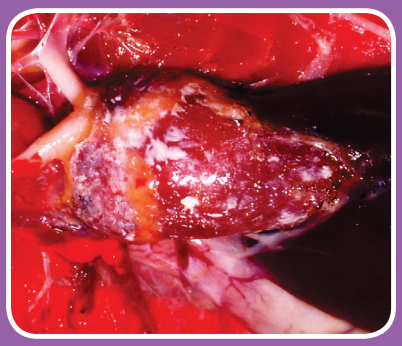
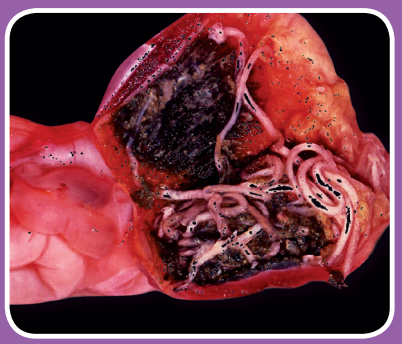
Second Edition

Pathology of Pet and Aviary Birds


Robert E. Schmidt
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WILEY Blackwell

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Second Edition

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9600 Garsington Road, Oxford, OX4 2DQ, UK

Library of Congress Cataloging-in-Publication Data

Schmidt, Robert E. (Robert Eugene), 1939-, author.
Pathology of pet and aviary birds / Robert E. Schmidt, DVM, PhD, Zoo/Exotic Pathology Service, Citrus Heights, California, Drury R. Reavill, DVM, Zoo/Exotic Pathology Service, Citrus Heights, California, David N. Phalen, DVM, PhD, Faculty of Veterinary Science, University of Sydney, Australia. – 2nd edition.
p. ; cm
Includes bibliographical references and index.
ISBN 978-1-118-82809-0 (cloth)
1. Birds–Diseases. I. Reavill, Drury R., author. II. Phalen, David N., author. III. Title.
[DNLM: 1. Bird Diseases–pathology. SF 994]
SF994.S36 2016
636.5′0896–dc23 2015014448

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Set in 9.5/12pt MinionPro by Aptara Inc., New Delhi, India

Printed in Singapore

1 2015

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Robert E. Schmidt, DVM, PhD, is a veterinary pathologist and consultant for Zoo/Exotic Pathology Service, Citrus Heights, California. He received his BS and DVM degrees from the University of California, Davis; his MS in veterinary pathology from Michigan State University; and his PhD in veterinary comparative pathology from Oklahoma State University. He is a Diplomate of the American College of Veterinary Pathologists and has been involved in diagnostic pathology of pet and exotic birds for more than 45 years. His professional affiliations include the Association of Avian Veterinarians, Exotic Mammal Veterinarians, The American Veterinary Medical Association, and the American Association for the Advancement of Science. He is a recipient of the Avian Pathology Award from the Association of Avian Veterinarians.

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David N. Phalen, DVM, PhD, earned his BA at the University of Chicago, his DVM from Cornell University and his PhD from Texas A&M University. He has been an avian practitioner for 32 years and is a Diplomate of the American Board of Veterinary Practitioners in avian practice. Dr. Phalen has spent the last 27 years studying the epizootiology, diagnosis, and control of diseases of aviary, companion, and wild birds and has published extensively in this field. He is currently an Associate Professor in the Faculty of Veterinary Science at the University of Sydney. He has received the Excellence in Avian Research Award from the American Veterinary Medical Foundation and was awarded the TJ Lafeber Practitioner of the Year in 2009.

Preface to the First Edition

The number of birds in captivity, as pets and breeders, and in ornamental and zoological collections has increased dramatically in the past 30 years. In many cases, wild populations of some of these species are threatened or have disappeared entirely, leaving the survival of the species to captive-bird breeding programs. With the growth in the bird-owning public has come a commensurate growth in the number of veterinarians providing care for birds and an enormous increase in the knowledge of the husbandry and diseases of these birds, including several comprehensive textbooks of avian medicine and surgery. Since birds are now common mainstream pets, there is also a need for diagnostic veterinary pathologists to be familiar with the diseases of these species.

The necropsy and related diagnostic services are an integral part of avian medicine. Both private and public collections are often large and closely housed. The death of a bird may be the first indication of a serious infectious disease, nutritional disease, or other management-related problem. Avian veterinarians and bird owners depend on pathologists to make an accurate diagnosis and provide advice on the significance of their findings.

Diseases of pet and aviary birds differ significantly from those of poultry. They also differ from many of the common diseases seen in wild birds, even wild birds of the same species. Much of the literature on the disease of pet and aviary birds is widely scattered in individual articles and in proceedings that most pathologists would not routinely review. Additionally, much information has never been published in any form. The goals of this book are to bring together in one volume a comprehensive review of the gross and histologic features of the diseases of pet and aviary birds and to provide a guide to ancillary diagnostics and a context in which to interpret the pathologic findings. While we feel this book will be a valuable reference for practitioners and students of avian medicine, helping them to understand the pathogenesis of the clinical manifestations of disease.

We have organized this material in a systemic format, so that pathologists faced with a diagnostic challenge involving a particular organ can hopefully go to the appropriate chapter rather than having to search through extraneous listings under etiology or by bird species.

For the most part, this book deals with diseases of common, and a few uncommon, pet birds. However, the authors have also included material relating to other avian species that private practitioners and pathologists might occasionally be expected to encounter.

Preface to the Second Edition

Eleven years have passed since the first edition of this book was published. During that time there have been many exciting advances in the fields of avian pathology and the medicine of pet and aviary birds. Additionally, the nature of avian medicine has changed. Veterinarians are now likely to be treating pigeons, backyard chickens, and other species of poultry, as well as, traditionally kept pet bird species. Veterinarians are also more likely to be treating birds with diseases associated with aging. The role and importance of the veterinarian in regard to aviculture continues. In general, the avian species that we now have in captivity cannot be replaced by birds from the wild so that maintaining their health and maximizing their breeding success is essential. Increasingly, captive breeding is also the last line of defense against extinction requiring significant veterinary input to maintain the health of small numbers of vulnerable birds.

Tissue biopsies and postmortem examination are an integral part of avian medicine. Biopsies inform treatment options and prognosis. Gross and microscopic postmortem assessments are essential if the impact of disease and inappropriate management practices are to be minimized. The second edition of *Pathology of Pet and Aviary Birds* is designed to assist the modern avian veterinarian and the avian pathologist so that they can maximize the information that they obtain from tissue biopsies and post mortem examinations. To this end the number of illustrations is increased and the figures are in color. The written content is also greatly expanded. These changes will allow practicing veterinarians and the avian pathologists in identifying the common and not-so-common diseases in the case material presented to them and understand the pathogenesis and epizootiology of the diseases they identify across a wide range of species.

Acknowledgments

The authors thank the many veterinarians who have contributed material that has led to this book. In particular, we would like to thank the following for the contribution of photos: Drs. Kristin Alhgrim, Duane Belote, Jennifer Blair, Scott Ford, Alan Fudge, Chris Griffin, Gregg Harrison, Irv Ingram, Isabella Langlois, Teresa Lightfoot, Douglas Mader, Tracy McNamara, Michael Murry, Chiara Palmieri, Brian Speer, Rhoda Stevenson, and Colin Walker.

1 Cardiovascular System

Normal structure

The bird's heart sits squarely in the middle of the coelomic cavity just caudal to the thoracic inlet. The axis of a normal heart deviates only slightly from the midline. Enlargement of any of the chambers may result in a change in the heart axis. The cranial ventral surface of the heart is in contact with the sternum, and the liver lobes cover the apex of the ventral surface.

The thin-walled atria have a scalloped surface and margins and are symmetrically located at the base of the heart. The right atrium is somewhat larger than the left. The right atrioventricular (AV) valve is a single muscular flap and is not membranous. The right ventricular free wall wraps around the heart from the caudal right lateral aspect of the heart to the cranial ventral surface of the heart. The wall of the right ventricle is approximately one-third to one-half the thickness of the interventricular septum and the free wall of the ventricle. This ratio, however, varies to some degree with the species, between individuals within species, and also varies depending on what level of the heart the measurements are taken.

The pulmonary and aortic values are essentially the same as those found in mammals. The left AV valve is membranous but is a continuous sheet and does not have clearly defined cusps. The valve is connected to papillary muscles by chordae tendineae. The brachiocephalic trunks immediately branch off the aorta as it leaves the heart. The first arteries to leave the brachiocephalic trunks are the carotids, which are relatively thin walled and narrow. The aorta arches to the right in the bird, as opposed to the left in mammals. Birds have a larger heart compared with body mass than do mammals. Myocytes have a smaller diameter (approximately one-fifth to one-tenth) than those found in mammalian hearts and a more rapid depolarization leading to a faster heart rate and relatively greater cardiac output. Purkinje fibers of the conduction system are relatively large as compared to those found in mammals.

Congenital anomalies

Most of the literature on avian heart anomalies concern chickens. Congenital lesions in pet birds are rarely described. Ventricular septal defects appear to be relatively common in umbrella cockatoos, and one of the authors (D.N.P.) has also seen them in cockatiels and an African grey parrot. The defects between the ventricles are typically 1–3 mm in diameter and are located in the interventricular septum just below the pulmonary and aortic valves (Fig. 1.1). Right- and left-sided heart failure typically develops in these birds between 1 and 3 years of age. Dilation of both ventricles is common, and the pulmonary veins are markedly distended (Fig. 1.2). Perihepatic effusion and cirrhosis of the liver with dilation of the hepatic veins may be present secondary to right-heart failure. Interventricular septal defects have also been associated with a truncus ateriosis in an umbrella cockatoo and aortic hypoplasia in a Moluccan cockatoo (*Cacatua moluccensis*).

Congenital aneurysms of the left ventricle are uncommon. One of us (D.N.P.) has seen several of these in cockatiels. All were small, typically 2–4 mm in diameter. A large left ventricular aneurysm (2 cm in diameter) was found in a mature blue and gold macaw. All of these emanate from the apex of the heart. There was no other evidence of heart disease in these birds and the lesion was not thought to impact the heart function.

An epicardial keratinaceous cyst presented as a yellow nodule containing caseous material. Histologically it was lined by stratified squamous epithelium, and the grossly noted material was laminated keratin. Based on the gross appearance, the differential diagnosis for this type of lesion would be an abscess. We have seen an African grey parrot with a focus of capillary proliferation in the myocardium (Fig. 1.3) that was considered to be congenital telangiectasis or possibly an example of a hamartoma.

In chickens, cardiac anomalies are thought to be associated with stress during organogenesis, including increased temperature and hypoxia. Vitamin deficiencies may also be responsible for these malformations in chickens. Aortic anomalies are reported in chickens and have been associated with excessively high or low humidity during incubation. Given that ventricular septal defects are seen most frequently in umbrella cockatoos, a genetic defect may be to blame for this anomaly in this species.

Pericardial disease

Pericardial lesions can be a manifestation of infectious, noninfectious, or neoplastic diseases.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

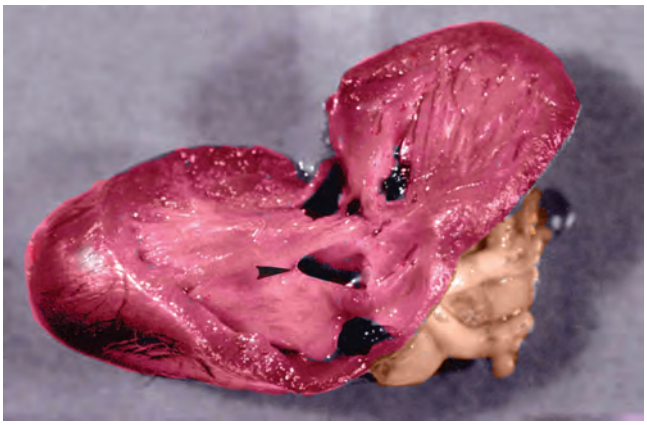

Figure 1.1 Interventricular septal defect (arrowhead).

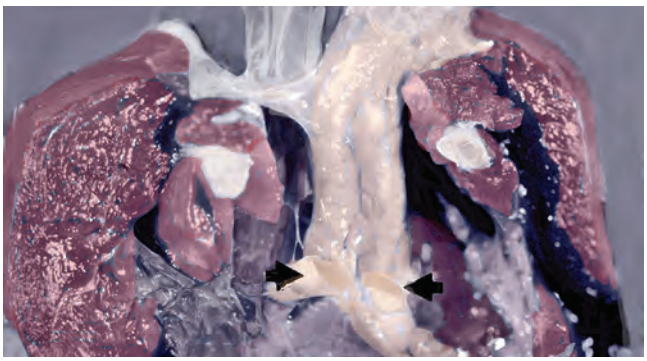

Figure 1.2 Marked distension of pulmonary veins (arrows) secondary to right-sided and left-sided failure in a bird with an interventricular septal defect.

Infectious disease

Infectious disease of the pericardium can be localized to the pericardium or may be just one manifestation of a systemic disease. A variety of organisms have been found to cause pericarditis, including numerous bacteria, including members of the Enterobacteriaceae, Mycobacteria, and *Chlamydia psittaci*, fungi and, occasionally, avian polyomavirus.

Pericarditis causes the pericardium to be variably thickened and gray to yellow-white, with red foci seen occasionally. The pericardium may have a shaggy appearance. In less severe cases, multifocal plaques are seen. There may be adhesions to the epicardium (Fig. 1.4). Pericardial fluid is increased, gray-yellow, and cloudy and may be flocculent. Histologically, bacterial and fungal infections cause edema, fibrin deposition, and an initial purulent response containing numerous heterophils and macrophages. Relatively more lymphocytes and plasma cells may be found in fungal infections. The pericardium may be adhered to the epicardium (Fig. 1.5).

With chronicity, there can be abscess formation. Macrophages and possibly giant cells as well as a more pleocellular response surround a central necrotic area. In both acute and chronic conditions, specificity depends on finding organisms that may be present.

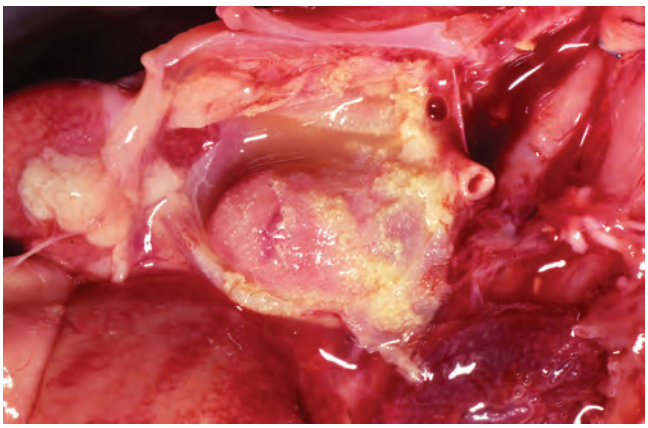

Figure 1.4 Epicarditis and pericarditis due to a systemic infection by *Chlamydia*. Grossly differential diagnoses include a variety of bacterial infections.

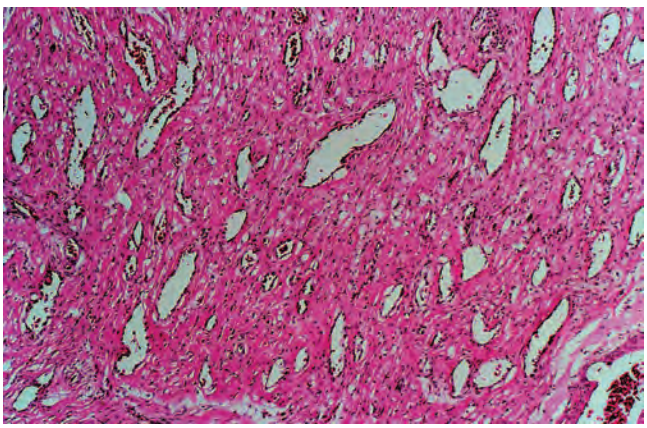

Figure 1.3 Congenital myocardial lesion comprised of irregular, dilated vascular channels.

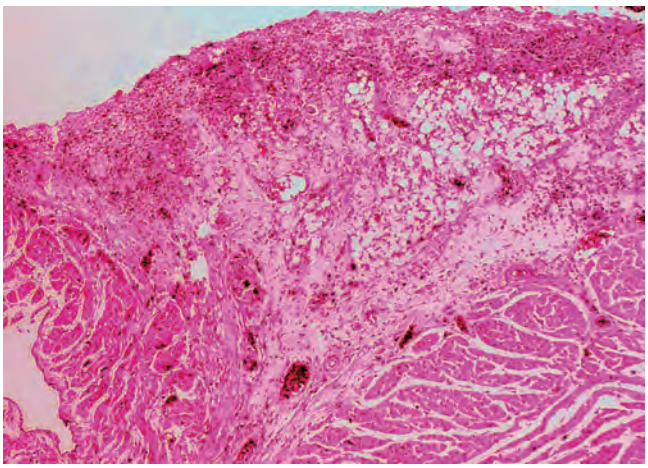

Figure 1.5 Chronic pericarditis/epicarditis. Note the diffuse inflammatory reaction and adherence of the pericardial tissue to the epicardium.

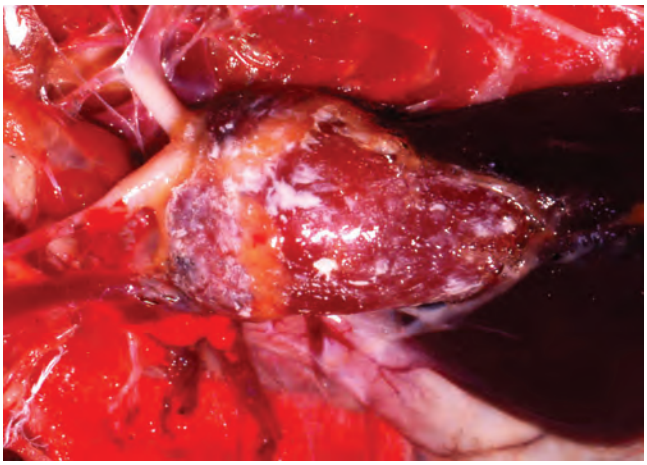

Figure 1.6 Severe pericardial and epicardial urate deposition. The lesion must be differentiated from infection.

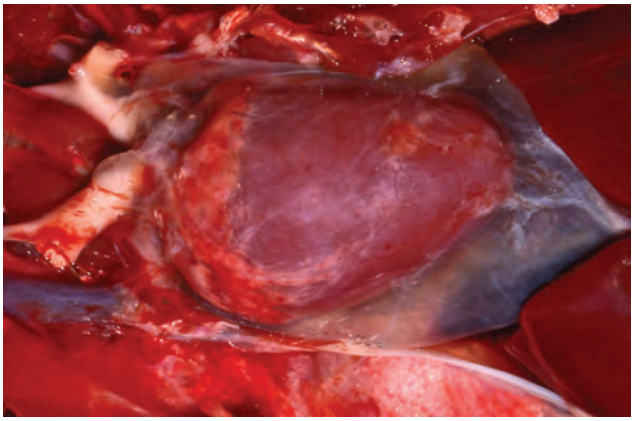

Figure 1.7 A large amount of partially coagulated proteinaceous fluid in the pericardial sac leading to cardiac tamponade. The fluid accumulation can be due to a number of causes.

Mycobacterial infections usually present grossly as large irregular masses that can mimic neoplasia. They are relatively firm, gray-white, and most often near the heart base. Early mycobacterial infections elicit a response of heterophils and macrophages. Organisms may be present infrequently. In advanced mycobacterial disease, the response will be primarily large macrophages with abundant light basophilic cytoplasm. Organisms can be seen within the cytoplasm with acid-fast stains.

Noninfectious disease

The pericardium is a common site of visceral urate deposition (gout). Grossly the lesion can be similar to an infectious pericarditis, with a thickened membrane containing gray-white plaques. However, pericardial thickenings associated with gout are typically white, smooth, and shiny as opposed to the yellowish, roughened, and dull exudates seen in infectious conditions. Flocculent material, along with an excess of turbid fluid, may be present in the pericardial sac (Fig. 1.6).

Histologically, urates may be crystalline or amorphous and are lightly basophilic on hematoxylin-eosin stains. Although the crystals dissolve in formalin, the remaining characteristic needle-shaped spaces can be found in most cases. Alcohol fixation and special staining can be used if there is any doubt that the lesion is gout. Depending on the duration of the urate deposition, there will be an inflammatory response comprised primarily of heterophils. Focal necrosis may also be seen.

Neoplastic disease

In mammals, sarcomas and mesothelioma have been reported in the pericardium. Primary pericardial tumors are not documented in pet birds, and we have not seen any examples of them.

Pericardial effusion

Effusion may accompany primary heart and pericardial diseases, as already discussed, and may be a part of systemic problems, including anything leading to right-sided heart failure or hypoproteinemia. Effusions may be transudates, modified transudates, exudates, or hemorrhage. The gross appearance will depend on the composition of the fluid. Within several hours of death, high-protein effusions will often become gel-like. In some instances the amount of pericardial fluid may be massive (Fig. 1.7).

Heart disease

Diseases of the heart can be divided into traumatic inflammatory, noninflammatory, and neoplastic. Infectious disease can be further divided into viral, bacterial, mycobacterial, fungal, and protozoal infections. Most diseases of the heart are confined to the myocardium, but, less commonly, lesions can also be seen in the epicardium and endocardium.

Trauma

Traumatic injuries to the heart are rare in cage birds, but extremely common in wild birds. Bruising of the myocardium is very common in birds that have been hit by cars or have had other blunt force trauma. Infrequently an atrium will be ruptured as the result of a proximal oblique coracoid fracture. Atrial rupture generally leads to a fatal bleed.

Infectious disease

Several viruses are known to cause myocardial lesions in pet birds. Polyomavirus is seen in a variety of psittacine birds and can also cause heart disease in finches. In budgerigars, gross lesions include hydropericardium, cardiomegaly, and hemorrhage. The myocardium may have patchy pale areas. Histologically there is coagulative myofiber necrosis and variable nonsuppurative inflammation and hemorrhage. There may be karyomegaly of myocyte nuclei, with margination of chromatin and inclusion body formation. Polyomavirus inclusions are usually pale or almost clear, or granular and basophilic.

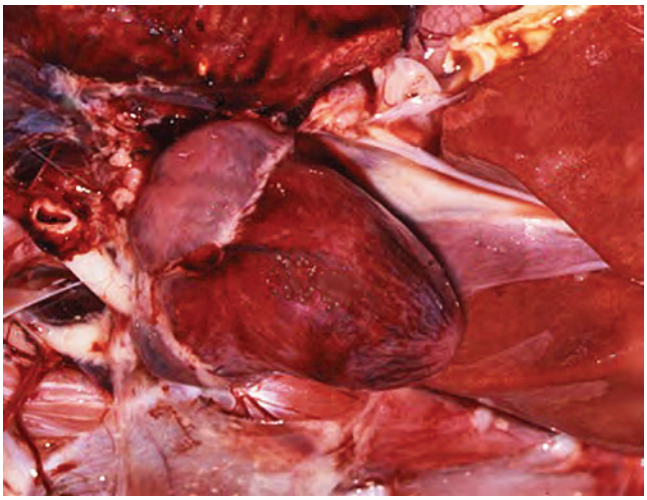

Figure 1.8 Polyomavirus infection causing patchy epicardial and myocardial hemorrhage.

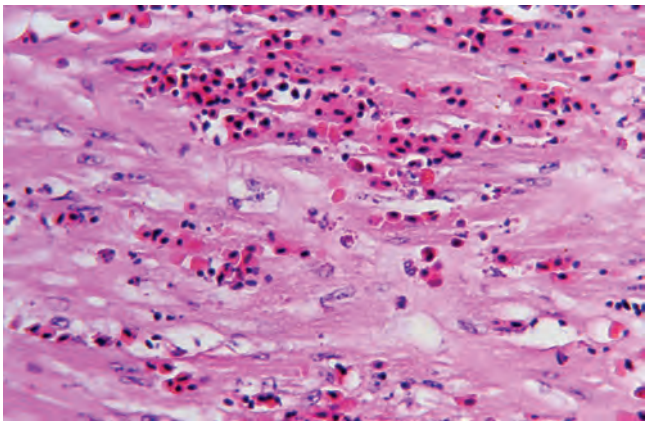

Figure 1.10 Severe myocardial degeneration and hemorrhage due to polyomavirus infection.

In nonbudgerigar psittacines, gross and histologic lesions vary somewhat from those seen in budgerigars (Figs. 1.8, 1.9, 1.10, and 1.11). Hemorrhage is a much more prominent feature of this disease and can be seen in subcutaneous tissues and serosal surfaces. Petechial and ecchymotic hemorrhages are often present on the surface of the epicardium. As the result of blood loss, birds are very pale and their muscles exhibit an unusual orange hue. If there is an inflammatory reaction, it is primarily lymphoplasmacytic. In finches, necrosis, inflammation, and inclusion bodies have been reported.

Avian Bornavirus infection resulting in proventricular dilatation disease affects a wide variety of psittacine and nonpsittacine birds, and heart lesions are relatively common. Grossly there may be slight dilatation of the ventricles, and occasional pale foci and streaks are seen (Fig. 1.12). Histologically, multifocal

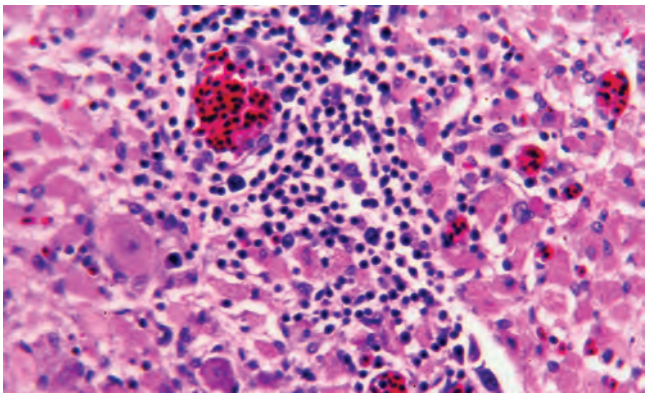

Figure 1.11 Nonsuppurative myocarditis in a bird with polyomavirus infection. Inflammation is seen infrequently in the heart in this disease.

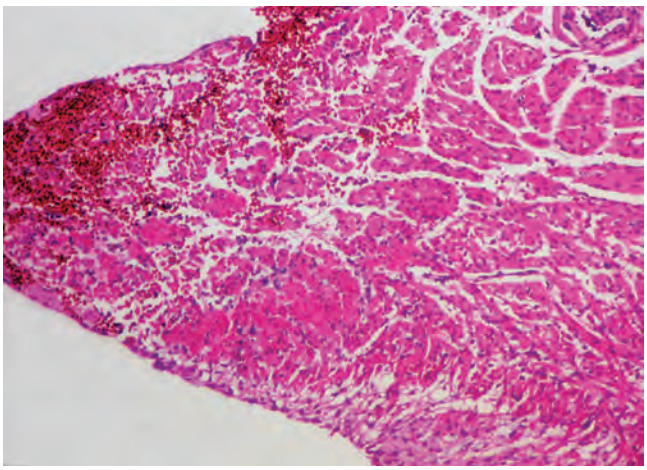

Figure 1.9 Focus of epicardial and myocardial hemorrhage in a bird with polyomavirus infection.

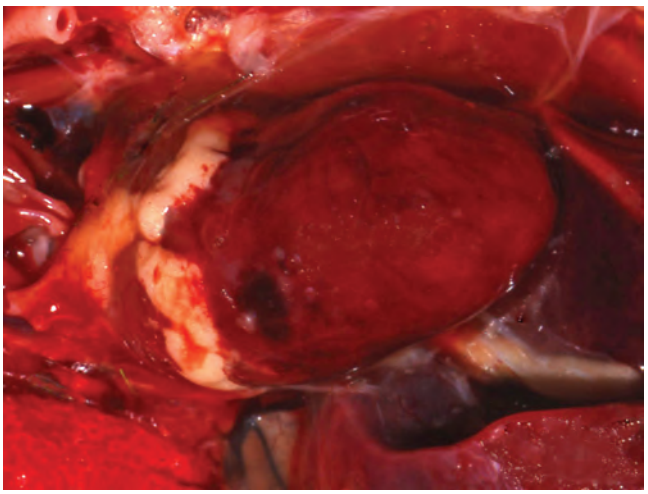

Figure 1.12 Foci of discoloration in the myocardium and asymmetrical dilatation of the ventricles of the heart of a bird with proventricular dilatation disease (Bornavirus infection). A focus of agonal hemorrhage is also seen, but hemorrhage is not a typical feature of this condition.

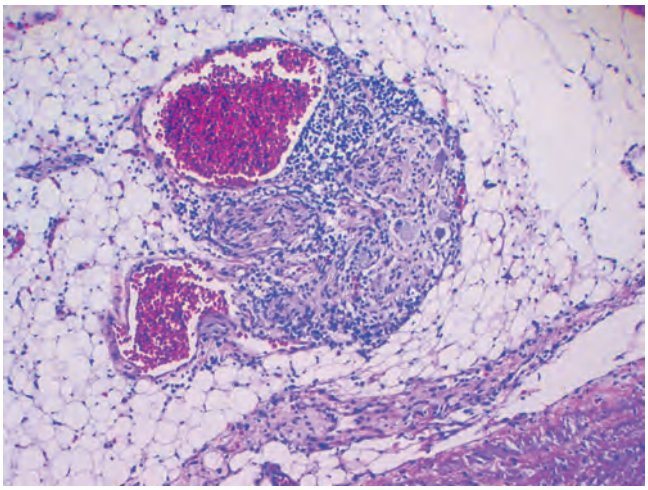

Figure 1.13 Epicardial ganglioneuritis in a bird with proventricular dilatation disease. A lymphoplasmacytic infiltrate is visible.

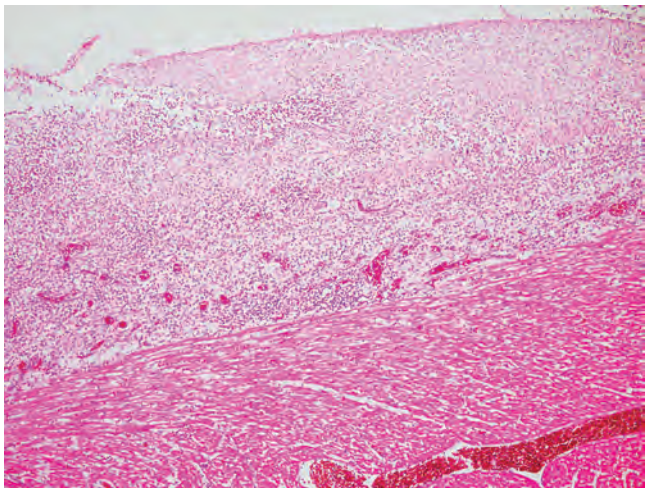

Figure 1.15 Severe chronic epicarditis in a pigeon with systemic salmonellosis. Nearly identical lesions can be caused by fungal infections and other bacterial infections.

lymphoplasmacytic and histiocytic infiltrates are seen in nerve ganglia (Fig. 1.13) and in the epicardium and myocardium, particularly near cardiac conduction fibers (Fig. 1.14). The conduction system may be involved, and, when severe, these lesions may cause the bird to die suddenly. Myocyte necrosis and, less commonly, fibrosis are seen.

Togavirus (eastern equine encephalomyelitis) is thought to be the etiologic agent of a disease described as avian viral serositis. Heart lesions in this disease include a fibrinous gray-yellow epicarditis. There may also be excessive cloudy pericardial fluid. Histologic lesions include the infiltration of lymphocytes, plasma cells, and histiocytes. Inclusion bodies are not seen, but ultrastructurally viral nucleocapsids are noted near cytoplasmic and intracytoplasmic membranes.

There is one report of a parvoviral myocarditis in canaries. A nonsuppurative myocarditis and viral particles were seen on electron microscopy. Myocardial necrosis is reported in systemic poxvirus infection but this is uncommon. The diagnostic features of the disease involve other organ systems. Myocarditis has been seen in cases of West Nile Virus infection. Grossly there may be gray-white foci and histologically a nonsuppurative myocarditis is present.

Bacterial infection of the heart can result in endocarditis, including valvular endocarditis, myocarditis, or epicarditis (Fig. 1.15), although in most cases at least two areas are affected. Bacterial heart disease may be the result of hematogenous spread of infection or direct extension from air sacs or adjacent tissues.

Primary gross changes in myocarditis are multifocal to confluent yellow-white foci (Fig. 1.16) that extend into the myocardium when sectioned. In advanced cases, large yellow nodules may be seen and must be differentiated from other types of infectious disease and neoplasia. Endocarditis may involve the wall and/or valves. Lesions are usually friable and vary from red-gray to yellow. Lesions may be seen on the chordae tendineae.

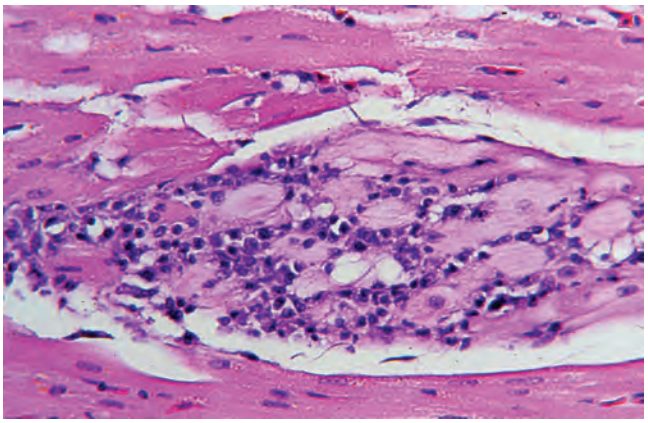

Figure 1.14 Lymphoplasmacytic inflammation in cardiac conduction fibers in a bird with proventricular dilatation disease.

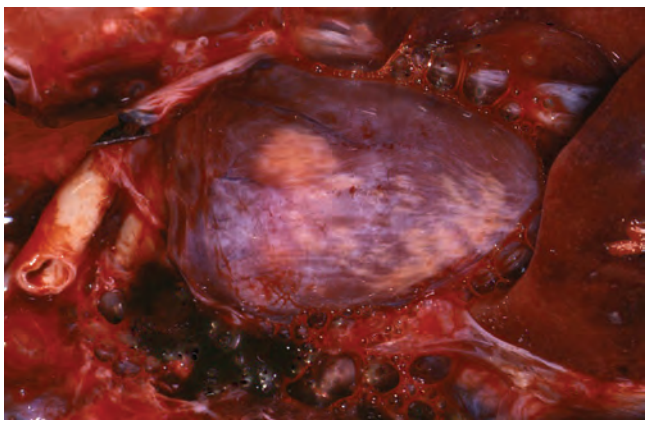

Figure 1.16 Severe bacterial myocarditis.

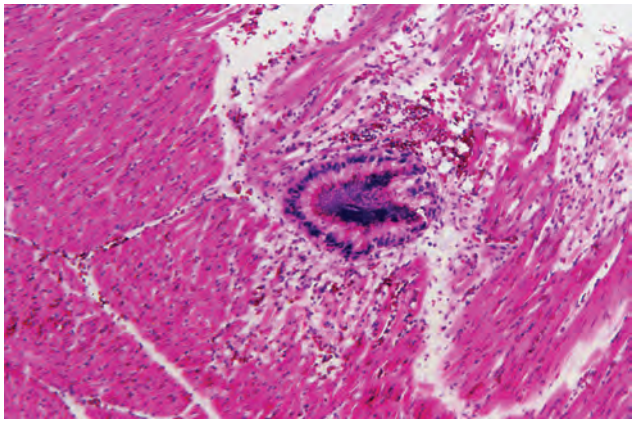

Figure 1.17 Bacterial myocarditis. Bacterial colonies are present in necrotic foci. A pleocellular inflammatory infiltrate is seen.

Valvular endocarditis is relatively rare, and, in our experience, the left AV valve is generally the only valve affected.

Histologically, bacterial infections vary with age. In early infections, there is acute necrosis and heterophilic reaction, and organisms may be seen (Fig. 1.17). As the lesion becomes more chronic, necrotic foci become surrounded by increasing numbers of macrophages, plasma cells, lymphocytes, and giant cells (Fig. 1.18). Organisms are usually seen in the center of these lesions. In endocardial lesions, in particular, fibrosis may occur as mural thrombi are organized. In cases of endocarditis, septic emboli may form, leading to disseminated infection in any other organ.

Mycobacterial infections are usually secondary to hematogenous dissemination or extension from cervical or thoracic air sacs. They usually involve the aorta or pericardium at the base of the heart and have been previously described. If there is myocardial extension, the lesion is similar grossly and histologically to those seen in the pericardium (Fig. 1.19).

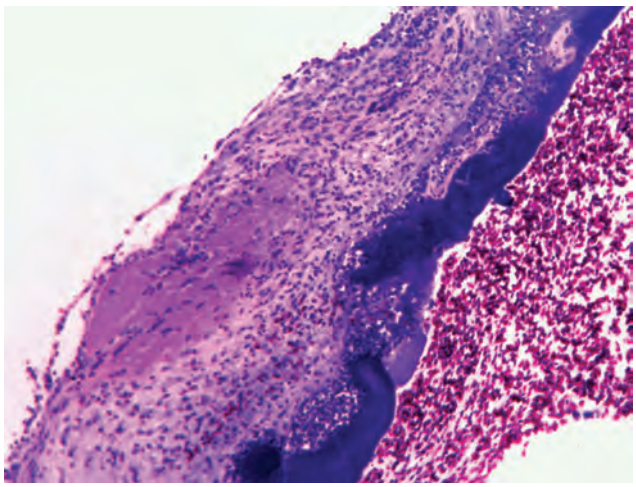

Figure 1.18 Severe valvular endocarditis. Large numbers of bacteria and a chronic-active inflammatory response are seen.

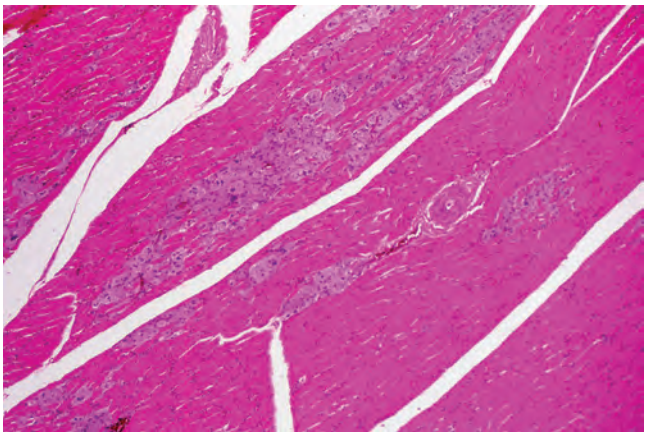

Figure 1.19 Mycobacterial infection of the myocardium. Numerous large macrophages are infiltrating the area. Granular material in the macrophage cytoplasm represents bacterial organisms.

We have occasionally seen myocarditis due to an intracellular bacteria that seems to be unique and unclassified. It is a Gram negative organism that has some morphologic features similar to *Helicobacter* sp. and also the organism called epitheliocystis in fish. There was no gross lesion seen. Histologically there was minimal inflammation and scattered myofibers contained small basophilic structures (Fig. 1.20). Ultrastructurally the organisms were within cytoplasmic vacuoles in degenerative myocytes. The organism has an undulating outer membrane, and a nucleoid with dense central masses and occasionally polar flagella (Figs. 1.21 and 1.22). The degree of inflammation associated with this infection can vary from little to moderate.

Mycotic infections of the heart are infrequent and usually the result of disease extension from air sacs. They usually involve the epicardium and superficial myocardium. Gross lesions are nodular or diffuse, gray-white, and friable (Fig. 1.23). If the fungal infection extends from an adjacent air sac, the fungus will sometimes produce conidia, giving the fungal plaque a green

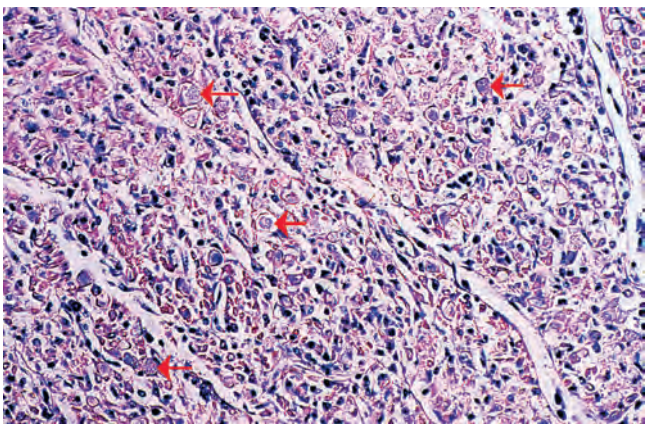

Figure 1.20 Myocarditis due to an unclassified intracellular bacterium. Note small organisms with myocardial fibers (arrows).

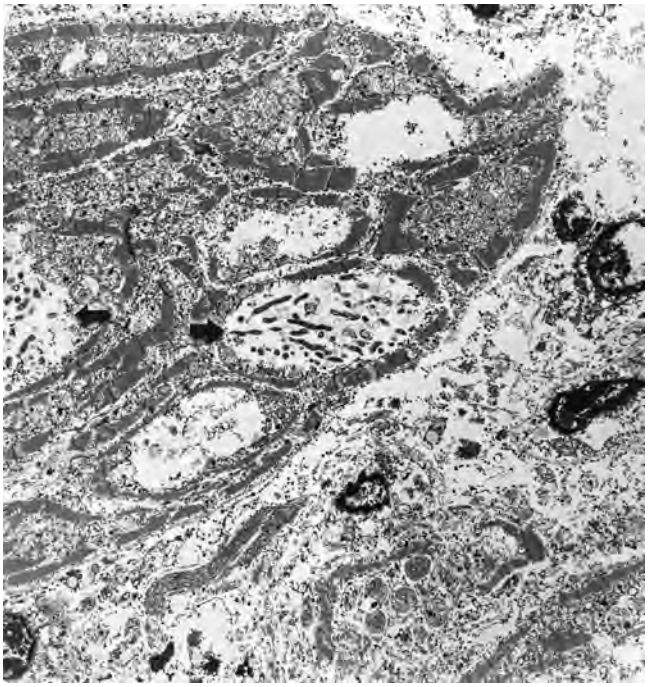

Figure 1.21 Unclassified intracellular organisms from Fig. 1.20. Ultrastructurally the organisms are within cytoplasmic vacuoles in degenerative myocytes.

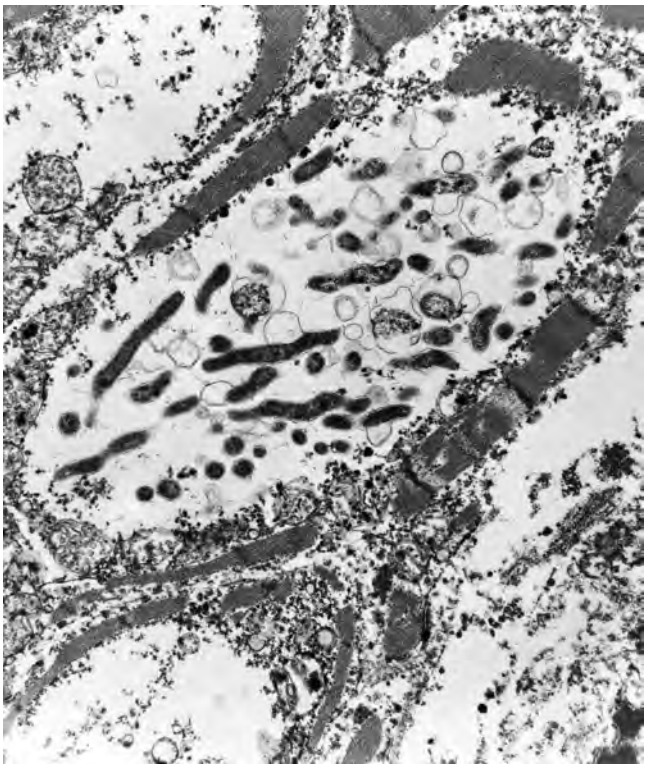

Figure 1.22 The organism has an undulating outer membrane, and a nucleoid with dense central masses and occasionally polar flagella.

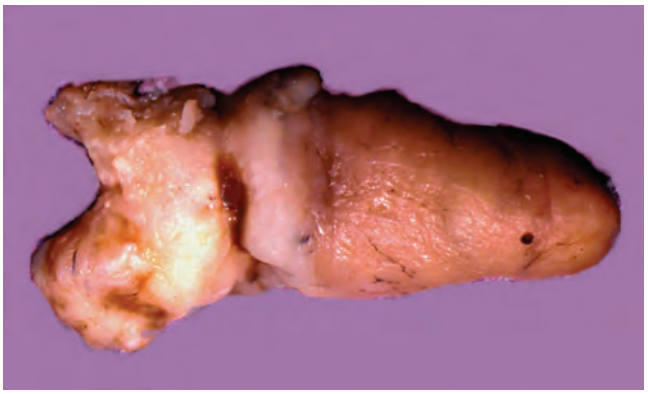

Figure 1.23 A large granuloma due to infection by *Aspergillus* sp. involving the atria and base of the large arteries. The lesion is not grossly specific, but should be suspected when more classical lesions of Aspergillosis are seen.

or black color. Histologically the lesions are similar to bacterial infections, with a pleocellular exudate whose character depends on chronicity. Fungal hyphae must be found for an exact diagnosis. *Aspergillus* is the most common organism involved, but a specific etiologic diagnosis requires that the organism be cultured or identified by molecular techniques.

Disseminated infection by *Aspergillus* sp., other mycelia fungi, and *Candida* sp. can develop in immunocompromised hosts, resulting in hematogenous dissemination to the heart. These lesions are grossly similar to bacterial infections of the heart, but fungal organisms are seen in necrotic foci. The inflammatory response is variable and involves both granulocytes and mononuclear cells.

Protozoal myocarditis is seen in some cases of systemic infection by *Sarcocystis* sp. *Sarcocystis falcatula* is a common cause due to the wide range of the definitive host, the Virginia opossum. The disease in most New World psittacine birds (macaws and conures) is usually subclinical, and the only evidence of infection is the incidental histologic finding of protozoal cysts in the myocardium at necropsy. Old World psittacine birds and some Amazon parrots have an acute disease with pneumonia and widespread dissemination of the organisms. Gross myocardial lesions are often not seen, but small white foci and streaks may be present in severe cases. Histologically there is a spectrum of myofiber necrosis, hemorrhage, and an inflammatory response comprised of lymphocytes, plasma cells, and macrophages. Newly formed cysts may be found (Fig. 1.24). Along with the brain and the lung, the heart is one of the common organs targeted by *Toxoplasma gondii* infections in birds. Bradyzoites and tachyzoites can be found in muscle fibers associated with inflammation (Fig. 1.25) similar to that caused by *S. falcatula*. In some instances inflammatory changes are seen but organisms are not found in the heart. Infections in cage birds are relatively rare but occur worldwide. Infections in poultry are common but rarely cause disease. Infections in wild birds are common, but the number of infections that result in disease is generally small.

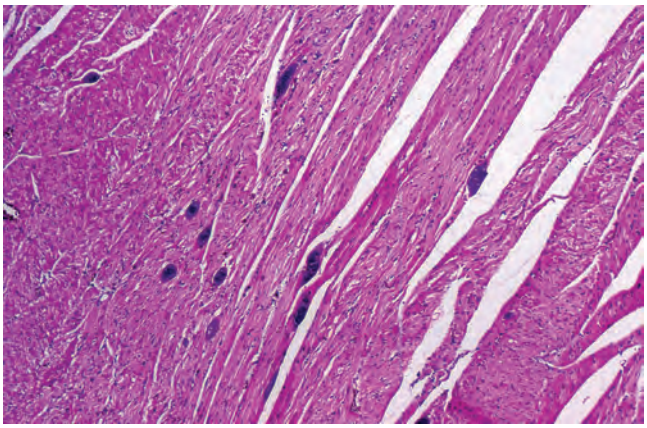

Figure 1.24 Multiple cysts of *Sarcocystis* sp. in the myocardium. Inflammation is usually not seen.

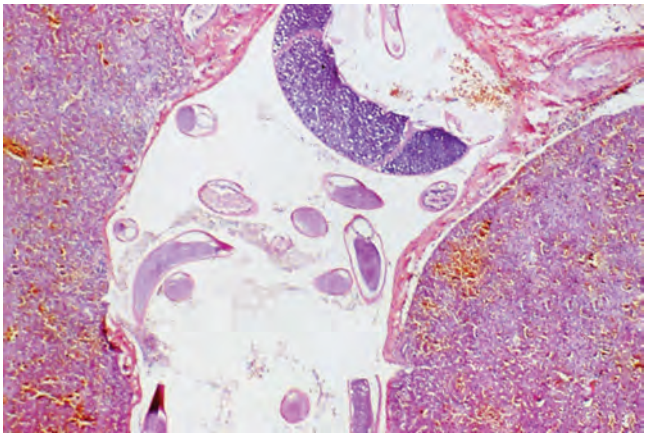

Figure 1.26 Filarid worms in a hepatic portal vein.

Filarid nematodes are an occasional necropsy finding in wild-caught cockatoos and occasionally other species and are particularly common in wild-caught African storks. These 1.5-cm white worms may be found in the right heart or in other vessels (Fig. 1.26). Histologically, adult nematodes may be found in hepatic and renal veins, and microfilaria are seen intravascularly throughout the body. In addition, focal endocardial hypertrophy and intimal hypertrophy of intramural vessels are noted. The intimal changes may be due to partial blood flow blockage by adults or a large number of microfilaria. Rarely, microfilaria are associated with embolic disease (Fig. 1.27).

Noninfectious disease

Inflammatory disease

Deposition of urates in the epicardium or occasionally myocardium results in grossly noted white-gray foci or streaks. Similar material may be seen in the pericardial fluid. Histologically the urates can be crystalline or amorphous and may elicit an inflammatory reaction comprised primarily of heterophils, although urate deposition without inflammation is also seen.

Nonseptic valvular endocarditis with formation of nodules and accumulation of inflammatory cells and fibrin has been seen as a secondary condition in cases of severe frostbite.

Inflammatory disease of undetermined etiology

Nonsuppurative myocarditis with no obvious cause occurs sporadically in birds. The possibility of autoimmune or immune-mediated disease should be considered in these cases even though not documented. It is known that certain peptides produced by *Chlamydia* mimic murine heart muscle-specific alpha-myosin heavy chains that can lead to nonsuppurative perivascular inflammation of the heart of mice. Since pet birds have a

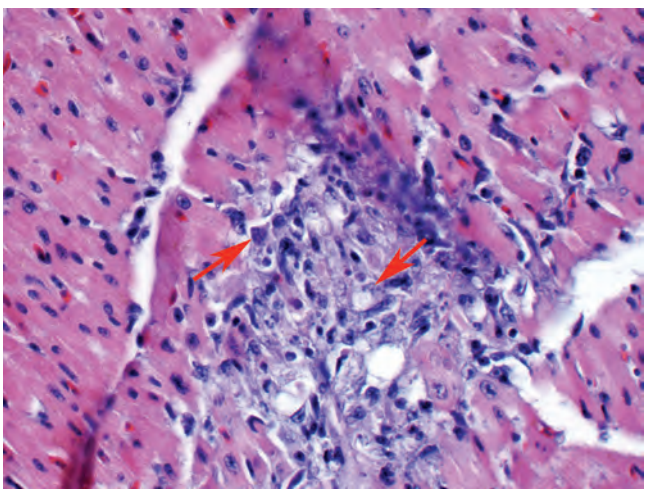

Figure 1.25 Myocardial necrosis and chronic inflammation associated with aggregates of Toxoplasma organisms (arrows).

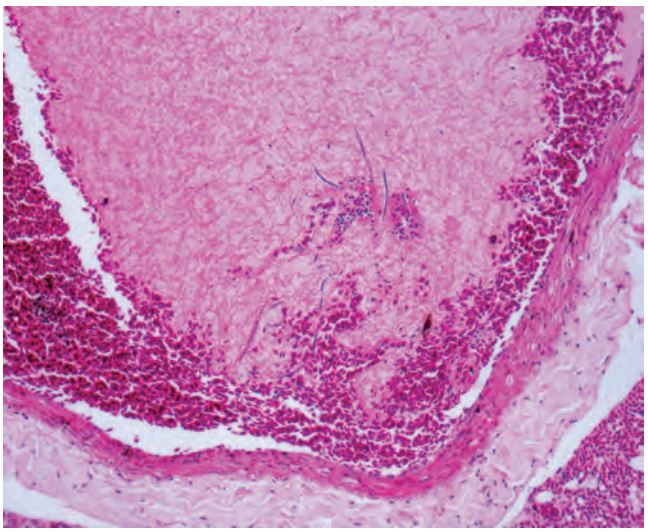

Figure 1.27 Microfilaria in a pulmonary thrombus.

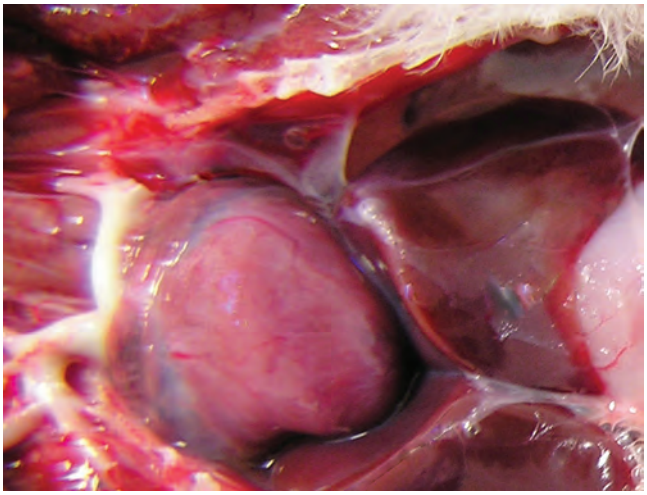

Figure 1.28 Serous atrophy of fat at the base of the heart. This change is consistent with a recent or longer term negative energy balance.

moderate incidence of chlamydial infection, perhaps the same mechanism that is seen in mice may be operational in birds.

Noninflammatory disease

Serous atrophy of fat

In cachectic birds, fat in the coronary grooves and epicardium may appear clear and watery as well as being reduced in amount (Fig. 1.28). Histologically adipocytes are small, and proteinaceous fluid may be present. Loss of heart fat is one of the first changes in birds experiencing a negative calorie balance, and it may even precede pectoral muscle atrophy.

Mineralization

Deposition of mineral may occur for several reasons, including dietary calcium/phosphorous imbalance, renal disease, and vitamin D_3 toxicity. It may also occur with excessive egg laying, but the pathogenesis is unclear. Mineral can be deposited in areas of myocarditis or myofiber necrosis of any etiology.

Grossly there are gray-white streaks and patches in the pericardium, epicardium, and/or myocardium. Gross differentiation from urates may not be possible, and both may be present in some cases. A spectrum of histologic changes can be seen, depending on the duration of the lesion. Evidence of primary inflammation or degeneration can coexist with myofibers containing a fine basophilic stippling along the cross striations. In some areas, there may be almost complete effacement of myofibers by mineral (Figs. 1.29 and 1.30).

Fat infiltration

Epicardial fat with some infiltration into the myocardium can be seen in birds and is not considered significant. It can, however, be excessive, and excessive fat is usually associated with obesity. Grossly the fat appears normal, but histologically there can be deep infiltration of the myocardium. Excessive amounts of fat may be a factor in heart failure, and the condition is seen in birds that die suddenly with no other morphologic change to explain death (Fig. 1.31).

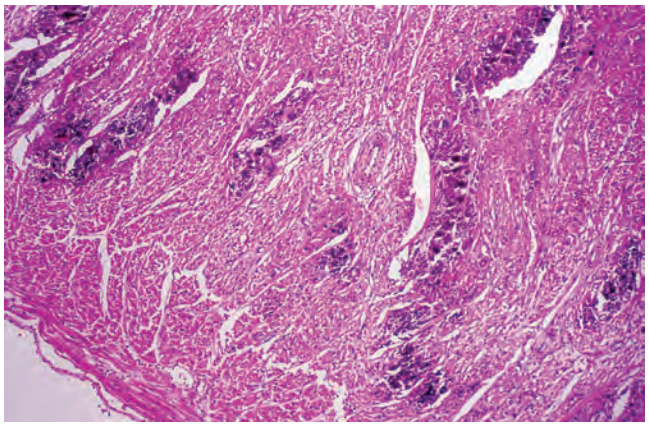

Figure 1.29 Multiple foci of myofiber mineralization in a bird with vitamin E deficiency.

Fibrosis

Fibrosis can occur after any insult to the heart that does not result in the immediate death of the bird (Fig. 1.32). Myocardial fibrosis is reported to occur in birds with atherosclerosis even though there is not necessarily coronary artery disease.

Lipofuscin

This is an intralysosomal pigment associated with excessive oxidation and polymerization of unsaturated fatty acids. It may accumulate in cells, including cardiac myocytes, secondary to a variety of disease processes. Although usually indicating emaciation or chronic disease, it is sometimes seen in young birds with acute clinical disease, possibly indicating a more chronic process than was expected. It is usually considered an incidental necropsy finding. If severe, the myocardium may have

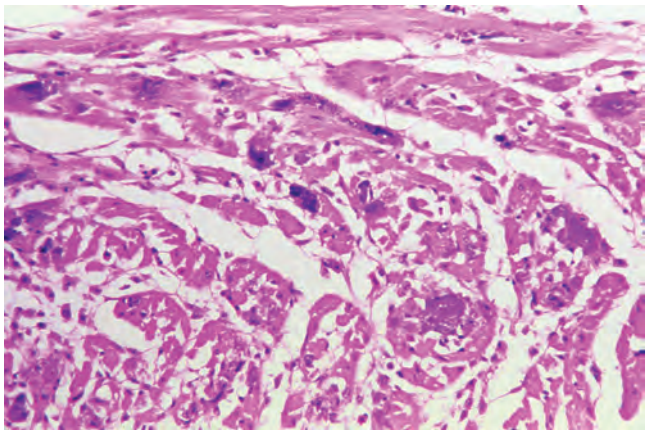

Figure 1.30 Myofiber necrosis and mineralization as a part of systemic changes in vitamin D toxicity.

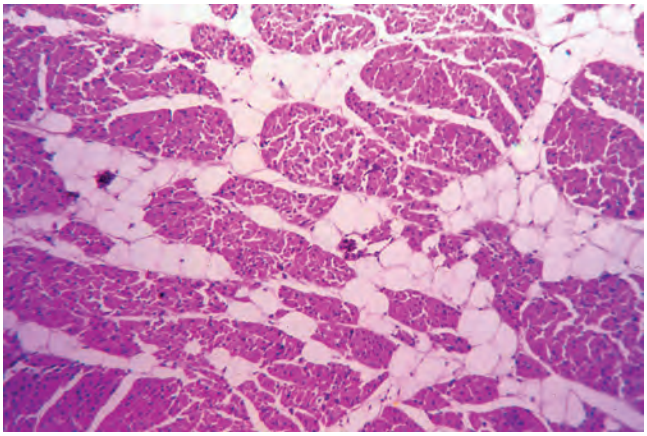

Figure 1.31 Severe myocardial fatty change probably associated with long-term feeding of a high-fat diet.

a brown discoloration. Microscopically, fine yellow-brown pigment is seen, primarily near the nucleus, but more diffuse in severe cases. One form of lipofuscin, ceroid, may occur in vitamin E deficiency.

Cardiomyopathy

Three forms of cardiomyopathy are described in mammals: hypertrophic, dilated, and restrictive. We have seen examples of the first two in pet birds. In both cases, the diagnosis is usually made on gross examination. Hypertrophic cardiomyopathy is characterized by ventricular thickening that leads to a diminution in ventricular volume. Dilated cardiomyopathy presents usually as a left-sided problem, with the left ventricle thin and flabby. In both cases, there may be no histologic change noted without quantitative morphometry and comparison to an age- and sex-matched bird of the same species. In some cases of dilated cardiomyopathy, the myofibers may appear obviously thin, with loss of sarcoplasmic detail, and, in some chronic cases, there has been evidence of fibroplasia, possibly indicating a previous insult. Restrictive cardiomyopathy is characterized by endocardial disease and fibrosis and could theoretically follow a variety of endocardial diseases, but we have not seen well-documented cases in pet birds.

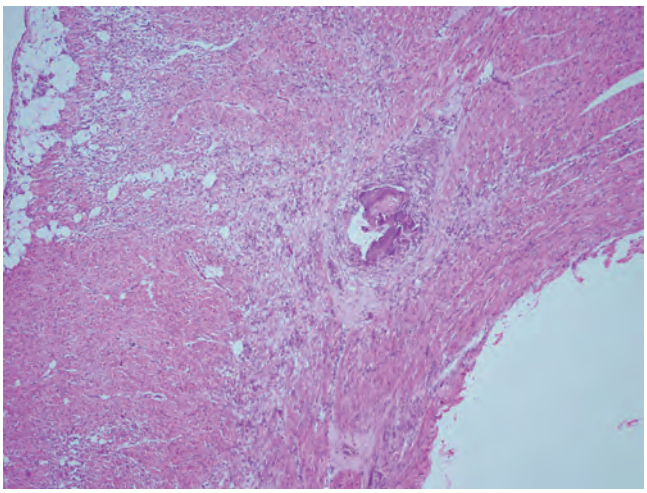

Figure 1.32 Mineralization, fibrosis, and fatty degeneration in a pigeon's heart. The cause of this lesion is not known, but may be the result of vascular disease resulting in ischemia.

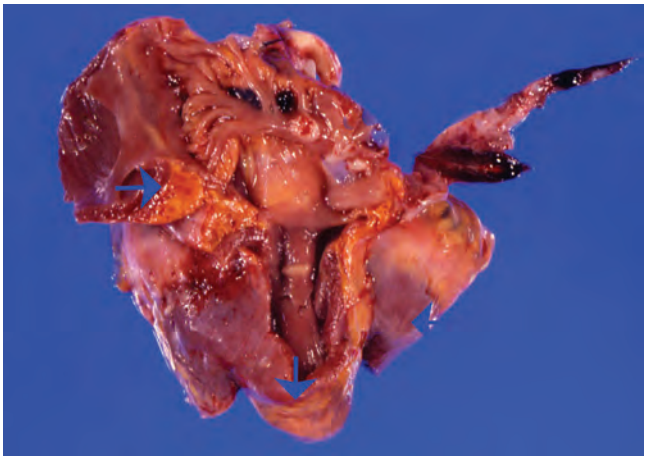

Figure 1.33 Myocardial degeneration due to vitamin E deficiency. Pale streaks and foci extend into the myocardium and on the epicardial and endocardial surfaces (arrows).

Myocardial degeneration

This may be the result of a vitamin E and/or selenium deficiency, vascular problems, and some toxicities. In many pet bird cases, the exact underlying problem is not determined. The gross appearance of an affected heart varies from having white streaks and patches to large pale areas (Fig. 1.33). In some chronic cases, the foci may appear as depressed areas. If there has been mineralization, affected areas are gritty when cut. Hydropericardium may be present.

Early histologic changes include contraction band formation, cross-striation loss, swelling, and hyalinization (Fig. 1.34). With progression, there is granulation, necrosis, and segmental fragmentation of myofibers. Microscopic mineralization may be seen, and, in chronic lesions, myofiber shrinkage and fibrous connective tissue proliferation are noted. No appreciable inflammatory response is seen (Fig. 1.35).

Myocardial degeneration is a prominent feature of a fatal disease of great-billed parrots. Also affected are the white matter and Purkinje cells of the cerebellum and skeletal muscles. The etiology is not known, but the lesions closely resemble those seen in poultry with vitamin E deficiency.

Endocardiosis

Noninflammatory swelling of true heart valves occurs occasionally. The cause is usually not determined. Affected valves are grossly swollen and usually smooth and firm. Histologically

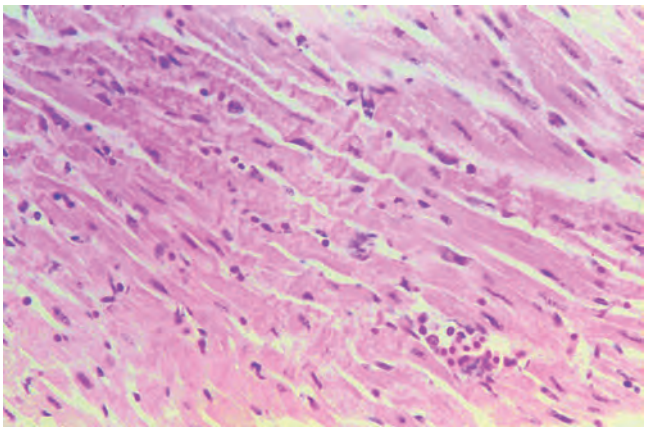

Figure 1.34 Contraction band formation and early myofiber fragmentation.

there may be hemorrhage, fibrous tissue proliferation, deposition of mucinous material, and cartilaginous metaplasia. Myxomatous degeneration of the left AV valve has been reported in an Indian ring-necked parakeet resulting in heart failure.

Heterotopic bone

This is seen sporadically in the myocardium. Its cause is usually not determined. Grossly the myocardium may feel gritty and histologically there is well-differentiated bone (Fig. 1.36).

Myocardial toxicity

Although a variety of drugs and chemicals are potentially cardiotoxic in birds, there are very few documented cases. Natural and experimental poisoning by avocados is seen in ostriches, canaries, cockatiels, and budgerigars. Gross lesions include subcutaneous edema and hydropericardium. Histologic lesions include myofiber degeneration and variable inflammation.

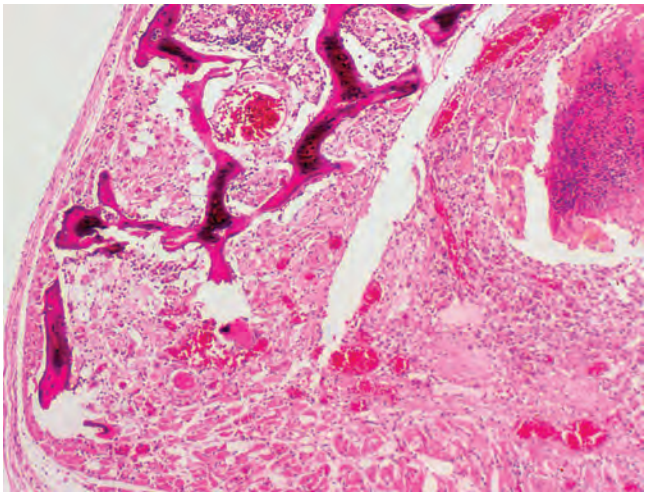

Figure 1.36 Diffuse production of heterotopic bone in the atrium of the heart.

Heterophils are seen in affected ostriches, but the lesion in canaries is characterized by nonsuppurative inflammation (Fig. 1.37). The toxic principle has not been determined.

Proliferative disease of the myocardium

Hypertrophy

Hypertrophic cardiomyopathy as a specific condition has already been discussed. Sporadic cases of myofiber hypertrophy are seen secondarily as compensatory responses to conditions that lead to an increased preload. These changes include pulmonary disease, vascular disease (especially atherosclerosis), congenital anomalies, and possibly chronic renal disease. Grossly the affected portion of myocardium is thickened and the lumen of the affected ventricle(s) is reduced. Histologically myofibers may appear to be normal, and without

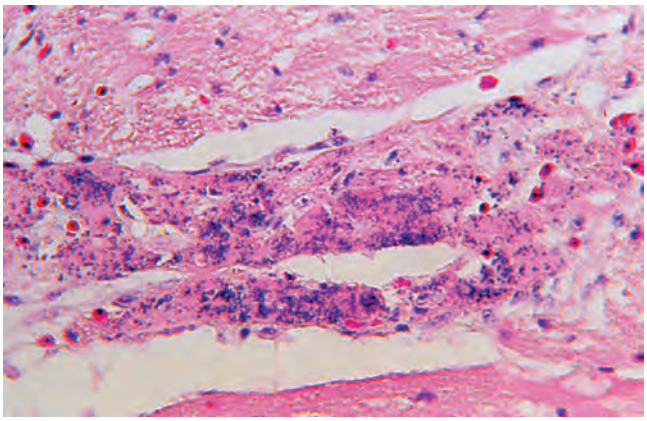

Figure 1.35 Necrosis of myofibers and severe mineralization in chronic nutritional myodegeneration.

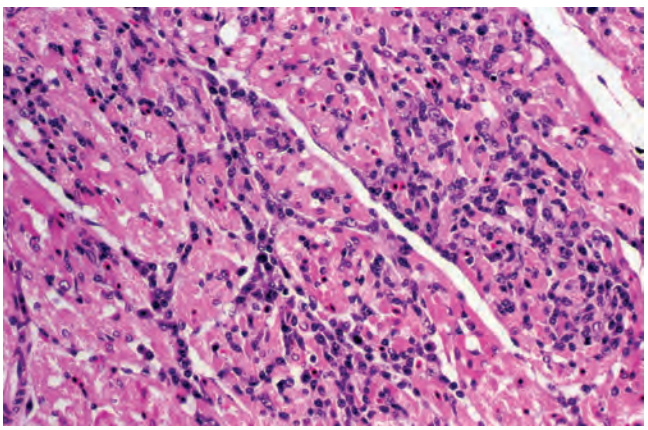

Figure 1.37 Myodegeneration, sarcolemmal proliferation, and nonsuppurative inflammation in a bird with avocado toxicity.

quantitative morphometry change can be difficult to discern. In more advanced cases, fibers may be thickened and lose their typical parallel appearance, and their nuclei may be enlarged.

Neoplastic disease

Several types of tumor are seen in the heart of birds. Rhabdomyoma or rhabdomyosarcoma is usually pale and firm grossly and may be multiple. Microscopically, strap and fusiform cells and cross striations are seen in routine sections of benign tumors. Sarcomas contain cells that may be fusiform, stellate, or strap-like, and cross striations are usually not present with hematoxylin-eosin-stained sections. Immunohistochemistry is often needed to prove the tumor is of striated muscle origin. Cell nuclei are enlarged and vesicular and may be multilobulated. Giant cells are often present. Rhabdomyosarcomas are infiltrative into surrounding myocardium.

Hemangiomas and hemangiosarcomas are found in the myocardium as red-black masses that may be friable and bleed easily. Histologically, benign tumors are comprised of well-differentiated vascular channels. Although histologically benign, these lesions interfere with normal cardiac function and do not have a benign behavior. Sarcomas are less well differentiated and may contain vascular channels lined by poorly defined endothelium, as well as solid foci.

We have seen primary fibrosarcomas of the myocardium. These tumors present as firm gray-white masses comprised of interlacing bundles and whorls of fibroblasts. Mitotic figures are typically abundant (Fig. 1.38).

Lymphosarcoma may involve the myocardium alone, or the heart may be involved as part of a generalized disease. Grossly the tumor is yellow-white or gray and may be diffuse or in multiple masses. Histologically lymphosarcoma is comprised of moderately undifferentiated pleomorphic lymphoid cells with variable mitotic activity (Fig. 1.39). They form infiltrative sheets in the myocardium. Occasionally, varieties appear to be primarily histiocytic (Fig. 1.40). The tumors caused by Marek's disease in chickens commonly infiltrate the heart (Fig. 1.41).

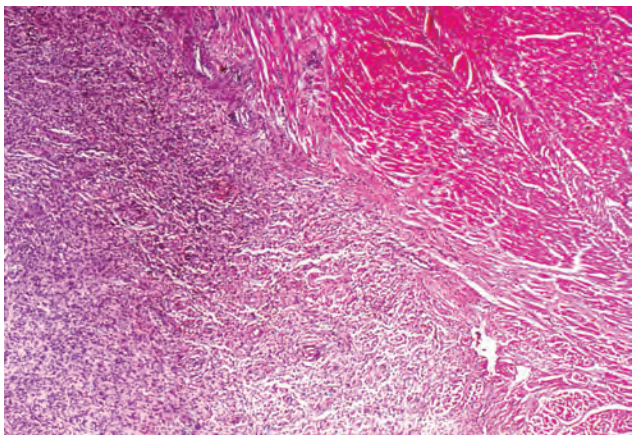

Figure 1.38 Fibrosarcoma replacing myofibers of the ventricle.

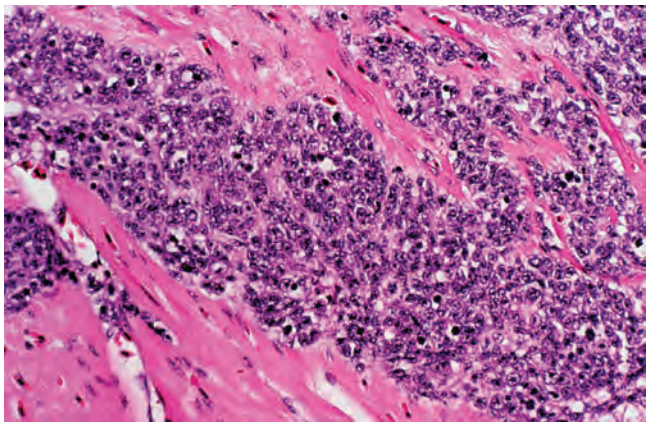

Figure 1.39 Lymphosarcoma infiltrating and effacing the myocardium.

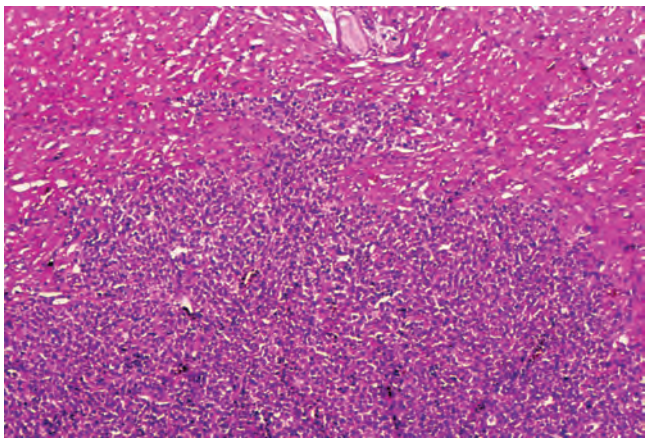

Figure 1.40 Myocardial histiocytosis. Compare the cell morphology with Figure 1.38.

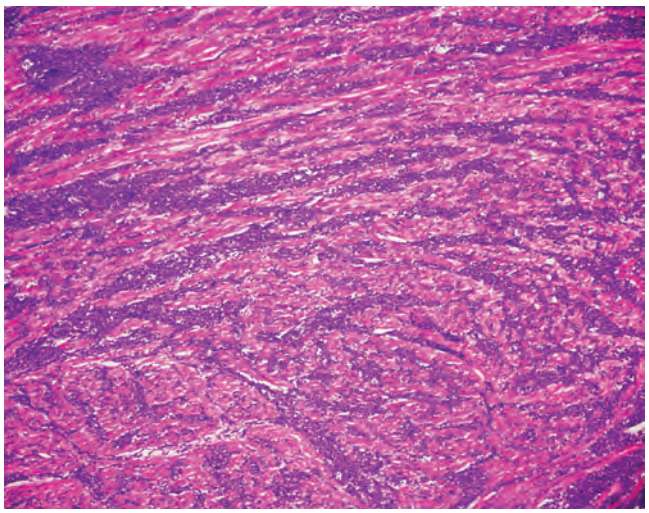

Figure 1.41 Marek's disease in a chicken. Neoplastic lymphocytes are seen infiltrating between muscle bundles.

Malignant melanoma may be found in the avian heart and is usually metastatic. These tumors are brown-black and may be multiple. Microscopically, poorly differentiated melanocytic cells form nests and sheets within the myocardium. Other metastatic tumors are rarely seen in the avian heart, but we have noted metastatic proventricular carcinoma in the epicardial lymphatics in a few birds.

The morphology of heart failure

A variety of conditions have been described that lead to heart lesions and subsequent death in birds. In addition, there have been many cases of pet birds whose presenting clinical sign was sudden death. In many of these cases, there is no gross or microscopic lesion. Sudden cardiac failure may be the underlying cause in many of these cases, and a careful and complete necropsy, as well as an investigation into the environment and husbandry of the bird, may be necessary to try and reach a conclusion as to possible cause.

The mechanism leading to acute cardiac death in any animal is often the creation of ventricular fibrillation or asystole. Factors influencing fibrillation include a long QT interval, hypokalemia, acidosis, imbalance in sympathetic/parasympathetic stimulation with a sympathetic dominance, and emotion. With sympathetic dominance, there is an exaggerated catecholamine reaction, reduced oxygen supply to the myocardium, and muscle spasm. The cardiac conduction system is described as anaerobic, with every cell functioning in an all-or-nothing capacity. Only a few cells are required for functioning, and problems can persist for some time until some insult leads cardiac failure. In chickens and turkeys, abnormal calcium regulation plays a part in the pathophysiology of heart failure. Although studies have not been done in pet birds, the mechanism may be similar.

Internal factors to consider in evaluating possible acute heart failure include disease in almost any other organ. In particular, there may be a relationship between the adrenal gland and the heart that leads to sudden death. With stress, there is an increase in interrenal cell (avian analog of cortical cells) hormone production that increases target organ sensitivity to the beta-adrenergic effects of epinephrine, leading to cardiotoxicity.

External factors may be obvious, such as a high-fat or other improper diet leading to obvious heart lesions. Less obvious is the possibility of the water supply being artificially softened, possibly causing electrolyte (potassium and magnesium) imbalances. In humans, soft water is apparently associated with cardiac problems. Although not documented in birds, evaluation of the water supply could be considered in ruling out unexplained sudden death.

The oculocardiac reflex results from pressure on or within the eyeball or stretching of ocular muscles. This results in a trigeminovagal reflex that leads to slowing of sinus rhythm and decreased conduction and contractility. This reflex has caused sudden cardiac failure in a pet bird.

Nonspecific stress is difficult to quantify and may be of different types and intensity. It is a factor in birds, particularly those in large aviary situations. Physical stress may be suspected if the owner is a good observer, but the possibility of mental or emotional stress as documented in humans is difficult to affirm. If environmental conditions include overcrowding, noise, and species/size mixture, some of the birds may certainly become stressed and die suddenly of no apparent cause.

In growing chickens there is a condition called sudden death syndrome (SDS). Affected chickens die suddenly and there is no apparent cause. Although the pathogenesis is not completely understood, some of the birds may have a predisposition to arrhythmia that leads to death. In some chickens there have been degenerative changes in cardiac myocytes and Purkinje cells.

Vascular disease

Inflammatory disease

Arteritis, phlebitis, and lymphangitis are infrequently encountered in pet birds. Bacterial infections can result in associated vasculitis in any organ. Histologically there is necrosis of the vessel wall and a response comprised primarily of heterophils. Microorganisms may or may not be present.

Mycobacterial arteritis is seen associated with lesions involving the pericardium and base of the heart. Lesions are similar to those that are seen in other parts of the heart (Figs. 1.42 and 1.43).

Fungi, such as *Aspergillus* sp., commonly invade the vasculature, resulting in the wide dissemination of fungal emboli that can cause vasculitis within any organ. In addition to necrosis and a pleocellular inflammatory infiltrate involving the vessel wall, organisms are usually present in the lumen and wall of the involved vessel or vessels.

Although not common in pet birds, paramyxovirus 1 (PMV-1) and togavirus (western equine encephalo-myelitis or WEE)

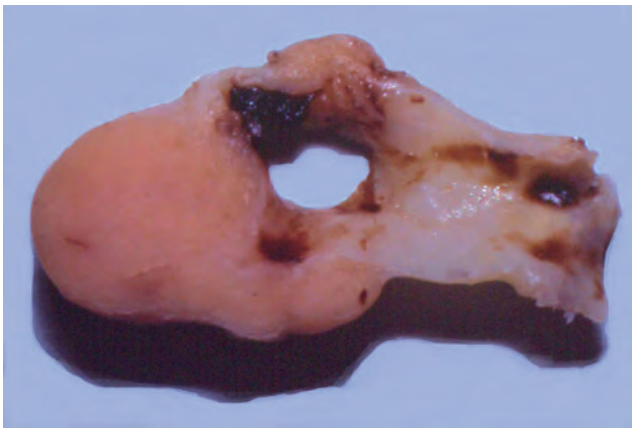

Figure 1.42 Chronic aortitis due to *Mycobacteria* sp. There is a large granuloma involving the wall of the aorta. Note the similarity of the lesion to that due to *Aspergillus* infection (Fig. 1.24).

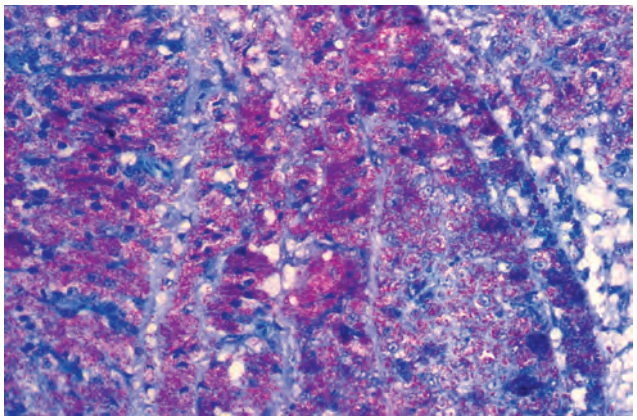

Figure 1.43 Acid-fast stain of diffuse infiltration of the artery wall by large macrophages containing acid-fast bacteria in a bird with mycobacteriosis.

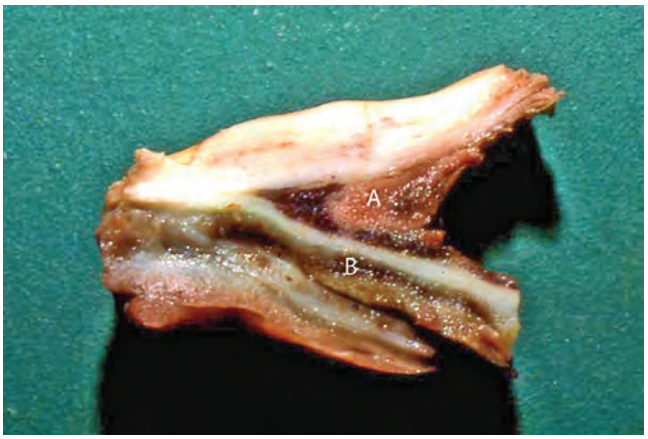

Figure 1.45 Separation of the aortic wall in a dissecting aneurysm. Original lumnen (B) and wall dissection (A).

can cause vasculitis. Grossly, in both infections, there will be hemorrhages, particularly in the serosa of the gastrointestinal tract. Histologically, vascular lesions of both infections are similar. Hemorrhage and edema are associated with hyalinization and degeneration of blood vessel walls, endothelial necrosis, possible thrombosis, and a variable mononuclear inflammatory infiltrate (Fig. 1.44).

Noninflammatory disease

Aneurysmal dilatation of blood vessels is not common in pet birds (Fig. 1.45). Occasional uncomplicated aneurysms are noted as variably sized dilatations in arteries. Histologically they are characterized by attenuation of the media, and there is usually no indication as to underlying cause, but they may be associated with atherosclerotic plaques.

Dissecting aneurysm is found in many avian species but is most often seen in the turkey and occasionally seen in the ostrich. These lesions are usually considered to be associated with a copper deficiency. A copper-dependent enzyme, lysly oxidase, is needed for connective tissue cross-linking of collagen and elastin in artery walls. Aneurysms begin with necrosis of elastin and arterial smooth muscle in the media, with subsequent hemorrhage and longitudinal dissection within the artery. Grossly there is dilatation and hemorrhage, and, on section, the dissecting band of hemorrhage is noticeable. Affected arteries may rupture (Figs. 1.46 and 1.47), with hemorrhage and clots noted in adjacent tissue and spaces. Thrombosis may also be present. Microscopically there is elastic tissue necrosis, acid mucopolysaccharide material deposition, hemorrhage, and variable inflammation that separate the arterial media.

Atherosclerosis

Atherosclerosis is perhaps the most common vascular lesion seen in parrots, especially aging populations of parrots. It can be found in any species of parrot and has been reported in many other species of birds. It is seen most often in Amazon parrots, particularly the blue-front Amazon parrot, African grey parrots, cockatiels, cockatoos, and macaws. It is also our experience that eclectus parrots are likely to develop atherosclerosis. Birds can be of any age, but most are 8 or more years old and many are more

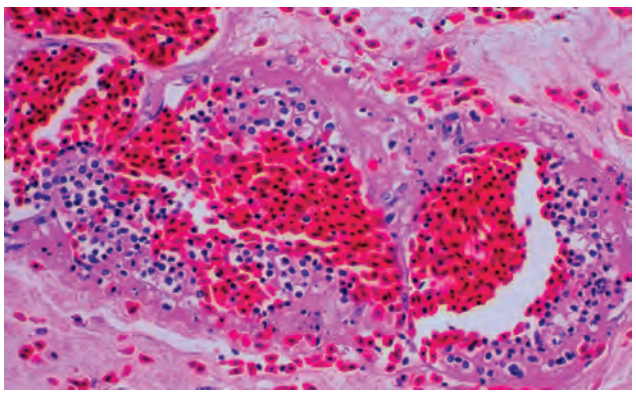

Figure 1.44 Vasculitis and degeneration of the vessel wall due to Togavirus infection.

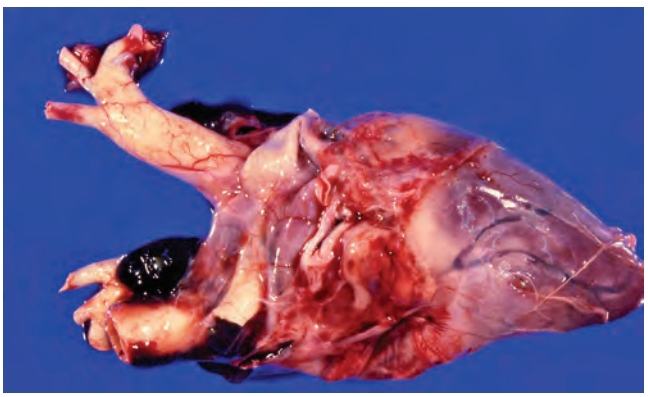

Figure 1.46 Ruptured aortic aneurysm with associated severe hemorrhage.

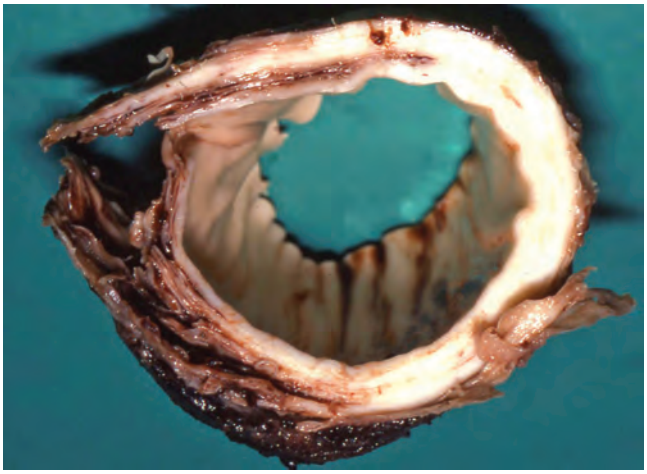

Figure 1.47 Rupture of the aortic wall. This is often the sequella of a dissecting aneurysm.

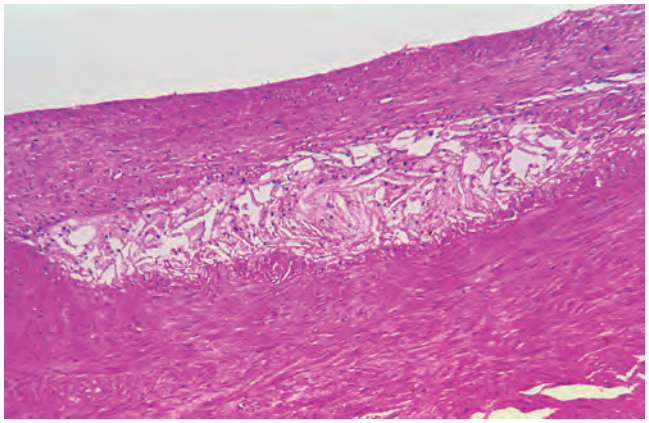

Figure 1.49 Early atherosclerotic lesion with foam cell and cholesterol cleft formation.

than 15 years old. The severity of lesions appears to increase dramatically in birds aged 20–30 years old. The prevalence of disease is very similar between sexes, but female birds may be more prone to develop severe lesions. Birds may die suddenly and be in excellent condition or be obese. Less commonly, atherosclerosis may cause a chronic disease that results in a loss of condition. Often there is a history of birds going through periods of a loss of awareness of their surroundings in the days or weeks prior to their death. Many birds have a history of being fed a diet rich in fat.

Lesions can be found in the aorta, brachiocephalic trunks, and pectoral and carotid arteries up to the level of the thyroids. Pulmonary arteries may also be involved but less commonly. Aortic lesions predominate in the ascending aorta and are uncommon in the descending aorta. Atherosclerosis of the coronary arteries is rare. Grossly the affected arterial wall is variably thickened and yellow (Fig. 1.48) and contains roughened yellow intimal plaques. Grading scales for atherosclerotic lesions have been extensively investigated and two have been developed. They are similar but not identical. Readers are referred to references by Beaufrère *et al*. and Fricke *et al*. for more detailed descriptions of these grading schemes. Microscopically the appearance of these plaques depends on the chronicity of the condition. Early lesions are characterized by fragmentation of the elastica and cell proliferation, and the deposition of extracellular substances resulting in thickening of the media. At approximately at the same time, fat-filled macrophages (foam cells) can be seen in the intima accompanied by an increase in extracellular matrix (Fig. 1.49). As the lesions progress, the number of foam cells increases, and as these cells die, there is the development of extracellular lipid that can include cholesterol clefts. Advanced lesions bulge into the lumen of the artery, have marked disruption of elastic layers, and form a fibrous cap. Fibrous changes continue in as the lesions mature, the atheroma is highly fibrous, and may contain little lipid. Mineralization also increases in the media of the diseased artery as the lesions become more severe. Chrondocytes are present in advanced lesions and may replace the smooth muscle cells in large areas of the media. Again in advanced lesions, there can be considerable narrowing of the vessel (Fig. 1.50). Microhemorrhage occurs variably.

Figure 1.48 Typical atherosclerosis. The aorta, brachiocephalic arteries, and carotid arteries are rich yellow colored and are thickened.

Many birds die because of a decreased blood supply to the brain as a result of severe narrowing of the carotid arteries. Infarction of the pectoral muscles occurs but is relatively rare. Likewise, it is rare to see ischemic disease of the heart. Atherosclerosis can lead to aneurysmal dilatation of the arteries. More commonly, it causes increased arterial resistance that affects the heart. Early changes in the heart include hypertrophy of the left ventricle, followed by left ventricular dilation, dilation of the left atria, right-heart dilation, and right-heart failure. Right-heart failure causes congestion, atrophy, and subsequently cirrhosis of the liver and is commonly accompanied by acites (Fig. 1.51).

Medial hyperplasia of vessels of the heart, liver, lung, and kidney have been associated with atherosclerotic changes in the

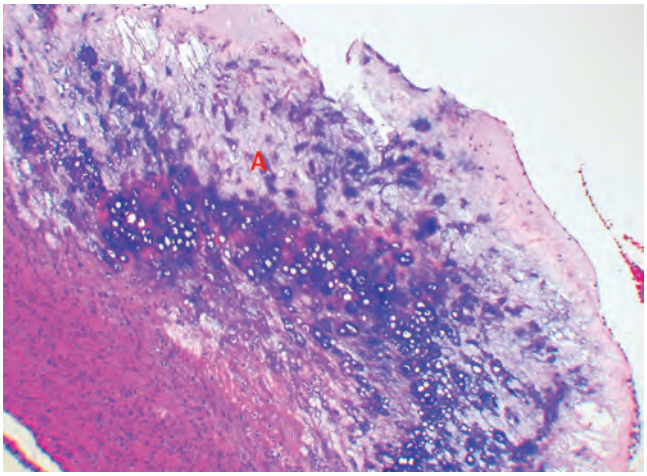

Figure 1.50 Severe arterial thickening due to atherosclerosis. Note the early chondroid metaplasia (A).

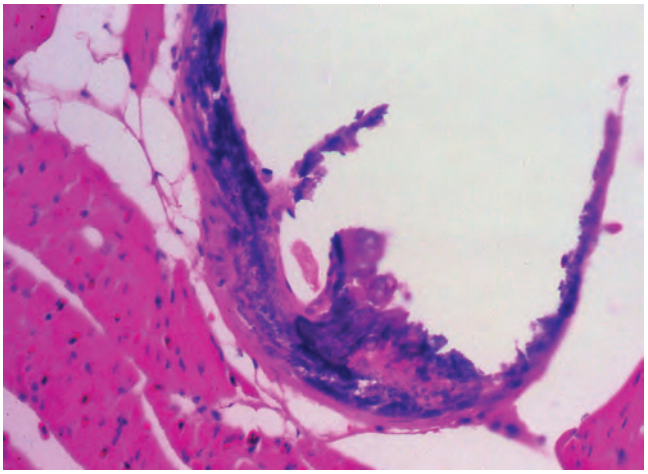

Figure 1.52 Mineralization of the arteriolar wall associated with a generalized problem due to chronic renal disease.

aorta and brachiocephalic trunks. Fibrosis of the myocardium has also shown a positive correlation with the severity of atherosclerosis of these vessels.

Mineralization

Mineralization of blood vessels with no other morphologic change is seen in cases of severe renal failure, chronic dietary imbalance of calcium and phosphorus, and vitamin D_3 toxicity. The change is typically in arteries or arterioles and can be found in any organ or tissue. The only gross indication may be a gritty feel to the tissue if the lesion is widespread or associated with other soft tissue mineralization. In larger arteries, raised, firm, irregular plaques may be seen that are usually gray-white and may have a shiny appearance. Histologically, all or part of the vessel wall may be affected (Fig. 1.52).

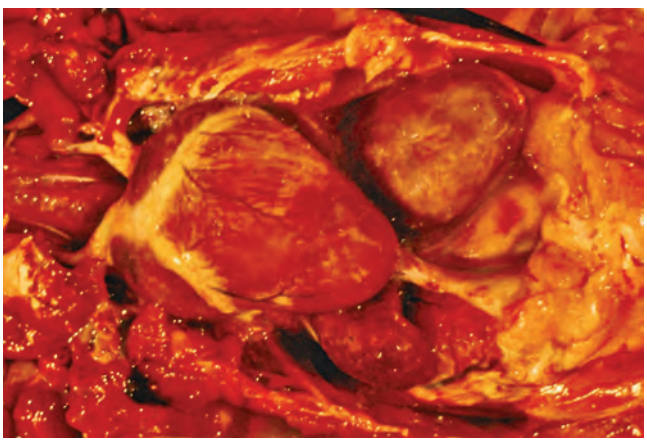

Figure 1.51 Left- and right-sided heart failure in a macaw with atherosclerosis. The spaces between the liver and adjacent air sacs were filled with a transudate. The liver is rounded and histologically was undergoing cirrhosis.

Amyloidosis

Among pet birds, amyloidosis is more common in the small passerines species but can occasionally be seen in other birds. Amyloid is deposited in a number of soft tissues and, in some cases, is found in the walls of blood vessels. This condition is usually not detected grossly. Histologically, affected vessels have a thickened media that has an amorphous, smooth appearance that is eosinophilic or amphophilic on hematoxylin-eosin stain. As in mammals, it is birefringent when stained with Congo red and viewed with polarized light (Fig. 1.53).

Thrombosis

Septic and nonseptic thrombi may be found in any tissue, depending on their cause (Fig. 1.54). Septic thrombi are often associated with valvular endocarditis, and bacteria may be present. Fungal infection that involves blood vessels may also lead to thrombi (Fig. 1.55). Secondary changes include infarcts and infection/inflammation in the involved tissue. Bone

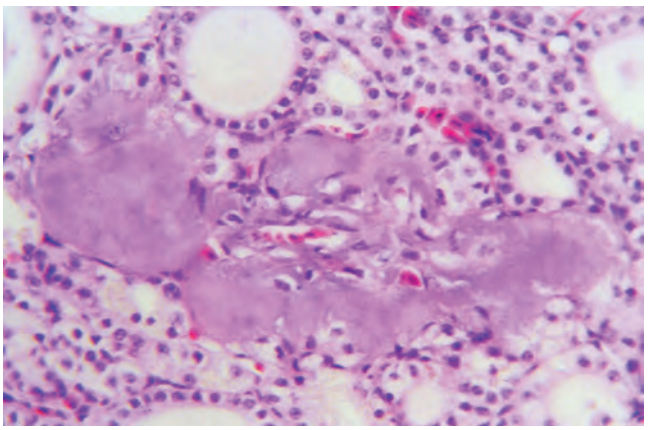

Figure 1.53 Amyloidosis of the arteriolar walls in the thyroid gland.

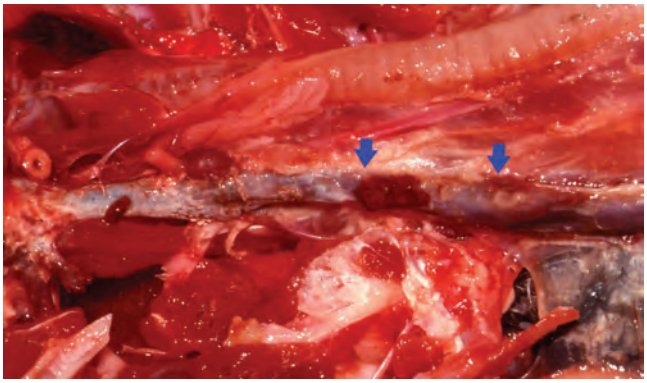

Figure 1.54 Thrombosis of the jugular vein (arrows). This can be associated with infectious or noninfectious causes.

marrow emboli are occasionally seen (Fig. 1.56), usually as incidental findings that did not appear to be a proximate cause of death.

Proliferative lesions

Vascular hamartomas have been found in the dermis/subcutis. These are comprised of proliferating, fairly well-differentiated vascular structures and are considered a malformation rather than true neoplasia. Hemangioma and hemangiosarcoma can occur in any organ but are most common in the skin and subcutis. Hemangiomas are usually deep red or black and have a smooth surface (Fig. 1.57). They are comprised of numerous fairly regular vascular channels lined by well-differentiated endothelium (Fig. 1.58). Occasionally, they are associated with adipose tissue proliferation leading to a tumor that has been called hemangiolipoma.

Hemangiosarcomas may be red-brown and have a roughened appearance with indistinct borders (Fig. 1.59). They contain

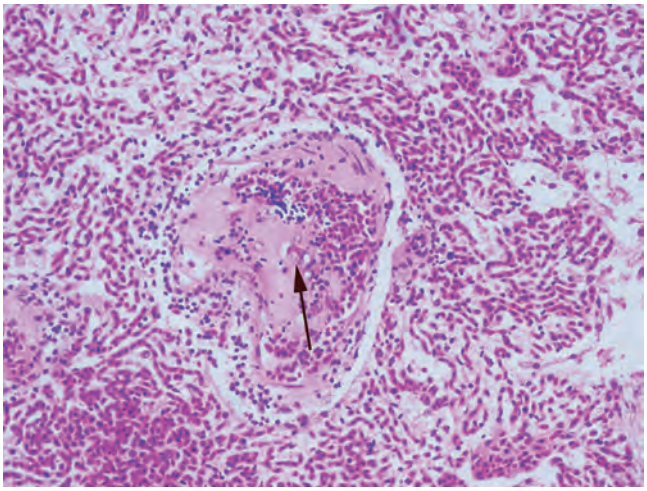

Figure 1.55 Thrombosis of a pulmonary artery as the result of vascular dissemination of an *Aspergillus* sp. infection. Arrows demonstrate fungal hyphae present in the thrombus.

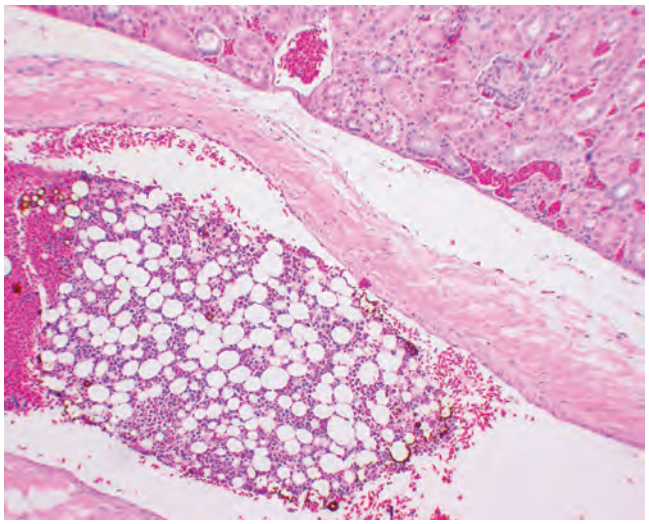

Figure 1.56 Bone marrow embolus with fat and vascular elements present.

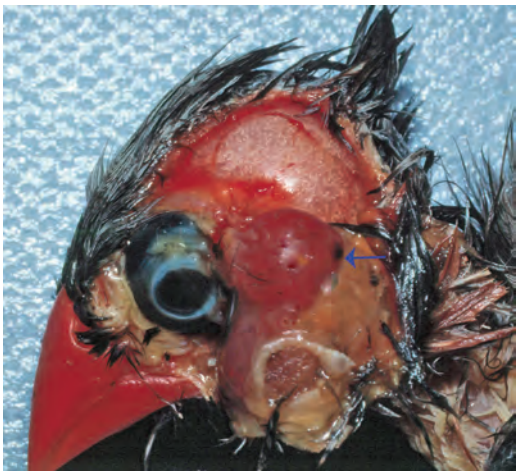

Figure 1.57 Red-brown mass typical of cutaneous and subcutaneous hemangioma (arrowhead).

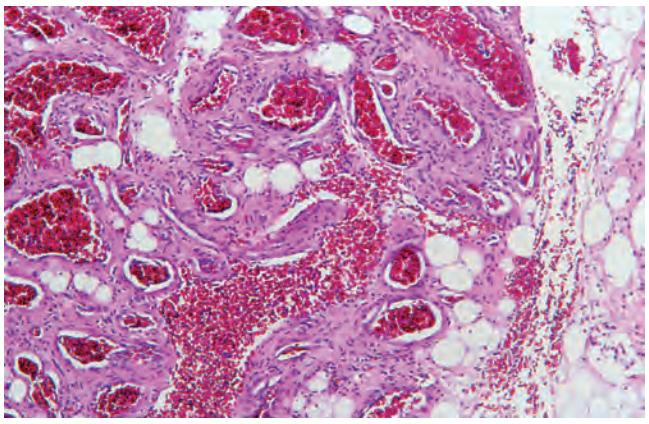

Figure 1.58 Typical appearance of hemangioma. Well-differentiated endothelial cells line the vascular channels.

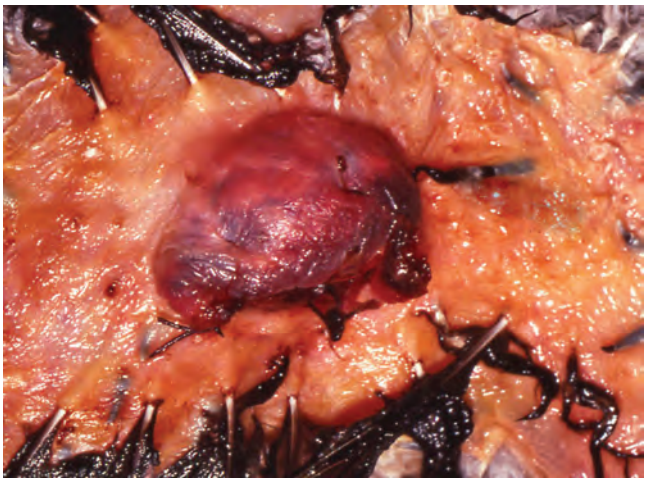

Figure 1.59 Hemangiosarcoma involving the skin and deeper tissues. The borders of the tumor are irregular. Compare with Figure 1.54.

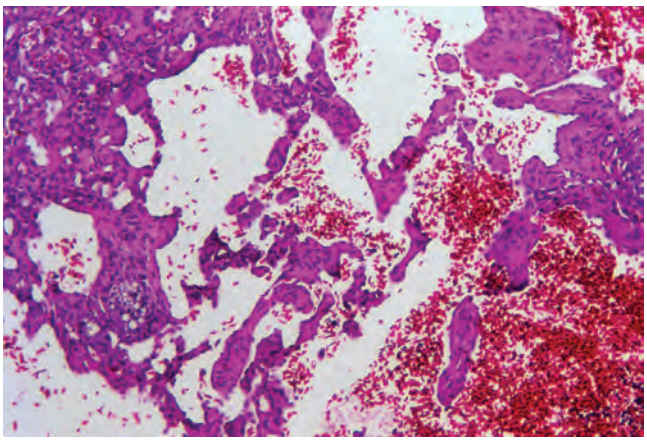

Figure 1.60 Poorly defined vascular channels and solid foci in hemangiosarcoma.

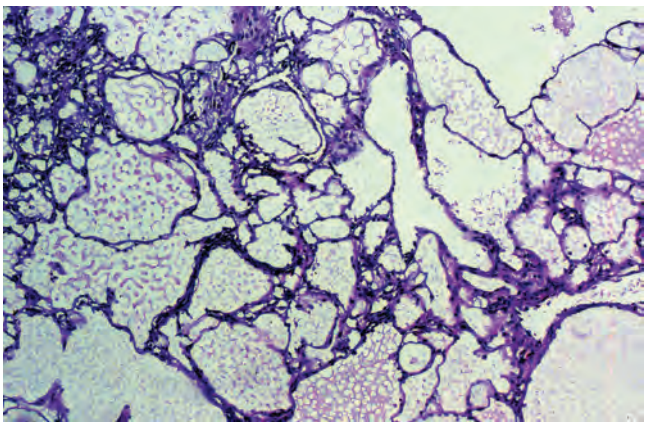

Figure 1.61 Lymphangioma comprised of dilated lymphatic channels containing proteinaceous material.

moderately undifferentiated or poorly differentiated endothelium and irregular vascular channels, as well as solid foci (Fig. 1.60).

Lymphangiomas are similar to hemangiomas, being lined by fairly well-differentiated endothelial cells. No erythrocytes are found in the channels, however (Fig. 1.61).

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2 Respiratory System

Normal structure

The cere is the thickened portion of integument that straddles the base of the nasal region. It may be feathered or bare, and it may or may not contain the nares (nostrils). In psittacines, the nares are located dorsally within the cere. Cockatiels and budgerigars have a well-developed cere compared to Amazon parrots. The cere of an Amazon is covered with tiny feather bristles (setae) (Fig. 2.1). Pigeons have well-developed ceres above the horn (rhinotheca) of their bills and behind the nares.

The vestibule of the nare is lined by a uniquely structured, keratinized, stratified squamous epithelium. The epidermis arises from a one- to two-layer thickness of basal cells, the stratum basale, that supports columns of epithelial cells, producing a corrugated surface. The uppermost cells in each column have pyknotic nuclei. The vestibular epithelium blends with the epidermis on the inner side of each nostril (Figs. 2.2 and 2.3).

Many species of parrots, raptors, and galliformes have an operculum or bony tubercule just inside the nares (Fig. 2.4). It is a rounded, keratinized structure that may act as a baffle to deflect and prevent inhalation of foreign material. The external nares open into the nasal cavity, which is tubular and separated into right and left chambers by the nasal septum. The nasal cavity has a threefold function of olfaction, filtration of airborne debris, and thermoregulation. Along the lateral walls of the nasal cavity are scrolls of cartilaginous and bony nasal conchae. The nasal conchae increase the surface area of the nasal cavity and, in most psittacines, are divided into three regions. The rostral concha is highly vascular and lined with stratified squamous epithelium. The middle and largest section has a mucociliary lining, and its cavity is continuous with the nasal cavity. The caudal section is lined by olfactory epithelium and does not open into the main nasal cavity. The olfactory epithelium is a pseudostratified columnar epithelium comprised of basal, olfactory, and supporting cells. This caudal section connects dorsally with the infraorbital sinus. African grey parrots, Falconiformes, and swifts do not have a definitive caudal nasal concha.

The infraorbital sinus is a large cavity under the skin primarily in the lateral region of the upper jaw. The right and left sinuses communicate in psittacines but not passerines. The infraorbital sinuses have openings directly into the nasal cavity or dorsally into either the middle or caudal nasal conchae. Numerous diverticula from the sinus extend around the eye and ear into the maxillary and mandibular beak and pneumatized sections of skull. These diverticula communicate with the cervicocephalic air sac at its caudal-most extent. In Amazon parrots, the diverticula can extend as far caudal as the seventh cervical vertebra. Stratified squamous epithelium lines the rostral infraorbital sinuses, and ciliated columnar epithelium with a few mucous glands are found caudally. Because of its position and poor drainage, this sinus is often involved in diseases of the upper respiratory tract.

The nasal cavity opens into the oropharynx via the choana, a median slitlike structure in the palate. The mucosa changes from the pseudostratified ciliated columnar cells with intraepithelial mucous glands of the nasal cavity to the stratified squamous epithelium of the palate. The palate surrounding the choanal slit is covered with keratinized papillae and supports the submucosal salivary glands.

The rima glottis is the laryngeal opening into the trachea. The larynx is comprised of four laryngeal cartilages. The cricoid cartilage is scoop shaped, with left and right lateral wings. The procricoid is small and articulates with cricoid wings on the dorsal midline. The two arytenoid cartilages form the margins of the glottis.

Closed cartilage rings that are shaped like overlapping signet rings form the avian trachea. The trachea is longer and wider than in a comparably sized mammal. There are some species variations of the trachea. Curassows and spoonbills have long tracheal coils between skin and pectoral muscle. In penguins and toucans, the trachea is divided at the cranial end of the neck into left and right tubes by a medium cartilaginous septum. Emus and ruddy ducks have an inflatable saclike diverticulum.

The syrinx is at the tracheal bifurcation within the thorax. The majority of birds have a tracheobronchial syrinx. Male ducks of the subfamily Anatinae have a syringeal bulla that is an asymmetric dilation on the left side of the syrinx (Fig. 2.5). Two primary bronchi form at the tracheal bifurcation, and they again branch into approximately 20 secondary bronchi.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

Figure 2.1 Detail of setae on the cere of an Amazon parrot.

The normal tracheal mucosa consists of ciliated pseudostratified columnar epithelium and mucus-producing goblet cells. The goblet cells are arranged as intraepithelial simple alveolar mucous glands in the proximal trachea and are more prominent as individual goblet cells in the distal trachea. The syrinx is lined by a stratified squamous epithelium. The primary and secondary bronchi are also lined with a pseudostratified ciliated epithelium and variable number of goblet cells.

The secondary bronchi give off a large number of small, tertiary bronchi that have a constant mean internal diameter. These tertiary bronchi, which are also known as parabronchi, anastomose with other tertiary bronchi. The walls of tertiary bronchi are thin, lined with squamous epithelium, and have thin

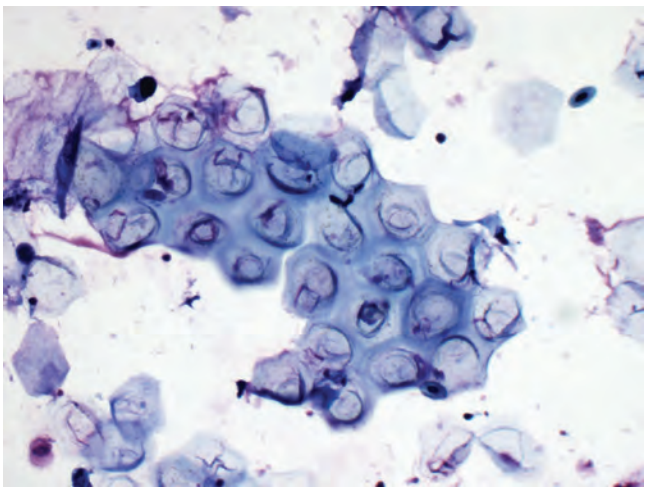

Figure 2.2 Cytology of normal vestibular epithelium.

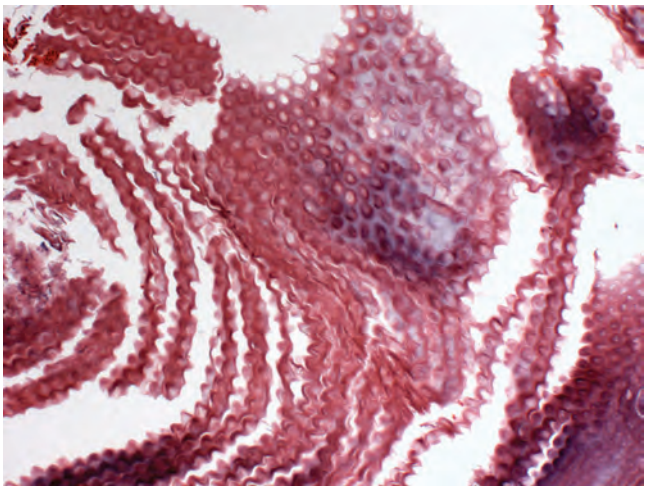

Figure 2.3 Histologic appearance of normal vestibular epithelium.

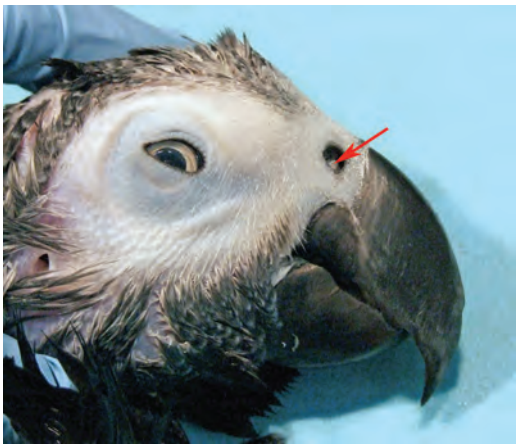

Figure 2.4 Normal appearance of nare with operculum (bony trabecula—arrow).

Figure 2.5 Normal syringeal bulla in a male duck.

underlying bands of smooth muscle (atrial muscles). These walls are perforated by numerous openings leading into small sacculations in the bronchial walls (atria). These atria are lined with flat or cuboidal epithelium. The atria are separated by atrial septa. Funnel-shaped infundibulae from the floor of the atria open into the air capillaries.

The air capillaries branch and freely anastomose with each other and are surrounded by a network of blood capillaries. This is the site of gaseous exchange. The blood–gas barrier is formed by endothelial cells, a common basal lamina comprised of a thin, electron-dense air capillary membrane that is frequently fused with a thicker, more lucent, blood capillary membrane, and the squamous epithelial cells of the air capillaries. The epithelial cells of the air capillaries have very thin cytoplasmic extensions, reminiscent of the mammalian type I pneumocyte. Macrophages are not normally found in air capillaries.

There are two functional, but not distinctly anatomic, systems of the avian lung. The phylogenetically primitive paleopulmonic lung includes the cranial pulmonary air sacs. This functional unit is present in all birds, and the airflow is unidirectional. The neopulmonic lung includes the caudal pulmonary air sacs, and air changes direction with each phase of breathing.

Air sacs are thin-walled structures with limited vascularity. They are an adaptation for more efficient respiration, insulation, and buoyancy in some birds. There are nine air sacs in most birds: the unpaired clavicular, and the paired cervical, anterior thoracic, posterior thoracic, and abdominal air sacs. The number of distinct air sacs and various diverticula will vary across avian families. The clavicular air sac extends into the humerus, coracoid, scapula, and clavicle. It runs adjacent to a main ventral nerve to the wing. Inflammation of this air sac can result in paresis of the wing.

The cervical air sacs are between the lungs, dorsal to the esophagus, and have extensions into the vertebrae. The cranial thoracic air sacs lie in the dorsolateral thoracic cavity. The caudal thoracic air sacs are caudal to the cranial thoracic. The abdominal air sacs penetrate into the intestinal peritoneal cavity. Except for the abdominal sacs, each air sac is connected directly to a secondary bronchus. The abdominal sac connects to a primary bronchus. The lining of the air sacs is a simple squamous epithelium with a basement membrane and underlying connective tissue. The air sacs have a similar histologic appearance to the peritoneum.

The cervicocephalic air sac is not part of the pulmonary air-sac system and is not used in gas exchange. It may function as insulation, as buoyancy control, or perhaps to support the head during sleep or flight. There are two divisions, the cephalic and cervical portions, and the cervicocephalic sac connects to the caudal infraorbital sinus. The cephalic division is not found in macaws. The cervical portion extends around the tympanic area and extends in two columns bilaterally down the neck. It is lined with a single layer of low cuboidal or flat squamous cells.

Respiratory disease

Upper respiratory system

Nasal cavity, sinuses, and pharynx

Cytology

The normal nasal and infraorbital sinus are lined with nonkeratinizing, stratified squamous epithelium. The sinus should have few bacteria, usually gram-positive bacterium.

Bacterial sinusitis, which is usually secondary to an underlying disease condition such as foreign material, tumors, or nutritional deficiencies, will show a septic, heterophilic or mixed-cell population. Chlamydia sinus infections often have a mixed-cell to histiocytic inflammation. The cytology of fungal sinusitis may support mats of fungal hyphae with a mixed inflammatory cell population.

Congenital disease

Choanal atresia is described in African grey parrots and an umbrella cockatoo (*Cacatua alba*). A persistent membrane or bony plate at the palate of the nasal cavity results in a closed choanal slit. This blocks the normal drainage of nasal secretions into the oral cavity. Young birds will present with a chronic nasal or ocular discharge, and, in some cases, the infraorbital sinuses will be distended with clear secretions.

Infectious disease

Viral disease

Systemic poxvirus infection can lead to necrotizing pharyngitis. Multifocal to confluent raised yellow foci are present (Fig. 2.6). Histologically there is ballooning degeneration of epithelial cells, with intracytoplasmic inclusions. Variable necrosis and

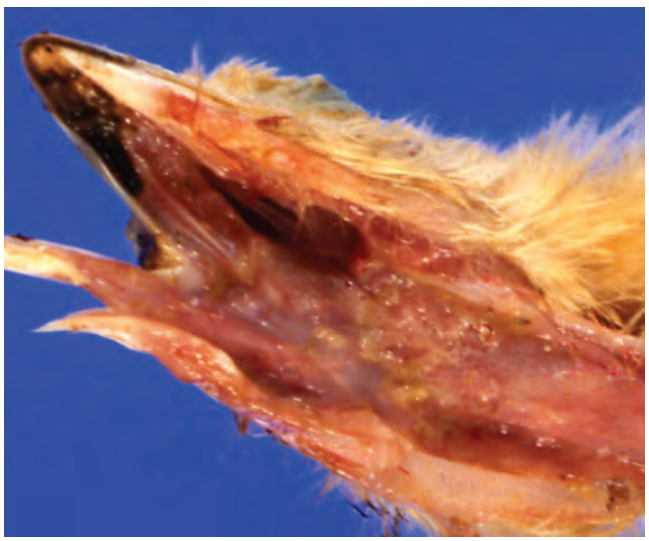

Figure 2.6 Proliferative and necrotic pharyngeal lesions due to poxvirus infection.

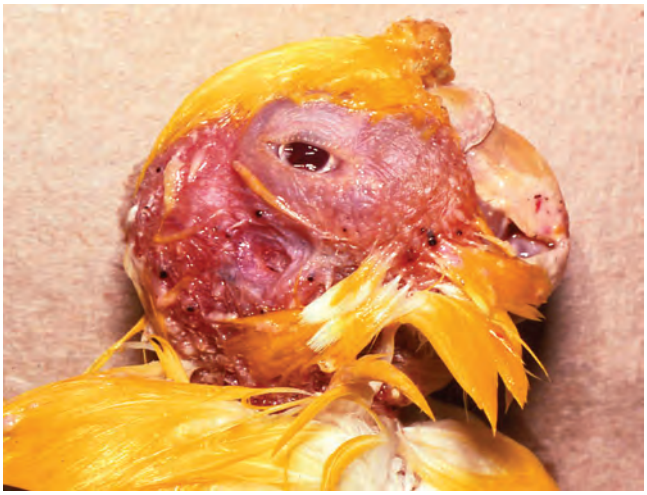

Figure 2.7 Marked swelling and feather loss secondary to sinusitis.

inflammation are present and there may be evidence of secondary infection.

Finch herpesvirus infection can cause disease throughout the upper respiratory system (see under trachea).

Bacterial disease

A number of gram-negative bacteria (*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Pasteurella*), and occasionally gram-positive organisms (*Enterococcus faecalis*, *Mycobacteria* spp.), *Mycoplasma*, and *Chlamydia* can cause a sinusitis. Acute sinusitis is characterized by a serous discharge, with swelling and redness in the orbital area and nares (Fig. 2.7). Histologically there is a thickening of the nasal mucosa or sinus membranes due to infiltrating heterophils, lymphocytes, and plasma cells, as well as hemorrhage, fibrin deposition, and tissue edema (Figs. 2.8 and 2.9).

Chronic sinusitis infections may be unresponsive to standard therapies due to resistant pathogens, masses from granulomas

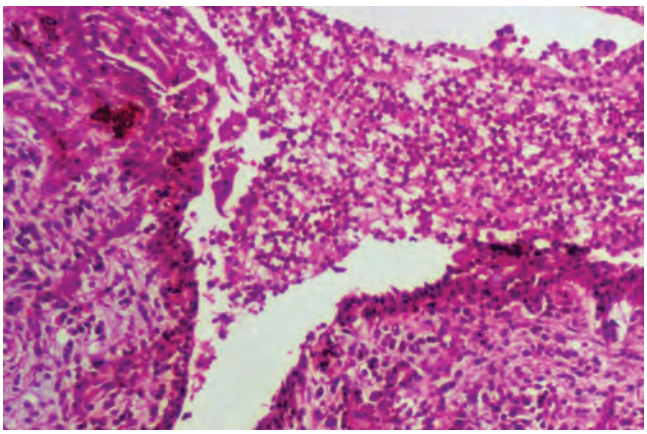

Figure 2.8 Partial necrosis, loss of mucosa and inflammatory exudate in a bird with bacterial sinusitis.

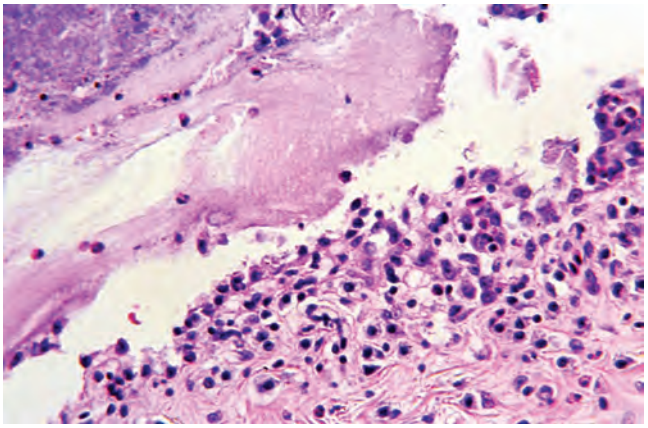

Figure 2.9 Bacterial sinusitis. Detail of a pleocellular inflammatory response.

or foreign bodies, or other disease agents such as protozoan infections. They are associated with a tenacious mucopurulent discharge and variable tissue distortion of the nares and beak or swelling of the periorbital sinuses and choanal slit region. There is loss or blunting of the palatine papilla and the formation of small pyogranulomas or granulomas in the mucosa. The lining respiratory mucosa may undergo metaplasia of the ciliated columnar epithelial cells to cuboidal or squamous cells and the inflammatory cells will be lymphocytes, plasma cells, and macrophages. The majority of chronic cases will have a focal lesion within the nasal cavity or diverticulae of the infraorbital sinuses. Such lesions include chronic bacterial or fungal granulomas, inflammatory polyps, unorganized caseous material, and mucoceles. Variable amounts of mucus and inflammatory debris may fill the sinus. A sequela to these chronic infections can be osteomyelitis and maxillary beak deformities.

Historically the sunken-eye syndrome of macaws is associated with chronic bacterial sinusitis. The enophthalmia that occurs appears to be a sequela of an infection in the infraorbital sinus diverticula around the eye. *Escherichia coli*, *Klebsiella* spp., and *Haemophilus* spp. have been isolated from these cases. Examination and imaging studies of the globes and periorbital soft and bony tissue are recommended.

Another specific syndrome attributed to a bacterial sinusitis is the lockjaw syndrome or temporomandibular rigidity of cockatiels. A number of microorganisms have been isolated from the sinuses of affected birds, including *Bordetella avium*, *Klebsiella* spp., *Aeromonas* spp., *Pseudomonas* spp., *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp., and *Bacillus* spp.

The disease generally affects young cockatiels 3–10 weeks of age, although it has been recognized in conures, cockatoos, and macaws. They initially develop a nasal and ocular discharge and swollen periorbital tissues that progress to an inability to open the beak. This results in death. Nasal passages, sinuses, and air spaces within cranial bones will contain inflammatory exudates consisting of fibrin, heterophils, and histiocytes. Histologic sections through the skull will have a necrotizing rhinitis and

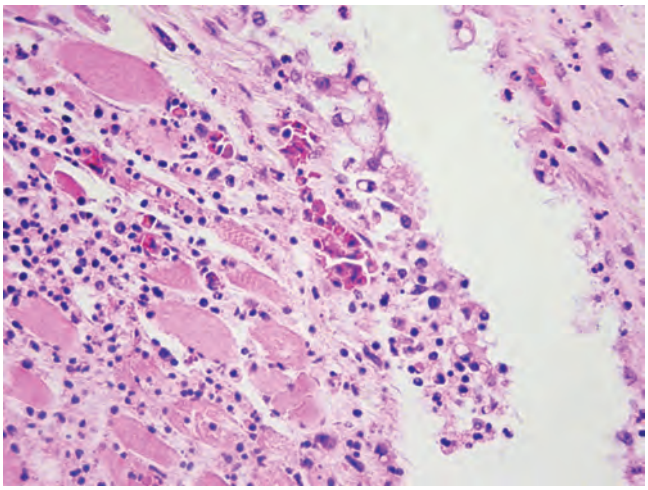

Figure 2.10 Detail of myositis and synovitis as seen in temporomandibular rigidity (lockjaw syndrome) of cockatiels.

sinusitis, as well as pleocellular and fibrosing myositis of the jaw muscles (Fig. 2.10). Osteomyelitis of the cranial bones and perineuritis are often present. The lesions in the sinuses and adjacent muscles of the temporomandibular joint are the most significant. Rarely, peracute hepatic necrosis, chronic hepatic fibrosis, splenic lymphocytic depletion, and subacute pneumonia with air sacculitis are present.

An unidentified spirochete has been associated with upper respiratory infections in cockatiels and lovebirds. The birds produce excess mucus at the choanae and into the trachea. The oral cavity is inflamed (choanal slit) and there may be ocular discharge and conjunctivitis/sinusitis. A thin gram-negative spirochete can be identified by exfoliative cytology. Based on PCR, the organism has been identified as a *Helicobacter* spp. It is speculated that the spirochete may interfere with normal ciliary function of the upper respiratory tract.

Mycotic disease

Members of the genus *Aspergillus* and the class Zygomycetes are capable of causing localized and/or disseminated disease. This group is characterized by the formation of hyphae in tissue.

Aspergillus is a ubiquitous, opportunistic fungus that grows readily in moist environments and on substrates such as wood shaving, corncob bedding, and seed hulls. It can be isolated from bird feces. *Aspergillus fumigatus*, *A. flavus*, *A. glaucus*, *A. oryzae*, *A. niger*, and *A. nidulans* have all been isolated from lesions in avians. *Aspergillus fumigatus* is the most common.

At least 11 species of the class Zygomycetes are regarded as medically important. The class includes the order Mucorales, containing the genera of the bread molds, such as *Mucor*, *Rhizopus*, and *Absidia*. This order is unique in that the hyphae are nonseptate or rarely septate. They are widespread in nature, thriving in organic material. They are also common laboratory contaminants. Infections involving *Rhizopus*, *Mucor*, and *Absidia* are reported in birds, although they are uncommon and usually associated with an underlying disease condition. The most common route of infection is by inhalation of the spores. There is a reported affinity of Zygomycetes to localize within blood vessels and the heart.

Localized lesions have been described in the trachea, bronchi, sinus, nasal cavity, and body cavity. In nasal cavity infections, the respiratory region of the nose is more susceptible than the vestibular region. Most mycotic rhinitis infections in psittacines start unilaterally and have a mucopurulent discharge. The fungal organisms tend to invade the sinuses, blood vessels, turbinate cartilages, and nasal bones. Mats of the fungal hyphae are supported within necrotic debris, hemorrhage, fibrin deposition, edema, and mixed inflammation. Cases of acute rhinitis or sinusitis have a large number of viable and degenerate heterophils.

More chronic lesions will have perivascular clusters of lymphocytes and plasma cells and hyphae associated with multinucleated giant cells and epithelioid macrophages. If severe and extensive, there can be associated osteomyelitis of the bones in the rhinosinus. Abnormal beak growth can be the result of this destruction. The underlying lesions may suggest mucosal epithelial metaplasia of vitamin A deficiency or a reaction to the chronic irritation from foreign material lodged within the nasal or infraorbital sinus.

Candidal infections are primarily diseases of the gastrointestinal tract; however, they have been isolated from lesions in the vestibular region of the nose. The proliferation of yeast and pseudohyphae are associated with hyperkeratosis of the nasal mucosal epithelium. There may be a variable inflammatory mixed inflammatory response.

Cryptococcal sinusitis, also known as turulosis or European blastomycosis, is caused by the saprophytic yeast, *Cryptococcus* spp. C*ryptococcus neoformans* (*var neoformans* and *var grubii*) and *C. gattii* (formerly *C. neoformans var gattii*) are two closely related siblings and are the primary pathogenic species. *Cryptococcus neoformans* has been recovered from a variety of environmental substrates including fruit, vegetables, unpasteurized milk, and hay. It is commonly isolated from the feces of birds, especially poultry and pigeons. Avian feces contain creatinine that the fungus uses as a source of nitrogen. This variety grows poorly at temperatures higher than 40°C. *Cryptococcus gattii* is associated with the flowers of the Eucalyptus camaldulensis (red river gum) and E. tereticornis. The gattii variety grows poorly at temperatures higher than 37°C.

Cryptococcus spp. infrequently causes disease in birds, possibly due to the protection by their normal bacterial microflora and high body temperature. The respiratory tract appears to be the portal of entry possibly because the upper respiratory tract has a lower mean temperature that may be predisposed to colonization. Dissemination to the central nervous system is not unusual with this fungus. The lesions are of a myxomatous gelatinous tan to white material within the nasal and infraorbital sinuses, lungs, air sacs, and brain.

Figure 2.11 Severe cryptococcal infection resulting in marked beak deformity.

In some cases, early diagnosis can keep the infection localized; however, there may be extensive tissue damage that like any process involving the nasal sinus can result in deformities of the beak (Fig. 2.11).

On exfoliative cytology, the organisms are narrow-based budding round yeast with a thick capsule. India-ink stains demonstrate the large heteropolysaccharide capsule. Histologically the numerous yeasts appear as "soap bubbles" separating the tissue's elements. They have infrequent narrow-based budding and are 5–15 mm in diameter. A variable and generally mild infiltration of heterophils, lymphocytes, plasma cells, and macrophages will be present (Fig. 2.12). Mucicarmine stain will help visualize the typical thick outer capsule.

Protozoa

Cryptosporidia has been recognized on respiratory epithelium in the nasal cavity, trachea, syrinx, and bronchi in a variety of raptors, including owls and falcons. Of the two species identified in birds, Cryptosporidium baileyi is most commonly associated with respiratory disease. The birds commonly develop a conjunctivitis, rhinitis, and tracheitis. The 4–6-μm spheroid apicomplexan parasites are at the apical border of mucosal epithelial cells. Histologically there is irregular epithelial hyperplasia with variable mixed inflammation. Grocott and periodic acid Schiff stains can be used to highlight the parasite.

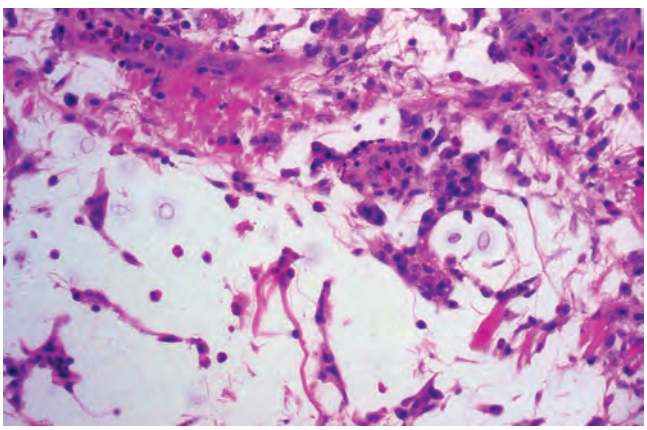

Figure 2.12 Sinusitis due to *Cryptococcus* sp. Note the numerous organisms and minimal inflammatory response.

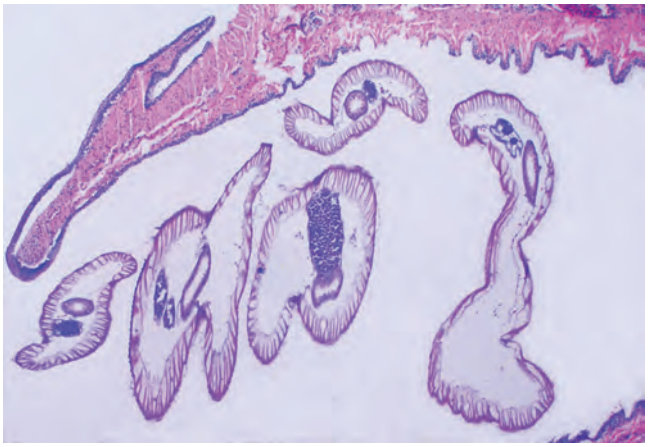

Figure 2.13 Nematode (*Aprocta* sp.) in the infraorbital sinus. No reaction is seen.

Metazoa

The nematode *Aprocta cylindrical* has been recognized within the nasal sinus, within the body cavity, and more commonly in the periocular soft tissues of European robins (*Erithacus rubecula*), a variety of African and Asia passerines, and a parrot. The lesion can vary in degree of inflammation based on association with secondary infections, especially fungal infections. Mucus may fill the sinus and there may be a mixed inflammatory response, although histologically minimal changes may be present even when nematodes are seen (Fig. 2.13). The nematode uses an invertebrate intermediate host, and the migratory locust (*Locusta migratoria*) is suspected to be the primary intermediate host in some geographic areas.

Noninfectious disease

Pet birds that are on a primary seed or cereal grain diet or have intestinal mucosal lesions which interfere with conversion of carotenoids to vitamin A may develop vitamin A deficiency. Hypovitaminosis A results in epithelial squamous metaplasia through poorly understood mechanisms of regulating gene expression of cell receptors as well as secreted proteins, which is manifested as hyperkeratosis of oral cavity, conjunctiva, nasal lacrimal duct, upper alimentary tract, and respiratory tract (Fig. 2.14). These cells may be found in washes or smears of the affected area (Fig. 2.15). In large parrots the epithelial changes will appear when vitamin A concentrations in the liver decrease below 50 IU/g (normal 500 IU/g liver).

Keratinizing epithelium that blocks the ducts of submucosal mucous glands is the typical gross lesion. These glands enlarge

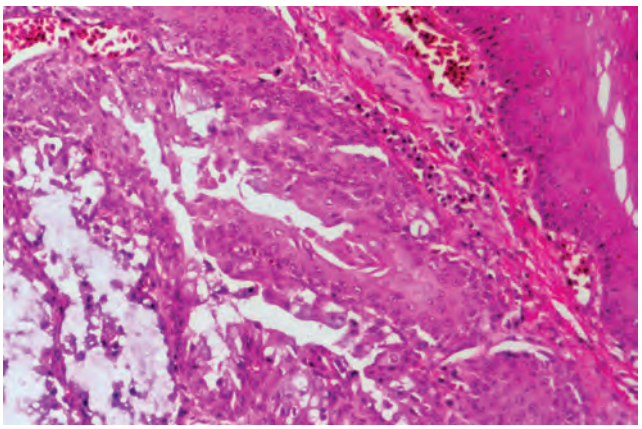

Figure 2.14 Metaplasia of pharyngeal and glandular mucosa in a bird fed with a vitamin A-deficient diet.F

and become secondarily infected, resulting in large keratin granulomas within the nasal or oral cavity. Some birds, especially African grey parrots, develop massive keratin rhinoliths (Fig. 2.16) that distort the nares and nasal sinus. The squamous metaplasia also alters the mucosal defenses, predisposing the bird to fungal and bacterial infections primarily of the respiratory tract.

Neoplastic disease

Rare polyps and mucoceles are described within the infraorbital sinus. These are associated with chronic sinusitis. The polyps are typical with a fibrous connective tissue core supporting hyperplastic mucosal epithelium. The mucoceles are of a mucinous cyst and sinusitis with marked goblet cell hyperplasia of the sinus lining.

Nasal/sinus carcinoma or adenocarcinomas

Carcinoma and adenocarcinoma of the upper respiratory system may arise from the nasal or sinus mucosa or from glandular epithelium. These tumors can become quite large, leading to distortion of the skull. They may impinge upon the brain in severe cases. Grossly the tumor is gray-white, firm, friable, and nodular (Fig. 2.17). Inflammation is common with exudates throughout the sinus. Histologically infiltrative cords and nests of neoplastic cells are usually seen within a moderate amount of stroma (Fig. 2.18). Invasion into the bony turbinates is common. Immunohistochemical staining for cytokeratin (CK AEI/3) was applied to one case. Immunoreactivity was variable (25–50% positive cytoplasmic reactivity) confirming epithelial origin.

Figure 2.16 Rhinolith formation secondary to vitamin A deficiency.

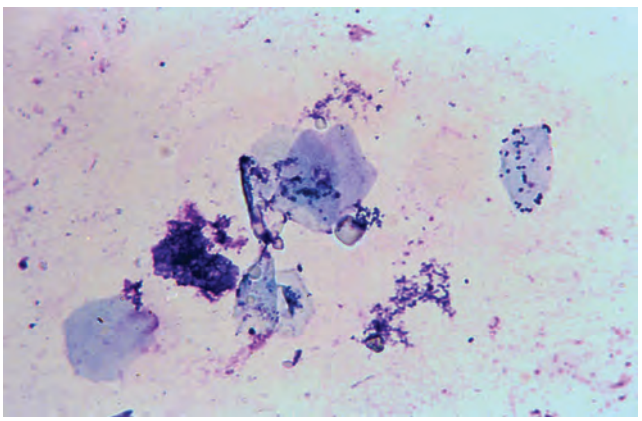

Figure 2.15 Cytology of sinus wash from a bird with a vitamin A deficiency. Keratinized epithelial cells and bacteria are seen.

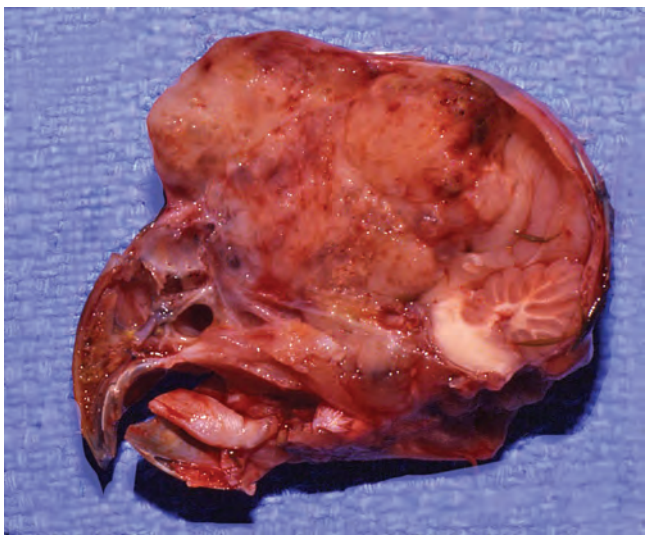

Figure 2.17 Nasal/sinus carcinoma with extension into the skull and brain.

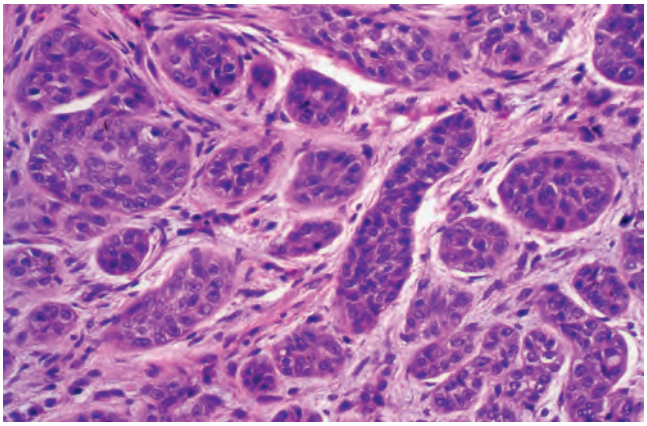

Figure 2.18 Nasal/sinus carcinoma. Numerous trabecular structures and nests are separated by moderate stroma.

Squamous cell carcinoma

Squamous cell carcinoma (SCC) is a malignant tumor comprised of nests and infiltrative cords of moderately undifferentiated to poorly differentiated squamous cells that frequently form central cores of compressed, laminated keratin ("keratin pearls"). In pet birds, the primary sites for SCC are the skin and upper gastrointestinal tract, including the beak, oral cavity, esophagus, crop, and proventriculus. SCC is a common tumor in budgerigars. SCC in the nasal sinuses and oral cavity has poorly defined borders and is associated with hemorrhage and necrosis of the surrounding tissues (Fig. 2.19). It is commonly associated with chronic stomatitis, and caseous material may be found within the mass. Multiple biopsies may be necessary for diagnosis as the inflammatory lesions and exudates may obscure the underlying tumor. It is a locally aggressive tumor that tends to recur. There are few reports of metastases.

Fibrosarcoma

Fibromas and fibrosarcomas are tumors that originate from fibrous connective tissue and are common neoplasms in pet birds. Fibromas are not reported in the upper respiratory tract, and fibrosarcomas are rarely described within the nasal infraorbital sinuses. The common sites of occurrence include the limbs, face, beak, syrinx, liver, small intestine, cloaca, spleen, air sacs, and lungs. Fibrosarcomas are gray-to-white firm masses with irregular and indistinct borders. Fibrosarcomas are locally invasive, rarely metastasize, and have a moderate to high potential for recurrence, giving them a guarded prognosis.

Figure 2.19 Squamous cell carcinoma of the oropharynx.

Lymphoma (lymphosarcoma)

Multicentric lymphoma is the most common lymphoid neoplasia in psittacine and passerine birds. Lymphoma may be more common in canaries, with an increased prevalence in males. However, male canaries, due to their popularity as songsters, may be the most common sex presented to veterinarians. Lymphoid neoplasms have been reported in many psittacine species. The reported ages of birds at the time of diagnosis ranged from 5 months to 30 years, with an average of 8 years.

A leukemic blood profile is uncommon in psittacine birds with lymphoid neoplasia. Canaries tend to have leukocytosis and lymphocytosis. Anemia (packed cell volume <35%) is common.

Diffuse or nodular involvement is characteristic of pet bird lymphosarcoma. Organs typically infiltrated include liver, spleen, kidneys, skin, bone, gastrointestinal tract, thyroid gland, oviduct, lungs, sinus, thymus, testes, brain, mesentery, trachea, fat, periorbital muscles, and pancreas. In the upper respiratory tract these tumors may present as periocular or choanal masses especially in Amazon and African grey parrots (Fig. 2.20). Grossly the lesions are firm and gray-white. Histologically normal tissue is effaced by a diffused sheet of immature lymphoid cells. Mitotic activity is variable.

Although lymphosarcoma in chickens is commonly associated with retrovirus (avian leukosis virus) or herpesvirus

Figure 2.20 Malignant lymphoma involving the sinus and entire facial region.

Figure 2.21 Beak distortion due to malignant melanoma.

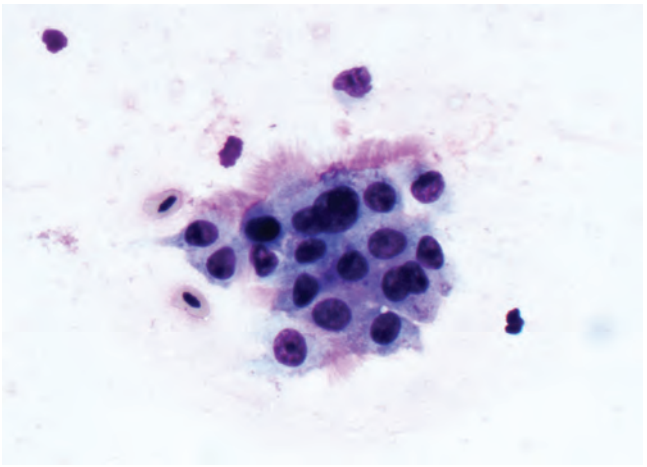

Figure 2.22 Normal tracheal mucosal cytology.

(Marek's) infection, there is no evidence to date of a viral link to the tumor formation in pet birds. Recent molecular investigations suggested a retroviral cause for multicentric lymphosarcoma in a starling. Retrovirus-induced lymphosarcoma has been suspected in other passerines but remains to be proven.

Malignant melanoma

Malignant melanoma has been recognized in the nasal sinuses as part of an infiltrative tumor involving the oral cavity and beak of African grey parrots, a thick-billed parrot, budgerigar, penguins, a variety of ducks and geese, pigeon, and zebra finch (Chapter 3). Tumors arising in the upper respiratory tract or oral cavity frequently distort the beak as they enlarge (Fig. 2.21). The tumor masses are black and firm with irregular borders. On exfoliative cytology the cells are arranged as individuals or clusters, round to oval, and supporting cytoplasmic granules. The intracytoplasmic granules in stained preparations are brown or pale blue to blue-brown, and in unstained preparations the granules are all brown. On histology, the infiltrative, pigmented melanocytic neoplasm is arranged in clusters and packets. The cells are round to ovoid with an eosinophilic cytoplasm containing small to moderate amounts of brown granular pigment and supported on delicate fibrous stroma. The cell nuclei are pleomorphic, with a vesicular and marginated chromatin and variably prominent nucleoli. Mitotic figures can be numerous. The cells have negative S-100 immunoreactivity but the dark brown pigment stains black with Fontana-Masson's stain for melanin. One tumor was immunoreactive negative for Melan A. Metastases are reported to many organs including the lung, liver, spleen, adrenal gland, pancreas, and bone marrow. Based on the reported cases, mitotic index, cellular atypia, and pigmentation are not correlated with malignancy. However, possible predictors of malignant behavior may be anisokaryosis and prominent nucleoli.

Trachea

Cytology: The normal exfoliative cytology collected from the trachea and primary bronchi is pseudostratified, ciliated columnar epithelium with goblet cells. Goblet cells are columnar, lack cilia, and have abundant cytoplasm with vacuoles and eosinophilic granulation. The nucleus is large, round to oval, and eccentric in location. The columnar ciliated cells have a nucleus situated at the opposite pole of the cell from the ciliated end (Fig. 2.22).

Viral disease

Herpesvirus

Herpesviruses are enveloped DNA virions that measure approximately 120–200 nm in diameter. The herpesviruses of the lltovirus genus are among the causative agents of respiratory disease in birds. Gallid herpesvirus I (GaHV-l), also known as infectious laryngotracheitis virus, causes severe respiratory disease in poultry. Passerid herpesvirus I (PaHV-l) is associated with tracheitis in Gouldian finches, *Erythrura gouldiae* (see in the following section). One or more herpesviruses also cause respiratory disease of parrots. Amazon tracheitis virus, a herpesvirus closely related to infectious laryngotracheitis virus, has been isolated from Amazon parrots (*Amazona* spp.) with tracheitis.

The herpesvirus outbreaks that primarily target the respiratory tract (Amazon tracheitis like virus) have been recognized in Amazon parrots, brown-throated conures, Bourke's parakeets (*Neopsephotus bourkii*), whiskered lorikeets (*Oreopsittacus arfaki*), and rosellas (*Platycercus* spp.). The tracheal mucosa and lungs appear edematous and congested. The histologic lesions range from the severe hemorrhagic or fibrinonecrotic inflammation that primarily affects the upper respiratory tract to a proliferative bronchitis with mild necrosis and syncytial cell formation. Type A nuclear inclusion bodies can be found in bronchial epithelial and syncytial cells (Fig. 2.23).

The defining lesions of Pacheco's virus (PsHV-l) are massive hepatic and splenic necrosis with syncytial cells and eosinophilic intranuclear inclusion bodies. Occasionally, intranuclear inclusions and necrotic lesions have been described in a variety of other tissues. Outside of the liver and the spleen, the pancreas,

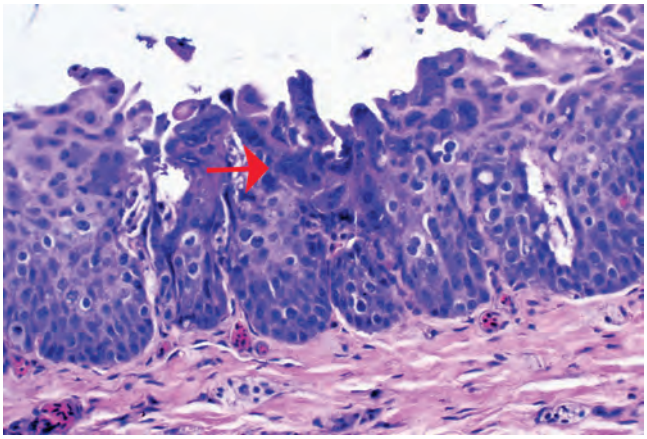

Figure 2.23 Pharyngeal necrosis and intranuclear inclusion body formation in herpesvirus (possible Amazon tracheitis) infection (arrow).

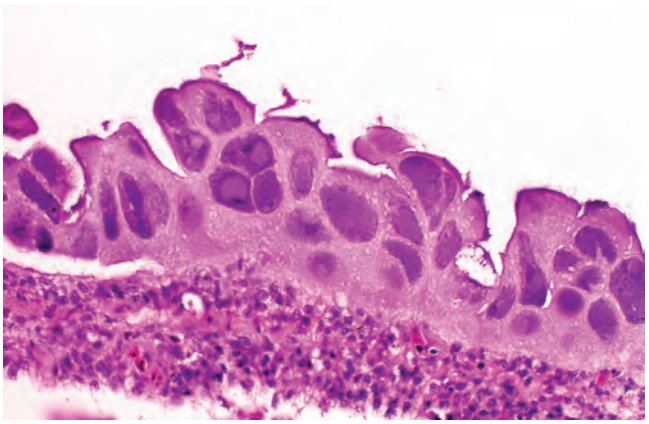

Figure 2.25 A finch with cytomegalic herpesvirus infection. There is marked mucosal proliferation with karyomegaly and intranuclear inclusion body formation.

crop, and intestine are most likely to contain lesions. Less commonly, kidney, endocrine organs, or cloaca are involved. It is unusual for Pacheco's disease to affect the respiratory system, but, when it does, the intranuclear inclusions have been observed in epithelial and syncytial cells of the larynx, trachea, and bronchi.

Finch herpesvirus

Finch cytomegalovirus was previously classified as a host-specific beta herpesvirus. Genetic sequencing is clustering this as an alphaherpesvirus within the genus Iltoherpesvirus. It appears to be a disease primarily of finches, especially Gouldian finches (*Er. (Chloebia) gouldiae*) and is characterized by high mortality, conjunctivitis, rhinitis, pharyngitis, tracheitis, and bronchitis. The prominent gross lesion is a hyperemic and edematous conjunctiva and respiratory mucus membranes (Fig. 2.24). The air sacs may be thickened with fibrin. The conjunctivae, syrinx, and bronchi will all have a hyperplastic epithelium with cytomegaly (exceeding 40 μm in diameter) and karyomegaly (Fig. 2.25). The esophagus and nasal conchae have focal diphtheritic lesions with the characteristic inclusion bodies. The viral inclusions are large intranuclear basophilic inclusion bodies within cytomegalic cells.

Polyomavirus

Polyomavirus, a nonenveloped DNA virus in the Papovaviridae family, commonly results in a pansystemic disease of nestling budgerigars and other psittacines. The most consistent lesions of polyomavirus include hepatic necrosis, membranous glomerulopathy, variable karyomegaly of hepatocytes and renal tubular epithelial cells, and large clear to basophilic intranuclear inclusion bodies of the splenic periarteriolar sheaths. The intranuclear inclusions have rarely been recognized within the bursa of Fabricius and the mucosa of the trachea, crop, and proventriculus (Fig. 2.26).

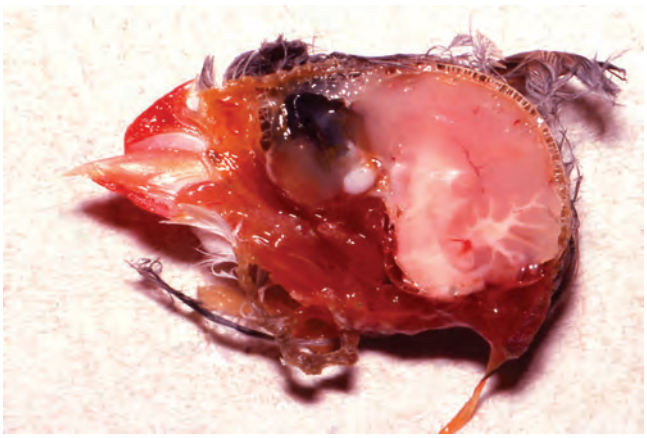

Figure 2.24 Rhinitis/sinusitis due to an alpha herpesvirus. Grossly there is hyperemia, edema, and a mucoid exudate.

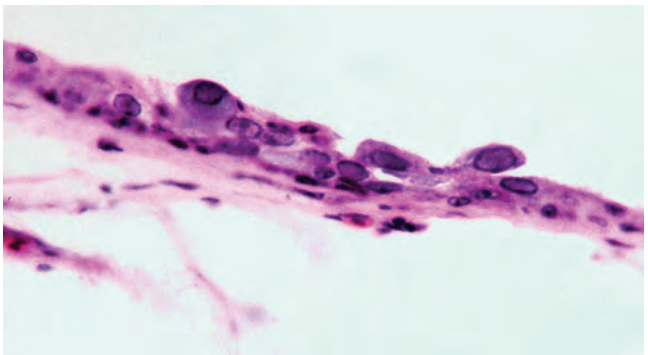

Figure 2.26 Polyomavirus infection leading to tracheal mucosal proliferation and intranuclear inclusion body formation. The changes are not as severe as those seen in cytomegalic herpesvirus infection and are unusual in polyomavirus infection.

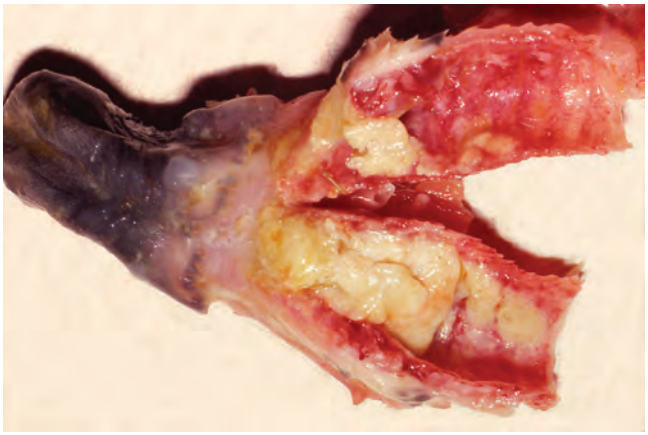

Figure 2.27 Caseous exudate in the trachea of a bird with systemic poxvirus infection.

Poxvirus

In some "wet pox" infections there can be a severe necrotizing lesion in a portion of the trachea (Fig. 2.27). The microscopic lesion is similar to that previously described.

Paramyxovirus (newcastle disease)

Newcastle disease may affect the respiratory system of chickens. Gross lesions can include tracheal congestion and hemorrhage and a mononuclear inflammatory infiltrate.

Bacterial disease

Enterococcus faecalis (formerly *Streptococcus faecalis*, 1990) is associated with a tracheitis, pneumonia, and/or airsacculitis of canaries and finches. This gram-positive coccus, which is part of the normal intestinal flora of many mammals and poultry, tends to be highly resistant to many commonly used antibiotics. The clinical signs are the same as for pox virus infection and Sternostoma mite infestation in passerines. Early lesions are of a heterophilic tracheitis with the accumulation of heterophilic exudates in the lumen. The more chronic lesion is of tracheal mucosal epithelial hyperplasia and a variable lymphocytic and plasmacytic inflammation.

Mycotic disease

The fungal organisms associated with cases of mycotic tracheitis are the same as those producing mycotic sinusitis. Localized fungal lesions have been described in the trachea bronchi, sinus, nasal cavity, and body cavity. The lumen of the trachea, syrinx, or bronchi will be partially to completely occluded with a white- to cream-colored fibrinocaseous plug (Fig. 2.28). Tracheal washes and brush cytology have identified fungal infections such as aspergillosis. One author (DRR) has observed an acute heterophilic inflammatory reaction in *Aspergillus* cases of the sinuses and trachea before cytology with fungal hypha or culture could confirm the disease (Fig. 2.29). As the fungal disease progresses, a mixed-cell to histiocytic inflammatory response develops.

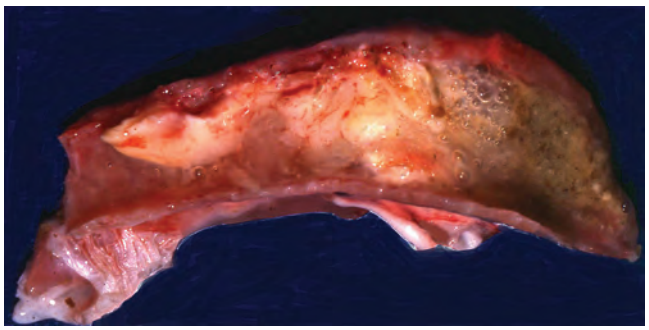

Figure 2.28 Severe tracheal aspergillosis with blockage of the lumen by exudate.

Histologically in the trachea and bronchi, the fungal mycelia penetrate the walls and combine with inflammatory cells to form caseous, granulomatous nodules (Fig. 2.30).

The syrinx is a common site of a primary focal fungal infection. Many pet birds will have a history of unsupplemented all-seed diet suggesting that hypovitaminosis A is a predisposing factor to the development of the tracheal lesions. Exposure to large number of fungal spores in the environment is also a possible cause for fungal tracheitis. One important but rare differential diagnosis is of mycobacteria tracheitis.

Parasitic disease

Protozoal disease

Trichomonads are flagellated protozoa that are primarily enteric pathogens. There are several closely related protozoa that have been isolated from lesions in the upper respiratory tract of birds. *Tetratrichomonas anatis* was isolated from the swollen infraorbital sinus, the nasal sinus, trachea, and the lower small intestine in ducklings. It is associated with a mucoid fibrinopurulent

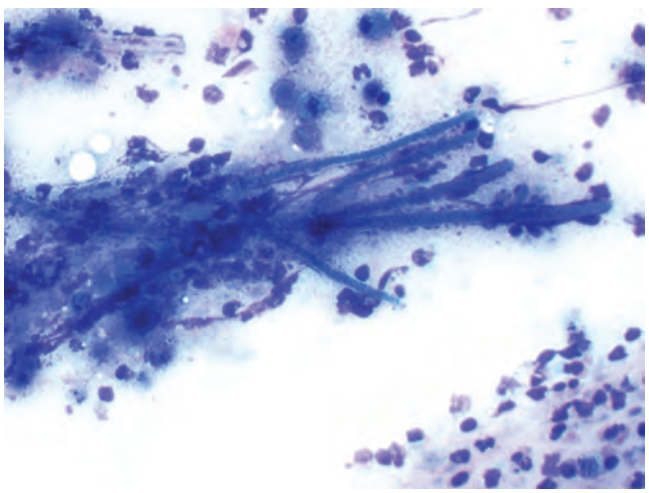

Figure 2.29 Cytology from the trachea of a bird with mycotic tracheitis. Hyphae and inflammatory cells are present.

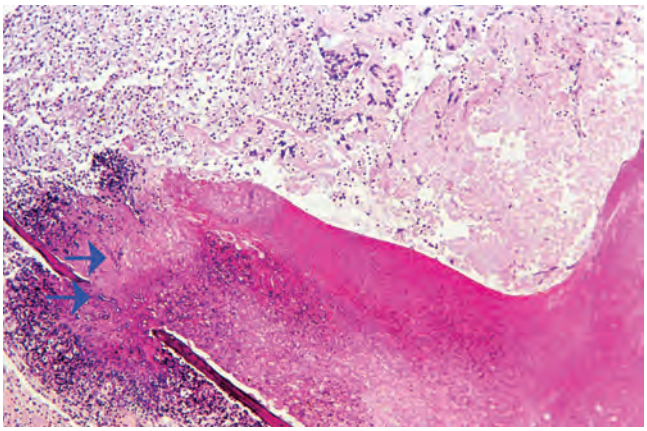

Figure 2.30 Tracheal/syringeal aspergillosis. Severe inflammation, fibroplasia, and exudate formation. A few organisms can be seen (arrows).

sinusitis and catarrhal rhinitis and tracheitis. There is marked hyperplasia of mucous cells in the epithelium, with excessive mucofibrinous exudate and many desquamated epithelial cells. Heterophils, some mononuclear cells, and erythrocytes are also present. Large numbers of pyriform-shaped protozoa stain purplish red with hematoxylin–eosin in the exudate.

Trichomonas gallinae, normally a pathogen of the digestive tract of Columbidae, raptors, and selected passerines, is found within lesions of the respiratory sinuses and trachea of these species. The mucosa is covered with superficial dry caseous diphtheritic membranes, and caseous material fills the tracheal lumen. Another common location for these lesions is the pharynx. These lesions are often large and caseous and may obstruct the choanal slit or the glottis. *Trichomonas* spp. are also associated with necrotic, caseated masses in the trachea of psittacines (Fig. 2.31). These protozoa are best visualized on wet mount preparations. The exudates from infraorbital sinuses and intestinal contents will have many motile protozoa with an undulating membrane and flagella. They are pear shaped, 12.20 μm long, and 8–12 μm wide, with a distinct nucleus (Fig. 2.32).

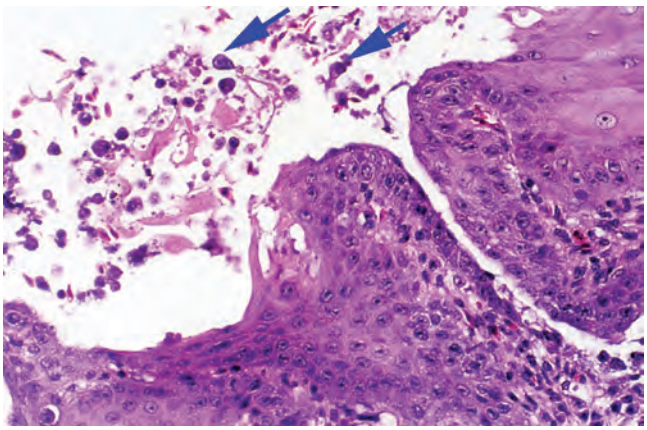

Figure 2.31 Trichomoniasis of the trachea. The mucosa is thickened, and organisms are seen within the lumenal exudate (arrows).

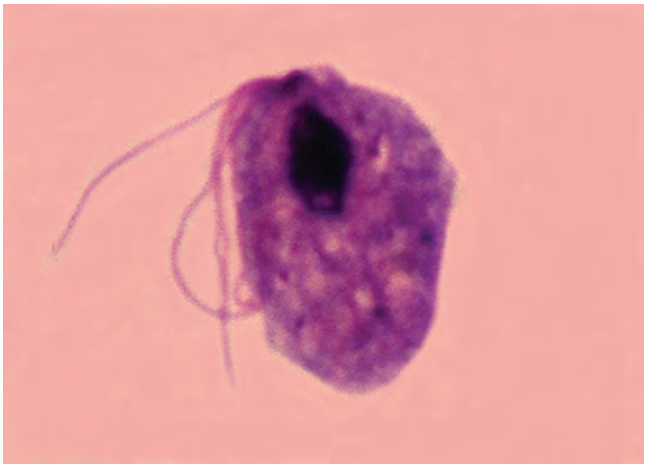

Figure 2.32 Detail of trichomonad from a smear of a lesion.

Nematodes

Syngamus trachea, also commonly known as the "gapeworm," is a well-described nematode infection in poultry. It has only been reported as occasional infection in a variety of other avian species including American robins, house sparrows, emus, magpie, barbets (*Trachyphonus erythrocephahs*), grouse, kestrels, various Columbiformes, and once in a psittacine. It is a large, robust, bright red helminth that inhabits the trachea and bronchi and appears Y-shaped because the male is attached to the female. The lifecycle is direct or indirect with earthworms, snails, and cockroaches serving as transport hosts. They produce large, ellipsoidal operculated eggs that can be identified on fecal parasitic examinations and direct smears of the oral cavity. The eggs can be confused with those of *Capillaria* spp. The birds typically present in respiratory distress and occasionally with blood in their oral cavity. Death may be due to obstruction of the trachea from the mass of nematodes and/or the inflammation.

Grossly the trachea will be hemorrhagic with many nematodes and eggs (Fig. 2.33). The lungs are firm, with irregular focal yellow areas of the parenchyma. The air sacs can be thickened and covered with yellow material (fibrin). The nematodes

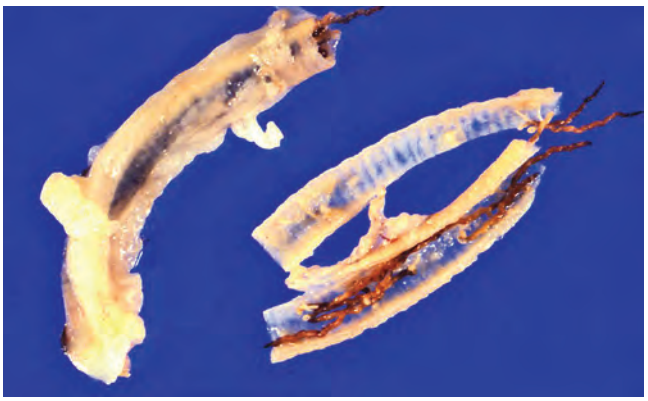

Figure 2.33 *Syngamus* sp. and exudate within the tracheal lumen.

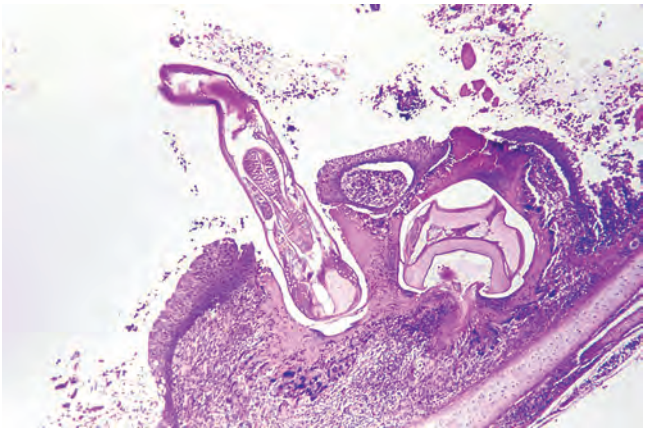

Figure 2.34 Tracheal infection by *Syngamus* sp. Note the swelling and inflammation associated with attachment of the parasites.

are associated with intense mixed-cell inflammation and associated hemorrhage, fibrin deposition, and edema (Fig. 2.34). Multinucleated giant cells and a large number of macrophages commonly aggregate around the eggs.

Arthropods

Sternostoma tracheacolum, a parasitic rhinonyssid mite, is the tracheal mite of canaries and Gouldian finches (*Er. gouldiae*). It is presumed to have a direct life cycle passing from parents to chicks. Aviculturists will use society finches to raise Gouldians in order to raise mite-free chicks. Air-sac mites are generally distributed throughout the respiratory system, especially in juvenile birds. Mites attach to the mucosa by embedding their legs into the connective tissue. Mucus from the host will coat the mites. They are recognized as small black masses within the lumen of the trachea (Fig. 2.35). The tracheal lesion associated with the mite is mucosal epithelial necrosis as well as mucosal hyperplasia with mixed inflammation. Heterophils, lymphocytes, and plasma cells will accumulate in the submucosa and extend between the tracheal rings. Mites have a brown, slightly refractile cuticle, segmented legs, and bands of striated skeletal muscle within the body cavity (Fig. 2.36).

Figure 2.35 Small black foci indicative of tracheal mites in a canary.

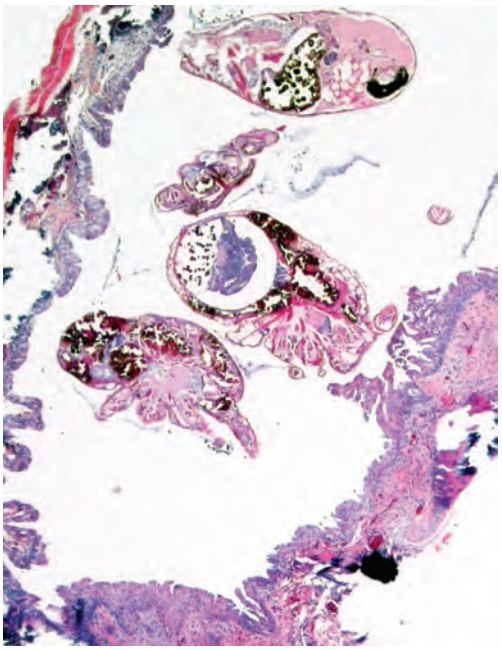

Figure 2.36 Tracheal infection by *Sternosoma tracheacolm*.

Inhaled toxins/irritants

Exposure to gases produced by undiluted sodium hypochlorite (5% chlorine bleach) appears to induce tracheal lesions that can result in death. Days after the initial lesion of tracheal hyperemia, multifocal diphtheritic membranes and caseous material covering the tracheal mucosa develop. These birds may also have yellowish, cloudy air sacs.

The histopathologic lesions of the trachea include epithelial deciliation, ulceration, squamous metaplasia, and epithelial hyperplasia. Death is considered to be the result of hypoxia secondary to blockage of the trachea or pulmonary congestion and, in some cases, sepsis secondary to invasion of bacteria through the altered tracheal mucosa.

Inadvertent inhalation of ivermectin diluted 1:10 with propylene glycol can result in respiratory distress and a necrotizing tracheitis. It was unknown whether the inhaled ivermectin or a carrier is responsible.

Foreign bodies lodging in the trachea are not an uncommon problem, although these are infrequently described in the literature. In cockatiels, millet seeds are the most common foreign bodies to become lodged at the tracheal bifurcation. Acutely the mucosa of the trachea becomes edematous, and heterophils infiltrate within the first few hours. As time passes, mixed cellular infiltrates, vascular compromise, and necrosis occur (Fig. 2.37).

Postintubation obstruction

Tracheal stenosis is an uncommon complication secondary to endotracheal intubation. Clinically acute respiratory distress develops about 2–3 weeks postintubation for gas anesthesia. Trauma to the tracheal mucosa from the endotracheal bevel tip or chemical irritation from cold sterilization are suspected to be

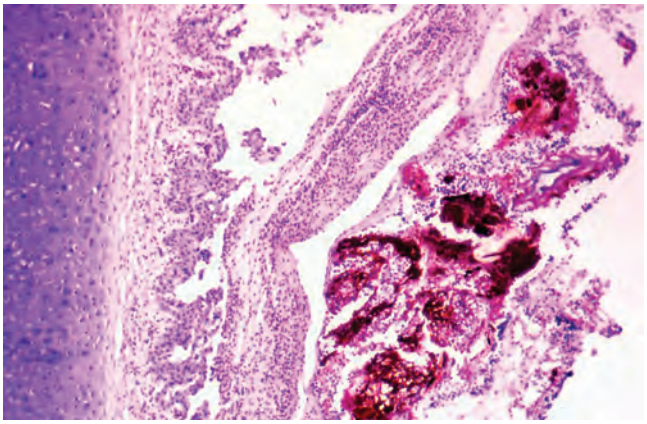

Figure 2.37 Foreign-material inhalation leading to an inflammatory response and fibrin production. Partial or complete tracheal blockage can occur.

causes. Grossly the tracheal lumen may be filled with mucous or fibrinonecrotic exudates. The submucosa histologically will be expended by granulation tissue. Ulceration, squamous metaplasia of the lining mucosa, and variable inflammation are common lesions recognized in tracheal obstruction (Fig. 2.38).

In a bird of prey (red-tailed hawk, *Buteo jamaicensis*), a xanthogranulomatosis mass developed at the site of previous endotracheal tube placement for surgery, approximately 3 weeks earlier. The mass resulted in an obstructive lesion and was successfully resected. The subepithelial mass consisted of fibroplasia, foamy macrophages, clusters of giant cells, a minimal to moderate lymphocytic infiltration, and a few cholesterol clefts. It is speculated that the lipid phagocytosis by macrophages may be secondary to hemorrhage, suppuration, or necrosis.

Neoplastic disease

Internal papillomatosis results in proliferative, gray-white growths on mucous membranes. Histologically they are frondlike projections of hyperplastic epithelium supported by thin, inflamed, fibrovascular stromal stalks. Mitotic activity is primarily in the polygonal basal cells, and mucin-producing cells may be present in the lining epithelium. The fibrovascular stroma will have varying infiltrates of plasma cells, lymphocytes, and heterophils. The lesions closely resemble those caused by papillomaviruses in mammals. To date, evidence for a papillomavirus in these lesions has not been found. However, many, possibly all, neotropical parrots (macaws, Amazons, and hawk-headed parrots) with internal papillomatosis are concurrently infected with psittacid herpesviruses (PsHVs). The age range in a series of Amazons was from 18 months to greater than 15 years. There is a cyclic regression and recurrence.

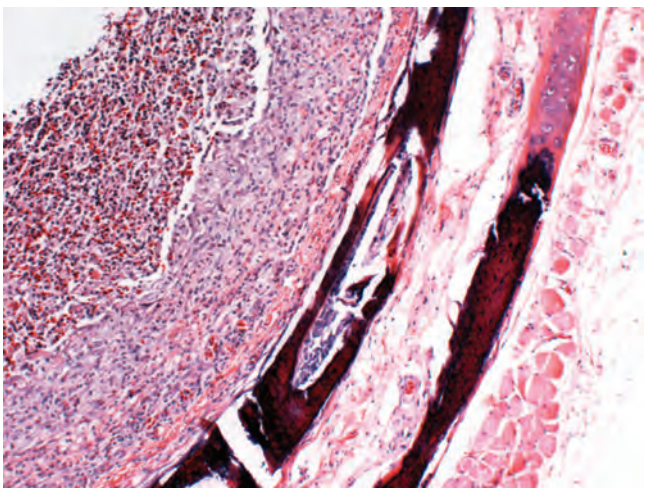

Figure 2.38 Tracheal stenosis secondary to endotracheal intubation.

Reported sites include the oropharynx, choanal cleft, conjunctiva, larynx, esophagus, crop, proventriculus, ventriculus, nasal mucosa, nasolacrimal duct, bile ducts, pancreatic ducts, and cloaca. Two of the most common sites for these lesions are the mucosa on the margins of the choanal slit and the mucosa of the glottis. Large papillomas in this location can interfere with breathing. There is a cyclic regression and recurrence of these lesions.

Tracheal osteochondroma

Tumors of the trachea are rare in birds. Tracheal osteochondroma, which is the most common tracheal tumor of dogs, was recognized in a psittacine bird. The tumor resulted in tracheal stenosis. The irregularly formed cartilage was ossified and protruded into the submucosal layer, and the cells were well differentiated.

Lower respiratory system

Lung

Cytology: The lung, air capillaries, and air sacs are lined with simple squamous epithelium. With airsacculitis and pneumonia there will be an increased number of inflammatory cells and background debris. Chronic chlamydial and fungal infections support a mononuclear leukocyte response with macrophages and plasma cells. Imprints of avian lung tissue have been diagnostic for atoxoplasma in finches.

Infectious disease

Polyomavirus

The common gross lesions of polyomavirus are hepatomegaly with necrotic foci, splenomegaly, an enlarged bursa of Fabricius with serosal hemorrhages, and widespread petechial and ecchymotic hemorrhages. In the classic cases of avian polyomavirus, there are either no histologic changes in the lungs, or the interstitium of the lung is expanded with mononuclear inflammatory infiltrates. Rarely large pale basophilic intranuclear viral inclusions can be identified within this mononuclear population (Fig. 2.39). Recently another form of avian polyomavirus was recognized in cockatoos. These birds have a chronic illness and

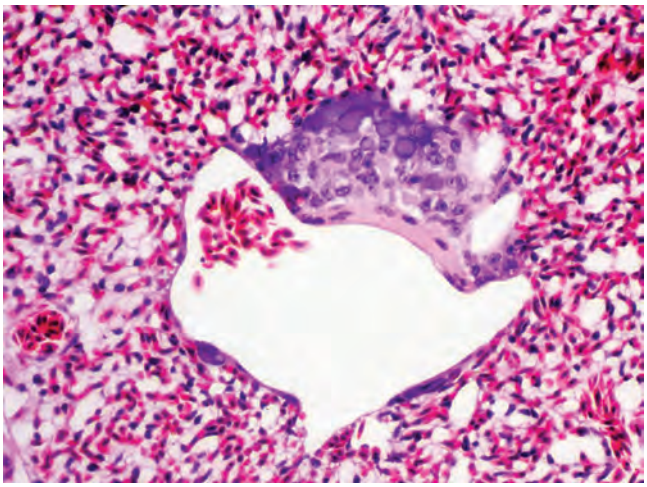

Figure 2.39 Bronchiolitis due to polyomavirus infection. Note the karyomegalic nuclei and minimal early inflammation.

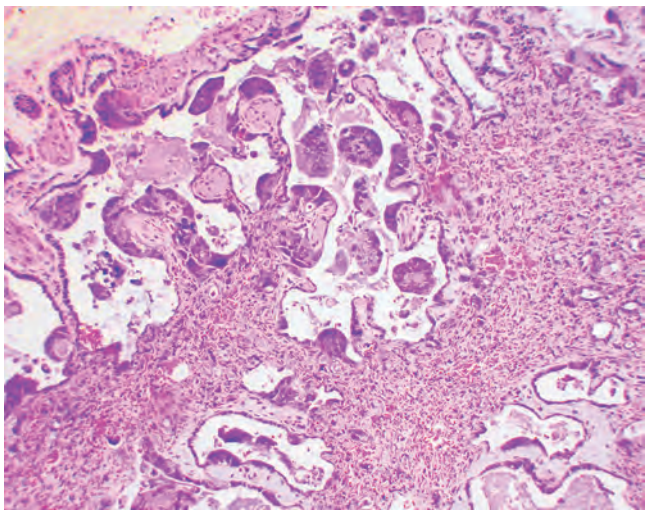

Figure 2.40 Pneumonia associated with Amazon tracheitis virus. There is inflammation and epithelial proliferation with syncytial cell formation.

are often poorly grown and emaciated. Grossly their lungs are moist and may have a decreased buoyancy. Histologically there is a diffuse interstitial pneumonia. There appears to be a proliferation of type II pneumocytes, and there is severe pulmonary edema and numerous viral inclusions.

Herpesviruses

The Amazon tracheitis virus, parakeet herpesvirus, and other herpesviruses may cause pneumonia (see the previous section on diseases of the trachea). The gross pulmonary lesions are edema and congestion. Within the lung, intranuclear inclusions are observed in epithelial and syncytial cells of the parabronchi. Similar inclusions and syncytial cells may also be present in the tracheal epithelium and air sacs. Amazon tracheitis virus is generally associated with severe hemorrhagic or fibrinonecrotic inflammation that primarily affects the upper respiratory tract as well as the lung (Fig. 2.40). Parakeet herpesvirus results in a proliferative bronchitis with mild necrosis and syncytial cell formation. An outbreak of respiratory disease characterized by dyspnea, lacrimation, nasal discharge, and death in Bourke's parrots has been linked by polymerase chain reaction (PCR) to a new herpesvirus in the lltovirus genus of the Alphaherpesvirinae subfamily. This virus is closely related to the clade of herpesviruses causing respiratory disease in other avian species.

Poxvirus

Avipoxviruses are epitheliotropic viruses that have cutaneous, mucosal (diphtheritic), and systemic presentations and in some outbreaks all three forms can be identified. Canary poxvirus, a virulent avipoxvirus, generally presents as a systemic infection and can cause up to 100% mortality in susceptible canary (*Serinus canaria*) flocks as well as other passerines such as finches and sparrows. Secondary pathogens of bacteria and/or fungus can significantly contribute to the mortality. Upper respiratory tract disease, pneumonia, airsacculitis, and splenomegaly may be evident. A common early lesion is of a periocular proliferative dermatitis and the most significant lesion is the proliferative bronchopneumonia.

Histologically, pox is characterized by marked epithelial hyperplasia and vacuolar degeneration of airway epithelial cells associated with small numbers of mixed inflammatory cells (Fig. 2.41). The lesions are progressive, starting in the nasal cavity as a proliferative rhinitis, continuing through the trachea, and finally reaching the lungs and airsacs. Scattered areas of coagulative necrosis may be present within the mucosa. The virus forms eosinophilic intracytoplasmic inclusion bodies (called Bollinger bodies in histological sections and Borrel bodies in impression smears) (Fig. 2.42). Cutaneous lesions may subsequently develop in birds surviving the initial lesions. Peracute to acute

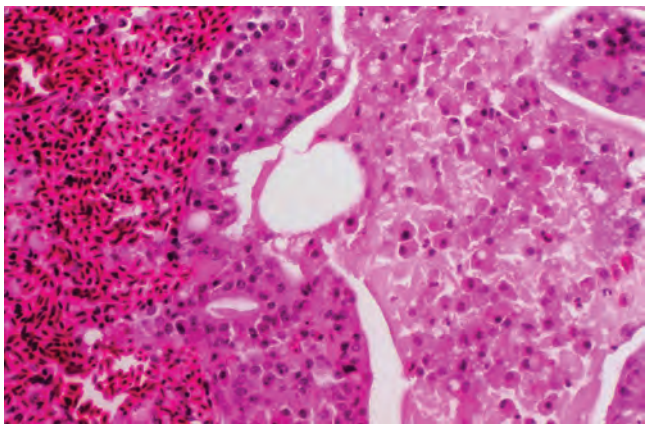

Figure 2.41 Bronchopneumonia due to systemic poxvirus infection. Variable epithelial proliferation is associated with congestion, as well as an inflammatory response and fibrin deposition within airways.

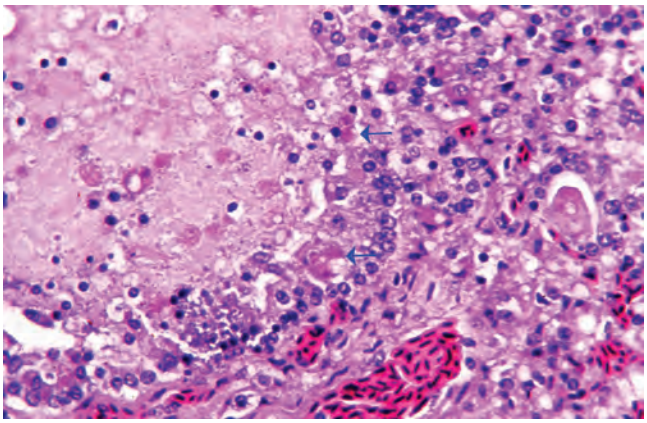

Figure 2.42 Detail of poxvirus-induced pneumonia. Note the epithelial proliferation and inflammatory response. Inclusion body formation is inconsistent, but can be seen (arrows).

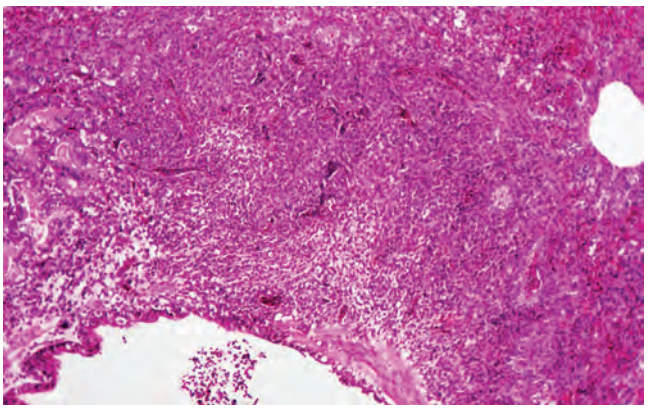

Figure 2.44 Severe bacterial pneumonia. Diffuse effacement of pulmonary parenchyma by inflammatory cells is seen.

systemic presentation of the infection is characterized by fibrinous inflammation of serous membranes, pulmonary edema, and fibrinous pneumonitis.

Bacterial pneumonia

This can occur from either inhalation of the bacteria or as part of a septicemic process. With the exception of some virulent bacterial organisms, most cases of bacterial pneumonia due to a systemic process are secondary to underlying viral infections or other diseases such as malnutrition. Grossly both processes will produce dark red lungs, occasionally with foci of abscessation (Fig. 2.43).

With inhalation, the bacteria can be seen within the lumen of bronchioles admixed with fibrin, small numbers of inflammatory cells, usually heterophils, and some hemorrhage. The inflammation, hemorrhage, and fibrin may extend into the surrounding air capillaries. The bacterial pneumonia of a systemic process generally results in diffused lesions. Abundant hemorrhage, congestion, fibrinopurulent exudates, and scattered bacteria efface significant portions of the lung (Figs. 2.44 and 2.45). Histologically bacteria may be identified within the cytoplasm of macrophages or within the lumen of vascular spaces indicating a bacteremia (Fig. 2.46), but they are often more readily seen on impression smears (Fig. 2.47).

Nocardia

Nocardia is a gram-positive bacterium with branching filaments and an irregularly granular and beaded appearance. It is variably acid fast. Pathogenic nocardia grow as saprophytes in the soil. The most common isolate from birds is *Norcardia asteroides*. There are rare case reports of infections in birds. In most avian cases, the primary site of infection appears to be the respiratory tract, with secondary involvement of other organs. The lung may have red-to-pink mottling, and the air sacs can appear thickened. The lungs and other tissues will also have multiple grayish white nodular lesions.

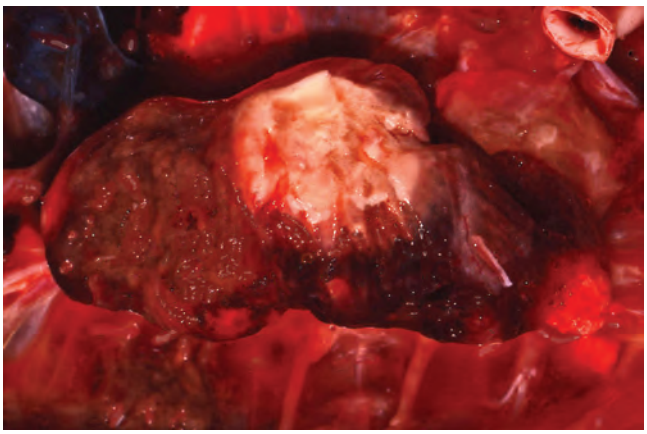

Figure 2.43 Bacterial pneumonia. Generalized discoloration and a focus of abscessation are seen.

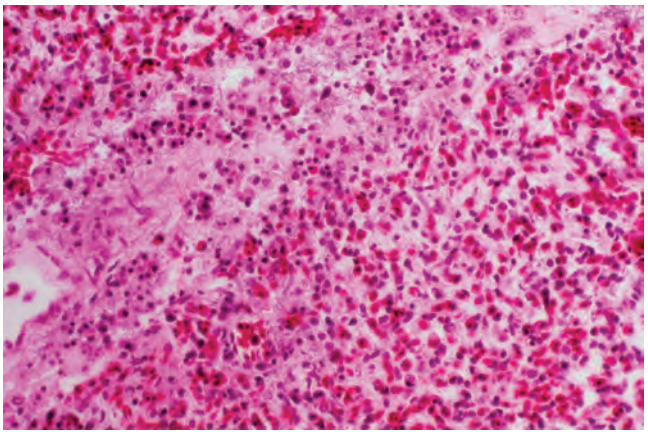

Figure 2.45 Detail of fibrin deposition and inflammatory infiltrate in bacterial pneumonia.

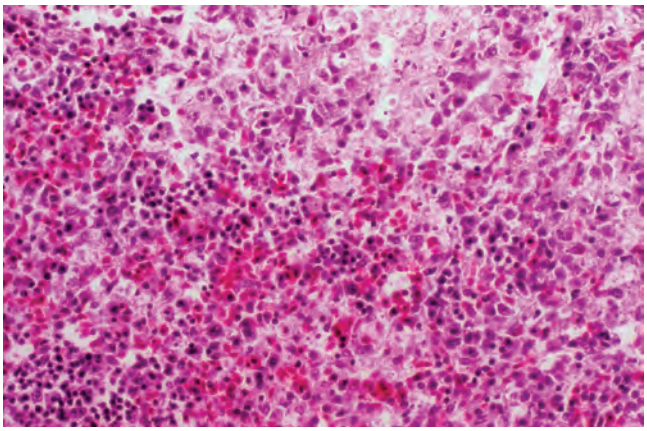

Figure 2.46 Pneumonia due to *Pseudomonas* sp. in an immunocompromised bird. Fibrin and inflammatory cells are seen, but bacteria are often difficult to see on routine stains.

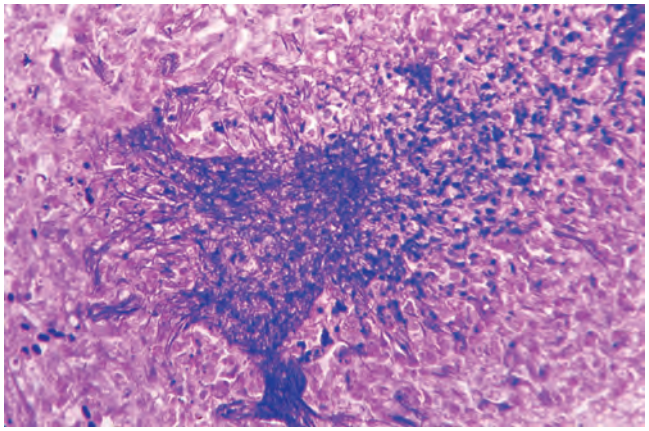

Figure 2.48 Pneumonia due to *Nocardia* sp. Numerous filamentous organisms are seen in a gram-stained section.

Histologically the lungs and other organs with the nodular lesions contain multiple, often confluent granulomas with central necrosis. The delicate filamentous bacteria are visible in the necrotic centers (Fig. 2.48). These organisms are acid fast when stained with Fite-Furaco. A mild fibrinous air sacculitis may also be recognized.

Mycobacteria

Mycobacteria are gram-positive, rod-shaped bacteria that stain with all acid-fast stains. In pet birds, *Mycobacterium avium* is most common although *Mycobacterium genevense* is frequently recognized. It is a slow-spreading, usually chronic infection of semimature to mature birds. The main portal of entry is the gastrointestinal tract, where the organisms penetrate the mucosa, colonize under the serosa, and once in the vascular system lodge in the liver, spleen, and bone marrow.

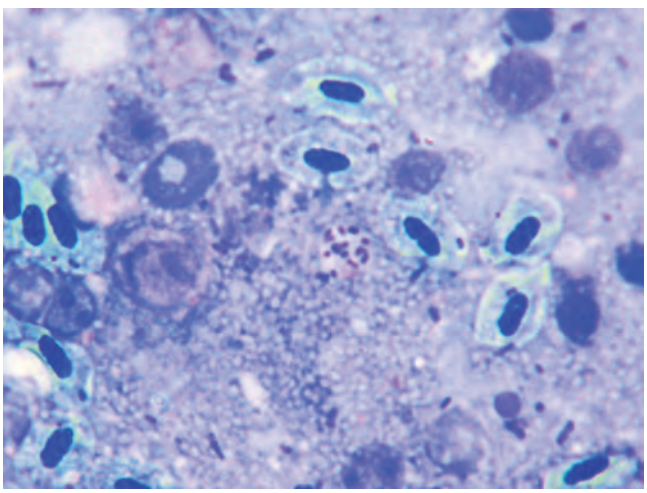

Figure 2.47 Impression smear of pneumonic lung with prominent bacteria seen.

The typical gross lesions are of organ enlargement, especially the liver and spleen, and a regional to diffuse thickening of the intestines. Multifocal to large, coalescing, firm, white masses may develop through the coelomic body cavity. In pet birds, the nodular masses (tubercles) do not calcify. The granulomas and granulomatous inflammation are commonly found in the liver, intestine, spleen, lung (Fig. 2.49), air sacs, bone marrow, and, uncommonly, kidney. The multifocal to coalescing granulomas will efface the normal architecture of the pulmonic parenchyma (Fig. 2.50).

A central core of granular eosinophilic matrix that is surrounded by multinucleate giant cells, epithelioid macrophages, and smaller numbers of infiltrating heterophils characterizes the granulomas (Fig. 2.51). Blood vessels will have accumulations of perivascular plasma cells and smaller numbers of lymphocytes with rare heterophils. Outlines of rod-shaped bacteria may be recognized within the cytoplasm of macrophages as well as identified within the core of the granulomas on hematoxylin–eosin preparations.

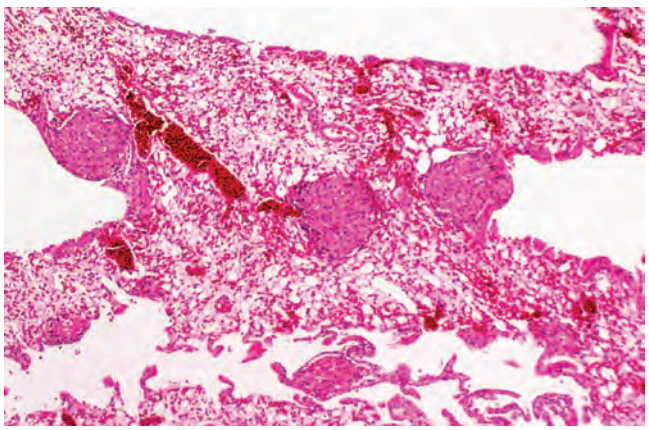

Figure 2.49 Early pulmonary mycobacteriosis with formation of discrete granulomas. Large macrophages contain organisms that are better visualized with acid-fast stains.

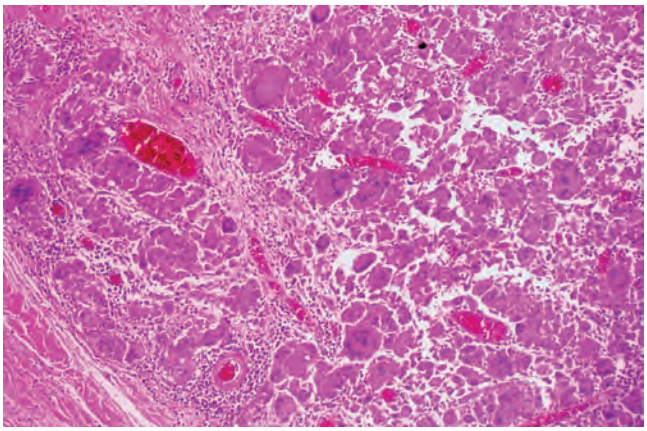

Figure 2.50 Severe pulmonary mycobacteriosis with effacement of parenchyma and a pleocellular infiltrate that includes giant cells.

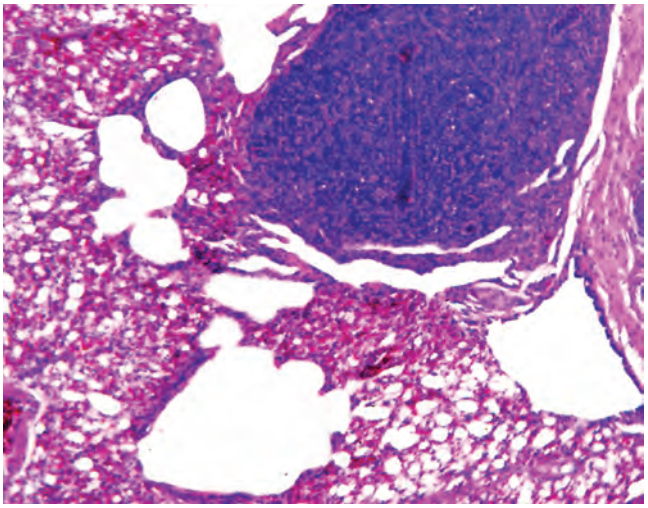

Figure 2.52 Pulmonary lymphoid nodule formation consistent with Mycoplasma infection.

Mycoplasma pneumonia

Mycoplasma infections of birds are poorly documented with the exception of poultry and some Passeriformes, where large outbreaks caused by *Mycoplasma gallisepticum* are described. For most cases the significance of isolates from lesions is unknown. The lung can have lymphocytic infiltrates in the tertiary bronchial walls and in the mucosa of secondary bronchi. The lymphocytic infiltrates may form prominent lymphoid nodules (Fig. 2.52). Focal perivascular infiltrates of lymphoid cells in lung parenchyma are also described.

Mycotic pneumonia

Aspergillus spp. are the most common fungi causing pneumonia in birds. Aspergillosis presents in several forms in pet birds. The lesions depend on the chronicity of the infection and the number of spores inhaled. Colonization may be limited to the site of primary infection. The spores grow on the mucous membranes of the lungs and in the air sacs. It can occur as a very acute systemic disease, due to an overwhelming dose of fungal spores. It can present as a chronic infection of the air sacs. In other forms, depending on the host's resistance, *Aspergillus* can be found in localized granulomatous lesions of the sinuses, trachea, internal organs, or body cavities.

The acute form results in multiple miliary granulomas of the lungs and air sacs. It is usually seen in young birds, raptors, waterfowl, poultry, and recent imports. Penguins, pelagic waterfowl, gyrfalcons, and birds, such as the ostrich, which originate from arid environments, are extremely prone to aspergillosis if moved to a warm and humid environment. Grossly the lungs appear dark red and wet and contain numerous small, white miliary nodules (Fig. 2.53). Histologically these are multifocal to coalescing foci of cell necrosis, hemorrhage, fibrin deposition, and edema. Large numbers of degenerate heterophils are present, as well as occasional fungal hyphae. These hyphae are usually branching and have internal septations (Fig. 2.54).

The chronic pulmonary and air-sac form is a slowly progressive disease. It occurs in immunocompromised birds exposed to

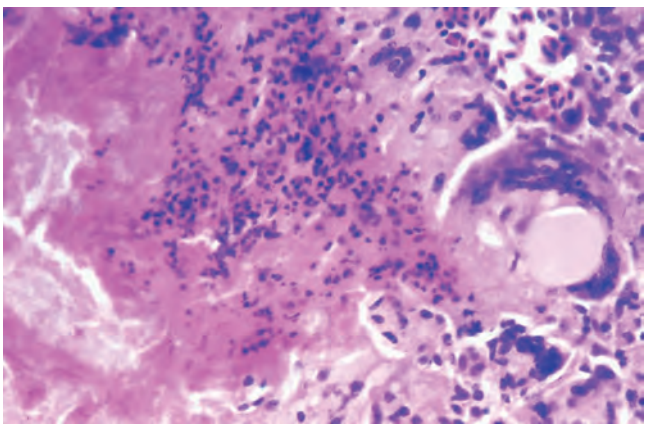

Figure 2.51 Chronic mycobacterial infection with formation of a large granuloma with a necrotic center.

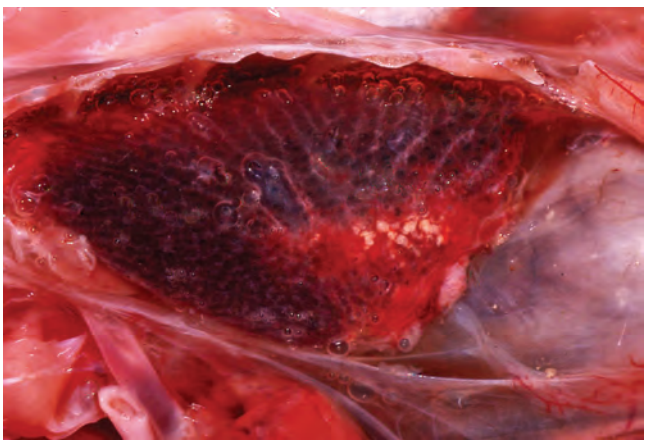

Figure 2.53 Severe pneumonia due to a fungus consistent with *Aspergillus* sp.

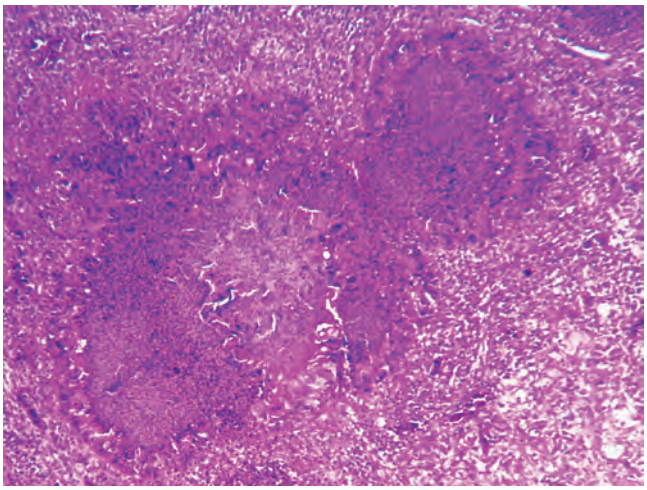

Figure 2.54 Multifocal coalescing granulomas seen in mycotic pneumonia.

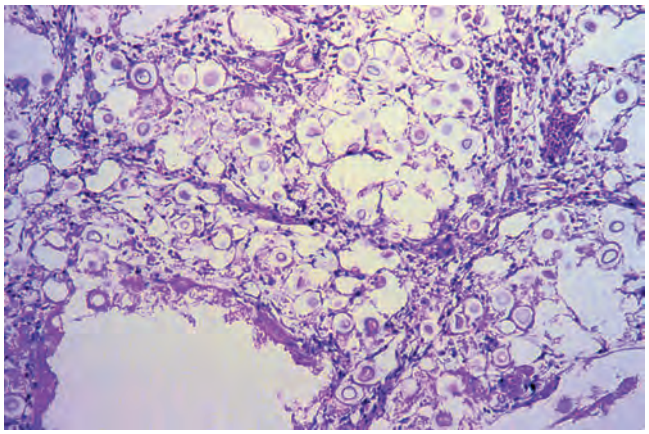

Figure 2.55 Severe mycotic pneumonia due to *Cryptococcus* sp.

persistent low levels of spores. Contributing factors can include recent importation, injuries, migration, inadequate nutrition, or long-term antibiotic therapy. Grossly the lesions include white-to-yellow plaques in the trachea, syrinx, bronchi, or on air sacs and other serosal surfaces, thickening of air sacs with or without caseous exudate, nodules in the lung parenchyma with caseous, consolidated, or necrotic centers, mycelial formation on air sacs or other serosal surfaces, and caseous nodules within organ parenchyma. From the air sacs, dissemination may occur following sporulation. Sites of secondary involvement include coelomic cavity, central nervous system, liver, intestines, kidney, pneumonic bone, adrenal glands, and spinal column.

Central necrotic cores surrounded by degenerate inflammatory cells and a variably thick capsule of multinucleated giant cells and epithelioid macrophages characterize the granulomas. Large number of fungal hyphae that have internal septations and branching can be identified.

Pulmonary granulomas and pneumonia can be caused by other fungi that produce tissue hyphae. These include *Penicillium* spp. and the class Zygomycetes, such as *Mucor*, *Rhizopus*, and *Absidia* spp. The hyphae of the Zygomycetes are recognized by the fact that they are nonseptate or rarely septate and do not dichotomously branched. The typical gross lesions consist of large granulomas in the lungs, free-growing sporulating mold in the air sacs, and emaciation. The granulomas efface the normal pulmonic architecture and are similar to those induced by *Aspergillus* spp.

Pulmonary cryptococcosis is generally an extension from the sinus infection (see the section on sinuses). The narrow-based budding yeast fills the pulmonary airways and is usually associated with mild and mixed inflammation (Fig. 2.55).

Protozoal pneumonia

Sarcocystis species are protozoa with an obligate two-host life cycle. At least six species of *Sarcocystis* infect birds. *Sarcocystis falcatula* appears to be the most significant in susceptible pet birds that are inadvertent hosts. The North American opossum is the definitive host, and cowbirds and grackles are the intermediate hosts. Asexual reproduction of the protozoa occurs within the intermediate host's endothelium. This stage can result in serious or fatal disease in aberrant hosts. In the normal host, schizogony is followed by formation of sarcocysts in muscles. The cysts are 20–25 μm long and may be macroscopically visible. They are packed with banana-shaped bradyzoites. The definitive host is infected when it eats the cysts within the muscle tissues. American or neotropical (Mexico, South, and Central America) psittacines are usually resistant to disease as adults, but clinical disease sometimes occurs. Old World psittacine birds of Australia, Asia, and Africa are highly susceptible to disease.

The primary gross lesion in susceptible species is severe pulmonary congestion, edema, or hemorrhage (Fig. 2.56). Histologically the lungs will be congested with some fibrin deposition, edema, and hemorrhage within tertiary bronchi. Lymphocytes and plasma cells accumulate around blood vessels and bronchi (Fig. 2.57). Multiple aggregates or clusters of small elliptical or crescent-shaped structures compatible with protozoal merozoites can be seen throughout the pulmonary vessels (Fig. 2.58). The clusters formed are long and sinuous and may resemble microfilaria. The merozoites do not stain well with Brown and Brenn, periodic acid-Schiff, or Giemsa. The organisms can sometimes be seen in impression smears of the lung (Fig. 2.59).

In birds with Leukocytozoon infection, schizonts have been seen in the lung (Fig. 2.60). *Toxoplasma* sp. can also cause pneumonia in birds. Identifying the organisms is necessary to differentiate the lesion from other forms of severe pneumonia with necrosis.

Mites

Sternostoma tracheacolum is the tracheal mite of canaries and Gouldian finches (see the previous discussion in the trachea section.) Mites can be distributed throughout the respiratory

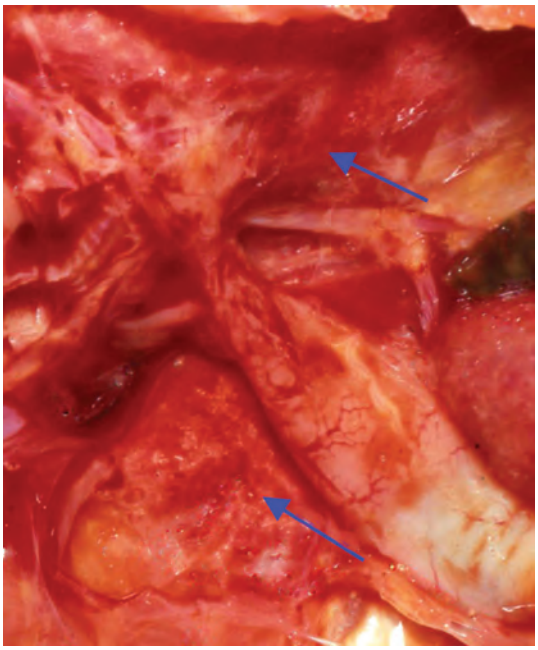

Figure 2.56 Pneumonia due to *Sarcocystis* sp. The lungs are collapsed and red (arrows).

system, especially in juvenile birds. Mites attach to the mucosa by embedding their legs into the connective tissue. Mucus from the host will coat the mites. The mites, when present in the lungs, remain within the lumen of the primary, secondary, and, rarely, the tertiary bronchi.

The mites have a brown, slightly refractile cuticle, segmented legs, and bands of striated skeletal muscle within the body cavity. In these sections, there are peribronchial infiltrations of lymphocytes, plasma cells, and macrophages that efface the normal architecture of the adjacent pulmonary parenchyma and transmigrate across the mucosal surface. The lumen of bronchioles will fill with proteinaceous granular eosinophilic

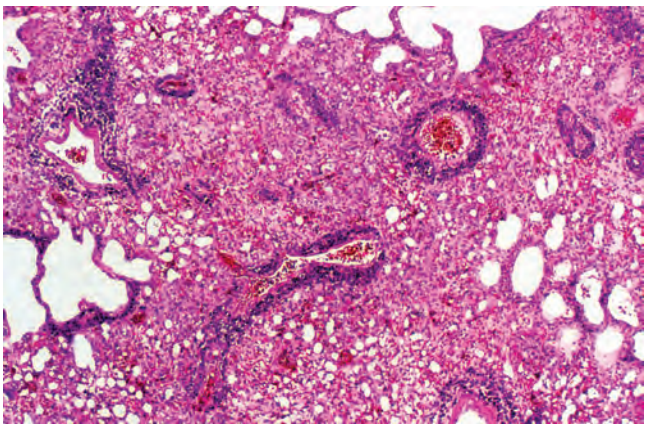

Figure 2.57 Pneumonia due to *Sarcocystis* sp. Edema and air capillary collapse are seen, and a dense lymphoplasmacytic infiltrate is seen around the blood vessels.

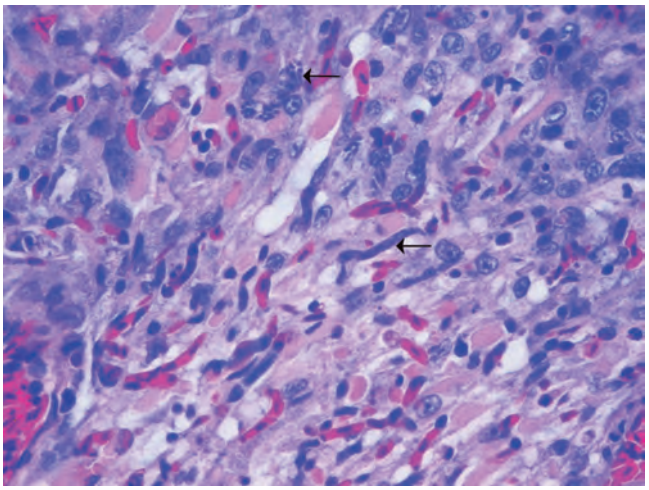

Figure 2.58 Meronts of *Sarcocystis* sp. These can be found in the endothelial cells of the lung (arrows).

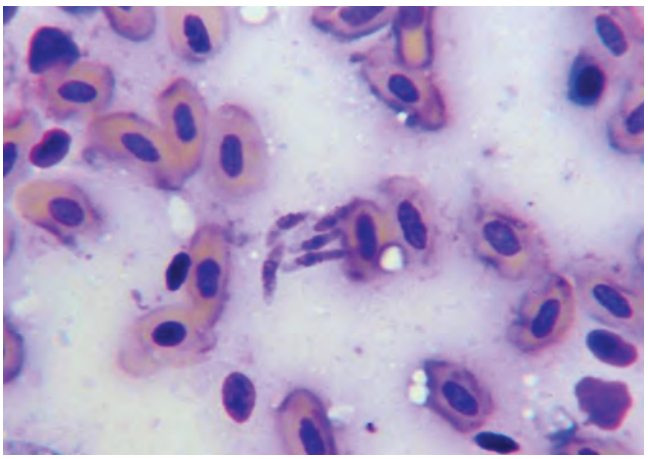

Figure 2.59 Impression smear from the lung of a bird with *Sarcocystis* infection. Characteristic crescent-shaped merozoites are seen.

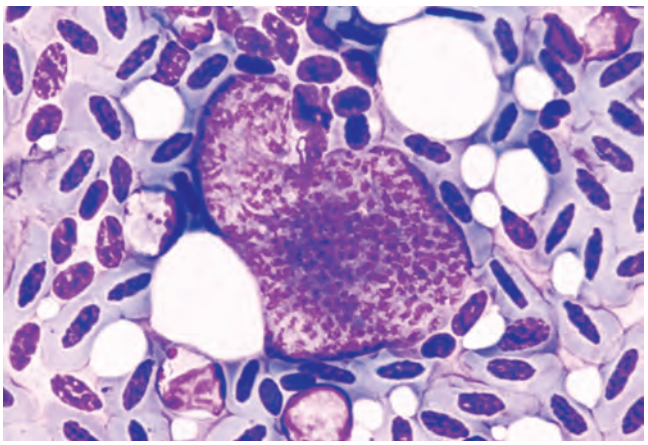

Figure 2.60 Schizont of Leukocytozoon in the lung.

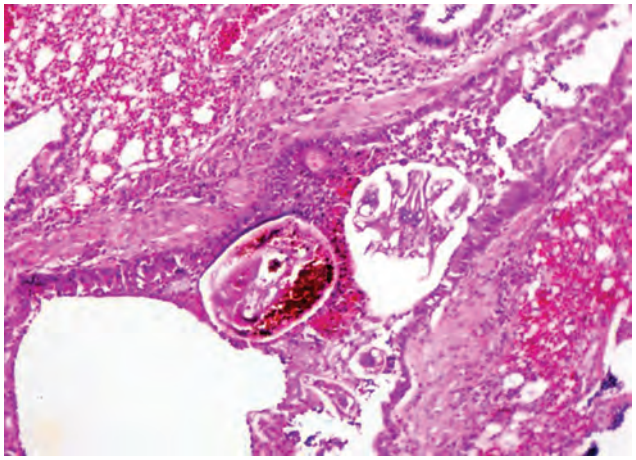

Figure 2.61 Inflammation and exudate in a secondary bronchus of a bird with respiratory mite infection.

material, cell debris, viable and degenerate heterophils, and bacteria (Fig. 2.61). This inflammatory exudate extends out into the adjacent air capillaries. The mites may also stimulate epithelial hyperplasia.

Pentastomids

Rarely pentastomid are described in the air sacs of various avian species. These are not associated with any lesions.

Nematodes

Microfilaria may occasionally be seen in the pulmonary vasculature.

Noninfectious disease

Airborne toxins

The best-documented reports of airborne pulmonary toxins are of those caused by inhalation of pyrolysis products produced from overheated polytetrafluoroethylene-coated cooking pans, stove tops, and coated heat lamps. The toxic products are made up of both gaseous and particulate materials. The acidic fumes cause direct damage to the delicate cell membranes of the lung tissue. The particulates are responsible for the necrotizing and hemorrhagic lesions. Other airborne toxins are aerosol sprays, cooking gas, carbon monoxide, tobacco smoke, and fumes from burned foods and cooking oils. Although the specific toxin is unknown, the operation of self-cleaning ovens has resulted in acute deaths. Compounds emitted from burned foods and other materials can be toxic.

Death after exposure to these airborne toxins is from acute pulmonary edema, hemorrhage, and shock. The birds consistently have severely congested lungs. Watery red fluid may exude from the trachea and nares. Within the severely congested lungs, the lumen of the tertiary bronchi, atria, and air capillaries are filled with abundant pale eosinophilic proteinaceous edema fluid. Multifocal to coalescing hemorrhage in the pulmonary interstitium often extends into air spaces (Fig. 2.62).

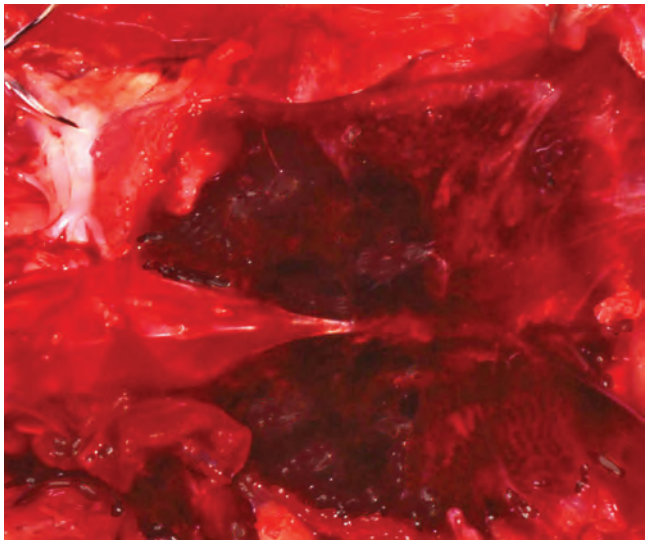

Figure 2.62 Severe hemorrhage associated with inhalation toxicity. This is typical of teflon and other toxicities.

Pale-staining edema fluid accumulates around most arteries and veins. Cardiac lesions are described and are of multifocal degenerate myocytes with deeply eosinophilic cytoplasm and deeply basophilic nuclei. Transmission electron microscopy shows tracheal mucosal and tertiary bronchiolar epithelium degeneration and ulceration with necrosis of air capillary membranes. One of us (DNP) has seen a case of failure of proper lung development in young chicks following exposure to new carpets. Air capillaries essentially fail to develop or the cells are killed in the process stopping development. Outgassing from new carpets and some new furniture can lead to serious respiratory problems in birds due to the volatile chemicals present. Histologically dense bands of well-vascularized tissue were separated by large clear spaces (Fig. 2.63).

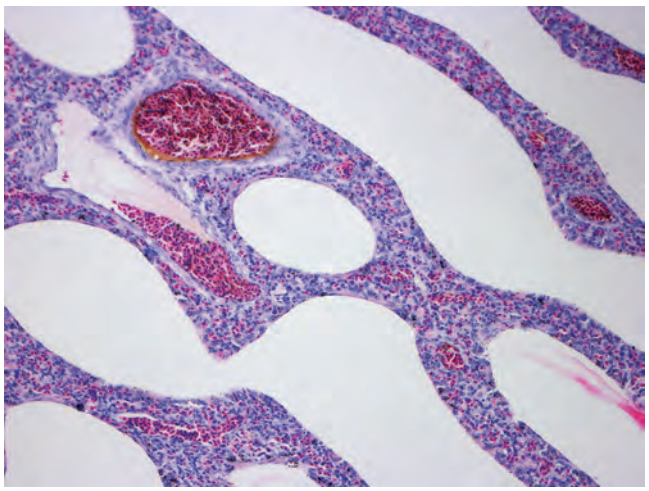

Figure 2.63 Immature lung tissue following inhaled toxin exposure (new carpet) in a young bird.

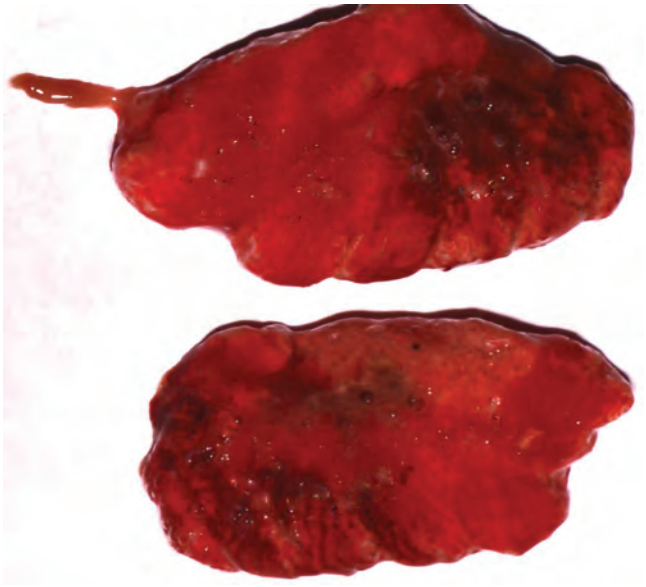

Figure 2.64 Pneumonia associated with foreign-body inhalation.

Chronic exposure to smoke will lead to damage in the secondary and tertiary bronchi, and eventually to a lesion similar to bronchiolitis obliterans in mammals.

Foreign-material inhalation

The inhalation of foreign material occurs most commonly in hand-fed nestling psittacine birds and sick birds that are being tube fed. The presence of the material will elicit an inflammatory response, with hemorrhage, congestion, fibrin accumulation, and edema. This will generally extend into the surrounding pulmonary parenchyma (Fig. 2.64). In peracute inhalation, little inflammatory reaction will be present, with a variable amount of congestion and edema (Fig. 2.65). More chronic lesions will result in accumulations of lymphocytes, macrophages, and multinucleated giant cells (Fig. 2.66).

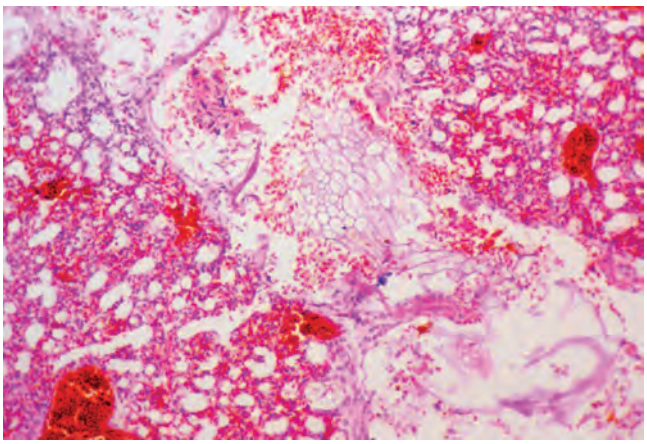

Figure 2.65 Acute foreign-body inhalation. Note the congestion and lack of inflammatory response.

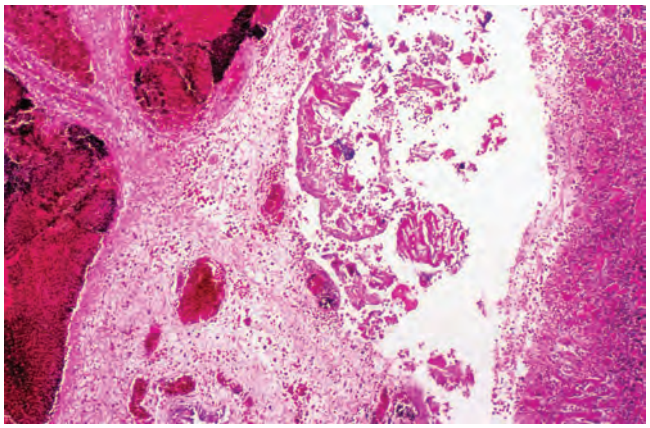

Figure 2.66 Foreign-body pneumonia. The foreign material is surrounded by fibrin, necrotic debris, and inflammatory cells.

Chronic obstructive pulmonary disease (macaw pulmonary hypersensitivity).

Chronic obstructive pulmonary disease (macaw pulmonary hypersensitivity) with polycythemia appears most common in the blue and gold macaw. Early diagnosis is difficult due to the reserve capacity of avian lungs and relative inactivity of macaws in aviaries. The lung lesions are generally advanced when polycythemia occurs. Grossly the lungs have a firm, rubbery texture and are moderately congested. Histologically there is extensive consolidation and a thickened interstitium with eosinophilic material and fibrous tissue with a mixed cellular infiltrate. There is partial or complete obliteration of the tertiary lumen. The prominent lesion is the atrial smooth muscle hypertrophy and some atrial loss due to fusion and epithelial bridging (Fig. 2.67). Uncommonly, there is a proliferation of parabronchial lymphoid tissue (Fig. 2.68) and in severe cases lymphoid nodule formation.

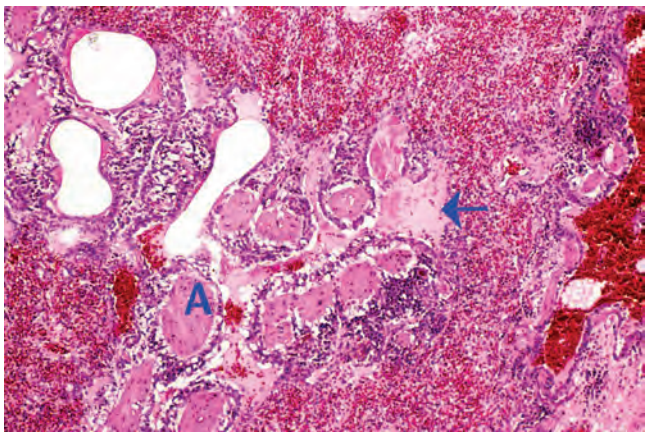

Figure 2.67 Hypersensitivity-induced pneumonitis in a blue and gold macaw. Note the edema (arrow). There is mild inflammation and hypertrophy of atrial muscle (A).

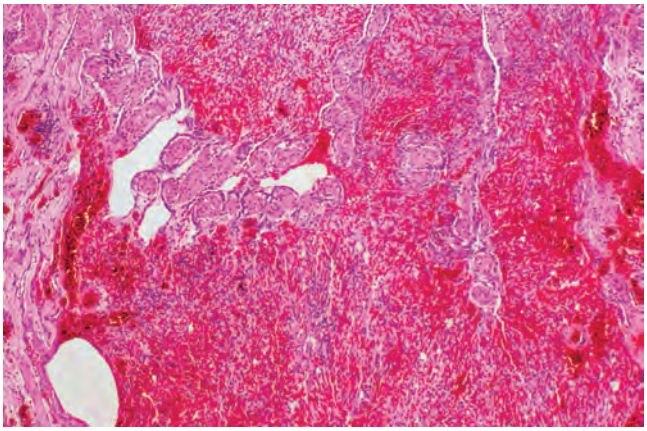

Figure 2.68 Severe congestion and air capillary collapse in a blue and gold macaw with hypersensitivity-induced pneumonitis. Minimal lymphoid cell accumulations can be seen.

Vaccine-induced reaction

A pulmonary lesion that has been associated with vaccine reactions in pet birds is suspected to be an anaphylactic reaction or type I hypersensitivity. Death occurs within minutes after the vaccination. The lungs are congested, and there is loss of the air capillary lumen due to collapse. Lacy, pale eosinophilic proteinaceous fluid can be identified within the bronchiole lumens (Fig. 2.69).

Heart-failure lung

Chronic pulmonary congestion can lead to capillary bleeding, which results in heart-failure cells and hemosiderin-laden macrophages. With pulmonary congestion, the capillaries become engorged and may rupture, resulting in intra-air capillary hemorrhages. The erythrocytes break down and are phagocytosed by pulmonary histiocytes. Cytoplasmic granular golden brown pigments or occasionally intracytoplasmic erythrocytes can identify these cells (Fig. 2.70).

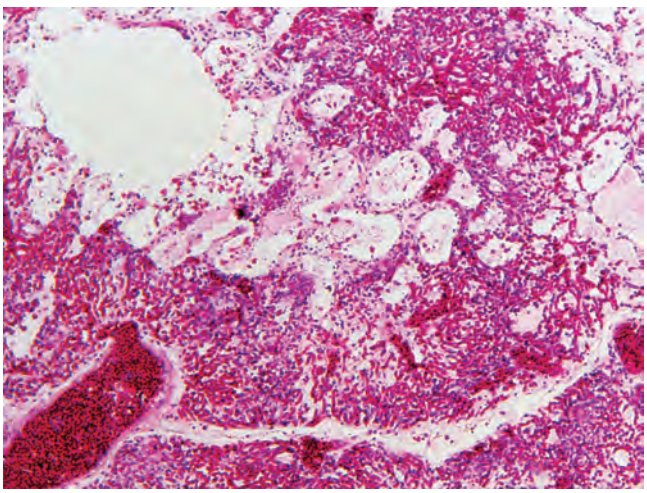

Figure 2.69 Acute vaccine-induced pulmonary collapse and congestion. Proteinaceous fluid is seen in bronchioles.

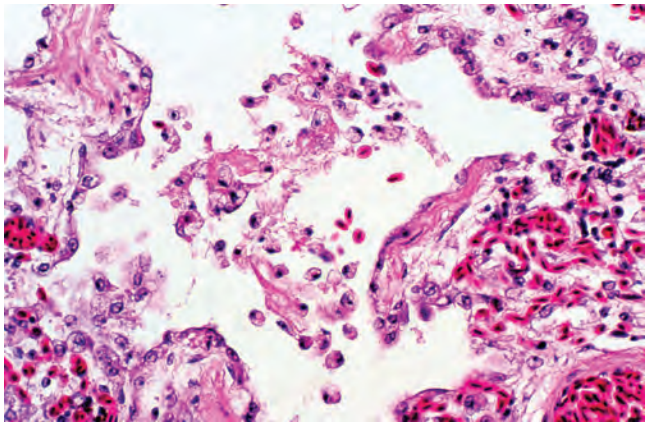

Figure 2.70 Macrophages and minimal erythrophagocytosis in the lung of a bird with congestive heart failure.

Endogenous lipid pneumonia

Lipid pneumonia is an incidental and uncommon lesion of pet birds. The etiology of the lesion is unknown, although in mammals it may represent a storage disease or acquired disorder due to reduced airway clearance. Many birds have concurrent atherosclerosis, liver disease, or other lesions in the respiratory tract. The gross appearance is of white foci typically subtending the pleura of the lungs. Histologically the tertiary bronchi are filled with proteinaceous fluids and histiocytic cells with foamy cytoplasm (Fig. 2.71).

Embolic pneumonia: yolk and bone marrow

Egg yolk pneumonia is similar to foreign-material inhalation pneumonia. The anatomy of the mesenteries provides access of the ovary and oviduct to the caudal abdominal air sacs. Any disease, trauma, or neoplasm of the reproductive tract during

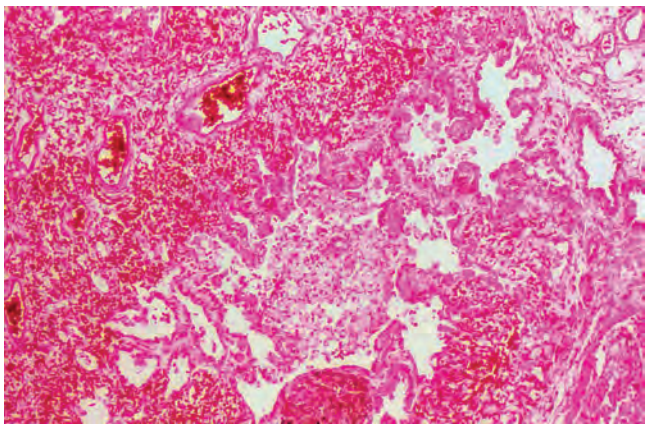

Figure 2.71 Endogenous lipid pneumonia. The exact cause is often not determined, but many birds with this condition have chronic hepatic disease.

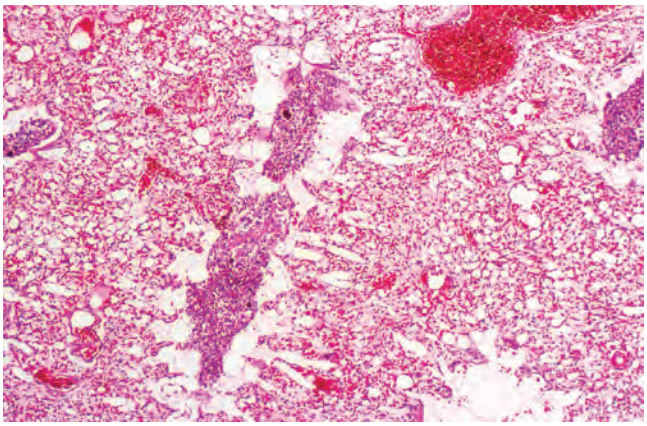

Figure 2.72 Retrograde yolk inhalation and pneumonia. In addition to yolk protein, there is edema and some fibrin deposition.

follicular development can result in the egg yolk material rupturing free into the intestinal mesenteric space. Any disease of the caudal air sacs allows the yolk into the respiratory system and inhalation into the lung.

The lungs, especially in the caudal fields, will be severely hemorrhagic and coated with the yolk. The yolk will be associated with hemorrhage, fibrin deposition, and edema (Fig. 2.72).

Pulmonary emboli from fat, bone marrow, and egg yolk have been recognized. These birds generally present in severe respiratory distress. On gross examination, the lungs will be diffusely and severely congested. The emboli are recognized as occlusions in pulmonary capillaries and arteries. The emboli may be associated with widespread, multifocal hemorrhages in tertiary bronchi and air capillaries. Bone marrow emboli are comprised of adipose connective tissue containing hematopoietic islands (Fig. 2.73). The egg yolk emboli, which are variably sized globular and amphophilic, may be the result of trauma and access of the egg yolk to the vascular system. Often an underlying cause of the yolk embolus is not determined.

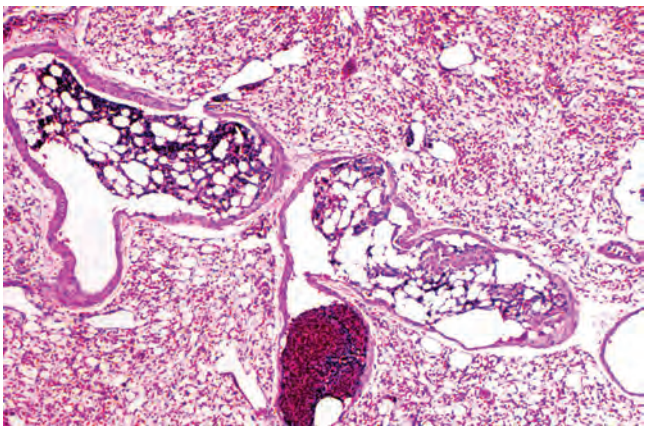

Figure 2.73 Bone marrow embolus in the lung. The cause may not always be determined.

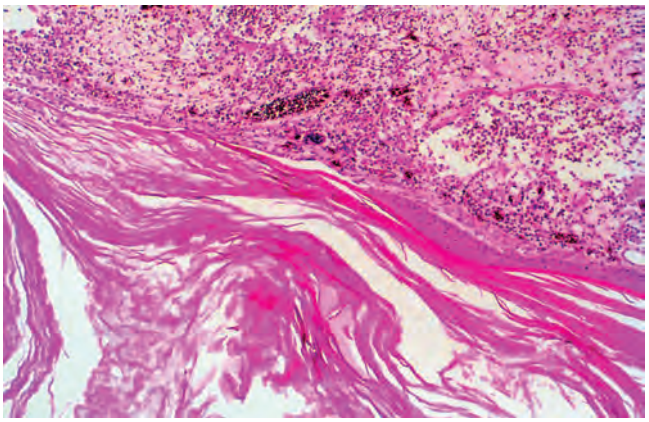

Figure 2.74 Severe squamous metaplasia of bronchial mucosa and hyperkeratosis in a bird with vitamin A deficiency.

Vitamin A

Pet birds that are on a primary seed or cereal grain diet or have intestinal mucosal lesions that interfere with conversion of carotenoids to vitamin A may develop vitamin A deficiency. Vitamin A deficiency results in epithelial squamous metaplasia, which will be manifested as hyperkeratosis of oral cavity, conjunctiva, nasal lacrimal duct, upper alimentary tract, and respiratory tract (nasal passages, sinuses, trachea, syrinx, and bronchi). This is characterized by the pseudostratified ciliated mucosal epithelium of the bronchi transforming into a stratified squamous epithelium (Fig. 2.74). In large parrots, the epithelial changes will appear after liver vitamin A decreases below 50 IU/g. The squamous metaplasia also alters the mucosal defenses, predisposing the bird to fungal and bacterial respiratory infections.

Pulmonary proteinosis

Eosinophilic, amorphous, or crystalline material is occasionally noted within the lumen of tertiary bronchi and air capillaries. It is interpreted as being proteinaceous, but its exact cause is not known. There is generally little to no inflammation. The significance of this uncommon lesion is also unknown (Fig. 2.75).

Pneumoconiosis

Pneumoconiosis (anthrasilicosis) is the focal accumulation of dust-laden macrophages in the interatrial septa of the tertiary bronchi. These lesions generally suggest exposure to airborne pollutants and appear incidental in sedentary pet birds. The lungs may have macroscopic miliary black foci, although usually the accumulations are not observed grossly. The histiocytic aggregates are located subtending the mucosa of the infundibula and atria of tertiary bronchi and around vessels. Rarely they occur in the lamina propria mucosae of primary and secondary bronchi. The histiocytes will have intracytoplasmic granular black pigments and refractile pale yellow crystalline material, which is birefringent with polarized light (Fig. 2.76). There may be infiltrates of lymphocytes and plasma cells associated with

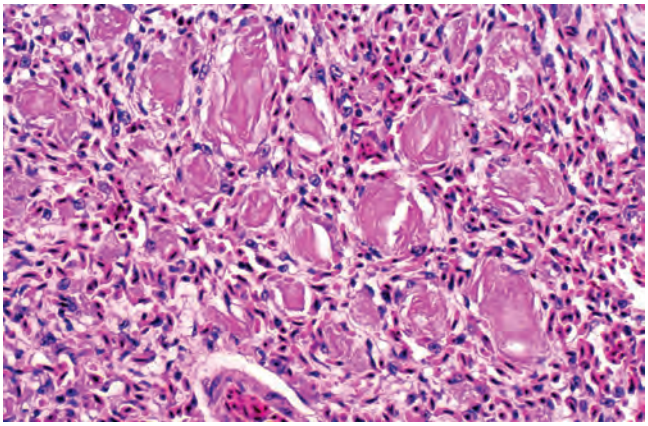

Figure 2.75 Pulmonary proteinosis/crystal formation. This is usually an incidental finding of undetermined cause, but it can involve large amounts of lung parenchyma in some cases.

the nodules. These nodular lesions can also develop under the mucosal epithelium of the air sacs where they are similar to those in the lung. When the crystalline material has been examined by transmission electron microscopy and x-ray spectra, most of the crystals are silicates. The silicates do not appear to elicit fibrosis in birds.

The death of a double yellow-headed Amazon parrot exposed to smoke from an oil furnace has been reported. It developed dyspnea and died 2 years later. Histologically its lungs were largely replaced by multifocal, coalescing granulomas comprised entirely of histiocytes, which contained fine back particles that were suspected to have originated from the smoke.

Pulmonary mineralization

Mineralization of the basement membranes of the pulmonary capillaries is seen sporadically in pet birds. Excess dietary calcium or severe renal disease may predispose birds to the development of this lesion. Excess dietary vitamin D has also been proposed to cause this lesion but was not found to do so in budgerigars fed diets containing excess D_3. Soft tissue mineralization may also be seen in the proventricular glands, myocardium, and kidney. The foci in the lungs are generally at the periphery and are characterized as linear, deeply basophilic granular material along the capillaries (Fig. 2.77). Hemorrhage into the pulmonary airways may occur.

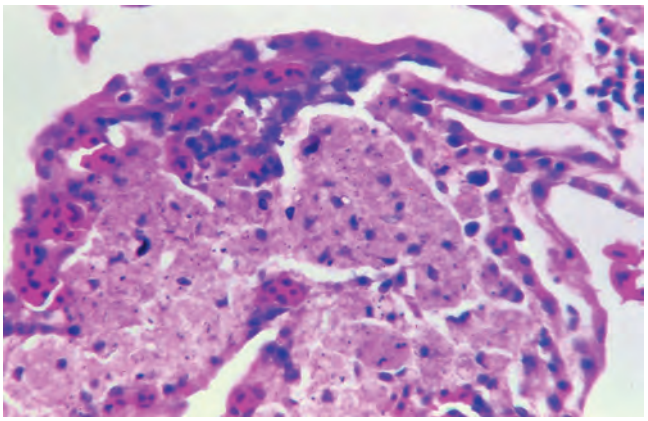

Figure 2.76 Pneumoconiosis. The partially birefringent pigment can be free or phagocytosed.

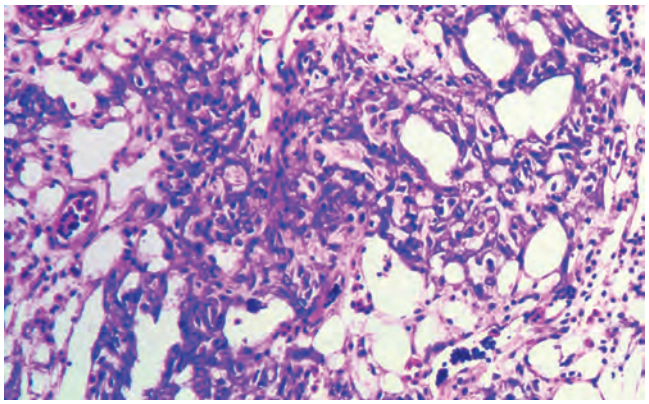

Figure 2.77 Diffuse mineralization of pulmonary basement membranes (basophilic material). This lesion is seen secondarily to several metabolic conditions and in vitamin D toxicity.

Osseous metaplasia

Small spicules of bone are occasionally found in the pulmonary parenchyma of older birds. These are small trabeculae or nodular foci of dense lamellar bone that expand and compress the adjacent parenchyma (Fig. 2.78). The significance is unknown although the lesions appear to be incidental findings.

Chronic pulmonary interstitial fibrosis

Chronic pulmonary interstitial fibrosis has been more frequently described in the European population of older psittacines, although it is also been seen in the United States in a number of psittacines. This syndrome is best described in older Amazon parrots (average age 20.5 years) and typically presents as

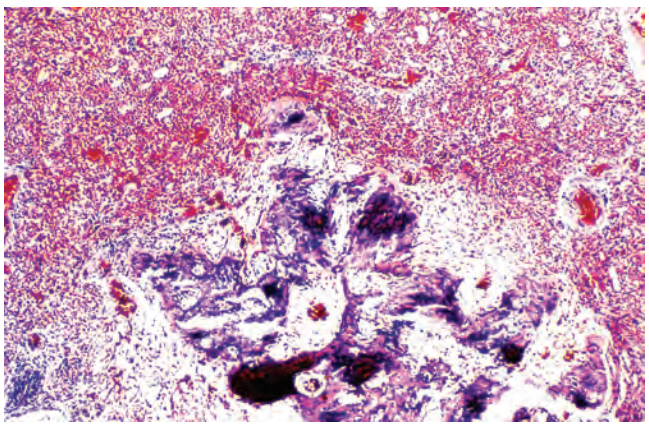

Figure 2.78 Small bone spicule (osseous metaplasia) in the lung.

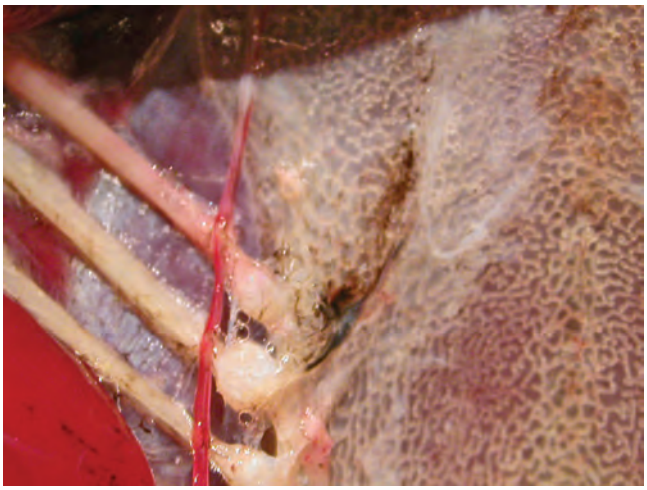

Figure 2.79 Melanosis in the lung of a cockatoo. This is a normal variation and seems to be somewhat more prevalent in cockatoos.

exercise intolerance. Most birds have a long history of respiratory disease. There is loss of functional lung tissue, pulmonary interstitial fibrosis, and generally cardiomyopathy consisting of right ventricular hypertrophy or right ventricular dilation. Some cases have an associated elevated packed cell volume as a result of an increase in erythrocyte size and an increased hemoglobin mass per erythrocyte. Venous blood gas may demonstrate hypoxia and hypercapnia. The cause of this syndrome was not identified but it was suggested that toxic substances, bacterial and chemical toxins, allergy, or viral infections could play a role in the pathogenesis of chronic pulmonary interstitial fibrosis in birds. In live birds, computed tomography is a valuable diagnostic tool (dilation of bronchi and variable thickened walls of the bronchi). Histologic lesions are the loss of air and blood capillaries combined with interstitial fibrosis in the remaining septa. In the functional lung tissue there will be variable amounts of smooth muscle hypertrophy of the tertiary bronchi, edema, and congestion.

Melanosis

Deposits of melanin pigment are seen in the lungs of some birds, particularly cockatoos. These are normal and do not cause any problem (Fig. 2.79).

Amyloidosis

In birds with many chronic conditions amyloid deposition is seen in the basement membranes of the lung.

Neoplastic disease

Fibrosarcoma

Fibromas and fibrosarcomas are tumors that originate from fibrous connective tissue and are common neoplasms in pet birds. Fibromas are not reported in the upper respiratory tract, and fibrosarcomas are rarely described arising from the air sacs and lungs. Fibrosarcomas are gray-to-white firm masses with irregular and indistinct borders. Fibrosarcomas are locally invasive, rarely metastasize, and have a moderate to high potential for recurrence, giving them a guarded prognosis.

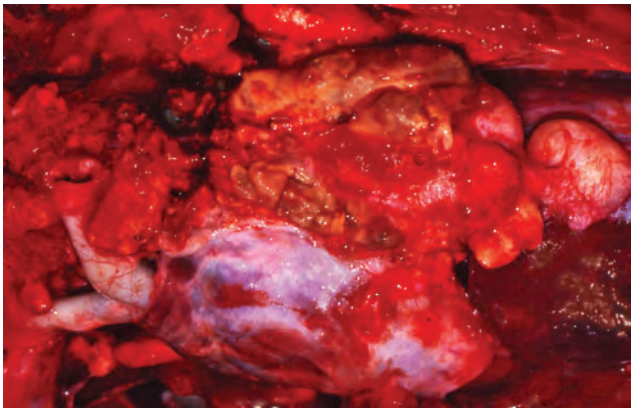

Figure 2.80 Carcinoma arising in the lung/air sac and expanding to replace lung and surrounding tissue completely.

Carcinoma

Primary pulmonary carcinomas are rare tumors of pet birds. The few cases reported may have arisen from the lung or the air sac. Grossly, multiple, slightly firm, tan-gray foci may be identified in the lungs. In cases suspected as arising from either the lung or air sac, there was extension of the lesion through the air sacs to bone, primarily of the right humerus. The patterns are variable from a trabecular and tubular neoplasm to a densely cellular sheet of pleomorphic cells (Fig. 2.80). The tumors are infiltrative and nonencapsulated (Fig. 2.81). The neoplastic cells are cuboidal to polygonal, with abundant eosinophilic cytoplasm and large round to oval nuclei. Cilia may be recognized on the apical pole. Metastases have been described to the vertebral column and extension into the humerus. The tumor invading into the humerus will be associated with periosteal new bone. Invasion into the vertebral column frequently results in the rapid development of ataxia and paralysis.

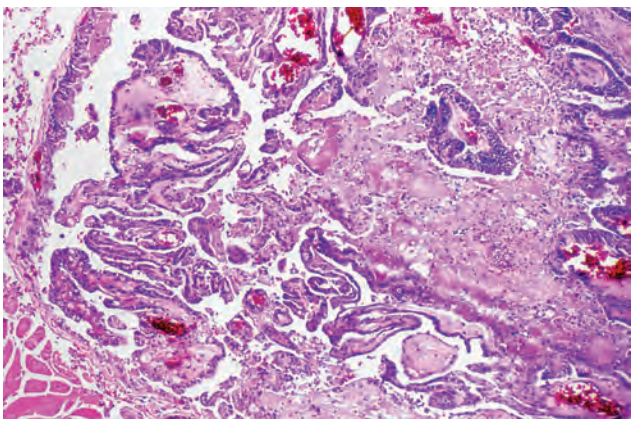

Figure 2.81 Pulmonary carcinoma infiltrating into skeletal muscle of the body wall.

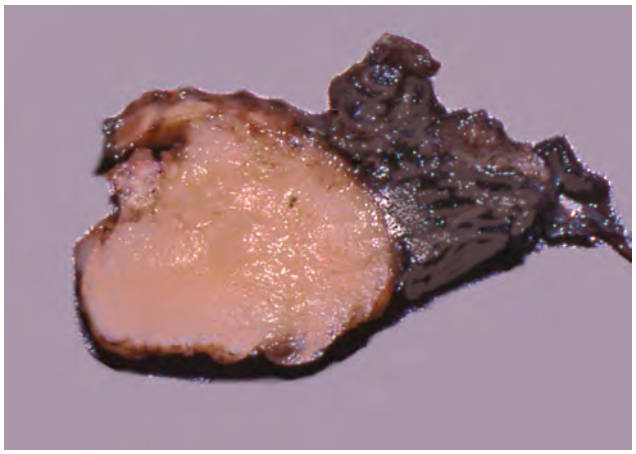

Figure 2.82 Polyomavirus-associated lung tumor in a cockatiel.

Undifferentiated pulmonary tumors of cockatiels

Massive discrete infiltrative pulmonary and air-sac tumors have been recognized in cockatiels. These tumors are large, firm, white-to-gray masses that replace areas of the lung (Fig. 2.82). Often the bird dies when a tumor extends into the thoracic inlet, collapsing the interclavicular air sac and compressing the trachea. In some early cases, the tumor mass appears to arise from the mediastinal tissues. These tumors are so aggressive that they may invade vertebra, resulting in paralysis. The neoplasm is comprised of sheets of closely placed cells. The supporting stroma is of fibrous connective tissue and occasional islands of epithelial components. There are regions in these tumors with differentiation toward fibroblastic, adipocytic, or chondroblastic cell types. Rarely the tumor will appear to be a liposarcoma but will contain islands of the more characteristic cells. Many cells have prominent karyomegaly and a pale intranuclear inclusion (Fig. 2.83). Electron microscopy suggests a virus that is morphologically consistent with polyomavirus within the nucleus (Fig. 2.84). Round foci of neoplastic cells compressing the surrounding parenchyma may also be seen in the spleen and less commonly in the liver and kidney.

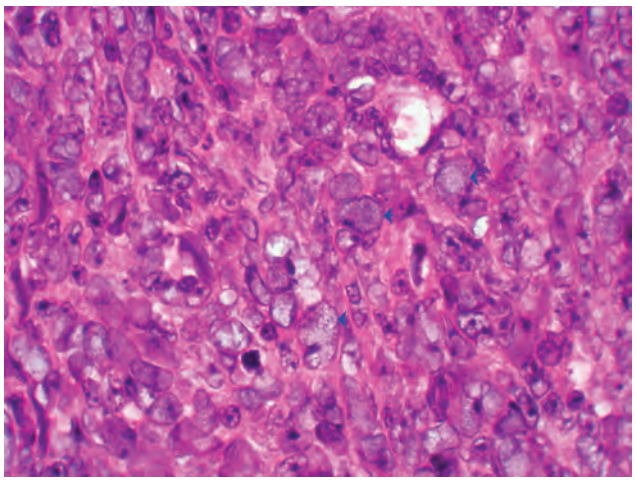

Figure 2.83 Undifferentiated lung tumor with numerous karyomegalic nuclei containing pale intranuclear inclusion bodies (arrowheads). Polyomavirus particles are found in some of these nuclei.

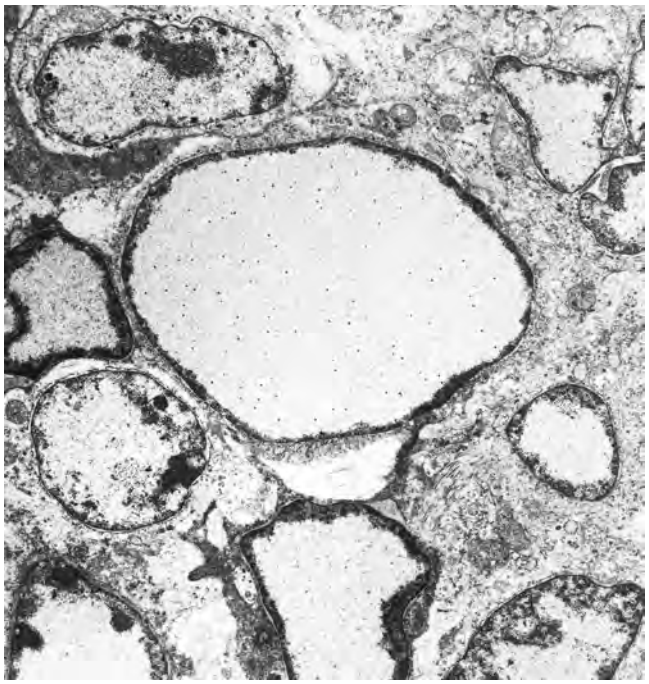

Figure 2.84 Detail of karyomegalic nuclei (Fig. 2.53). The small dark foci are viral particles.

Metastatic tumors

Tumor metastases to the lungs of pet birds include adenocarcinoma and carcinoma from various primary sites, fibrosarcoma, hemangiosarcoma, liposarcoma, lymphosarcoma, melanoma, mesothelioma, and osteosarcoma (Fig. 2.85). Identification of the primary site may be necessary for diagnosis in the case of poorly differentiated neoplasms. Immunohistochemistry has

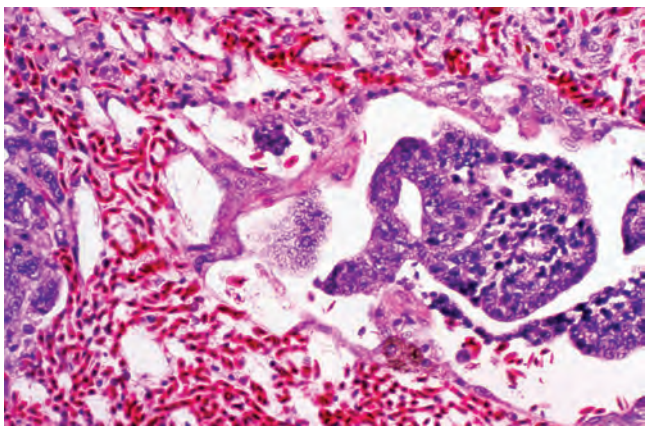

Figure 2.85 Metastatic renal carcinoma in the lung.

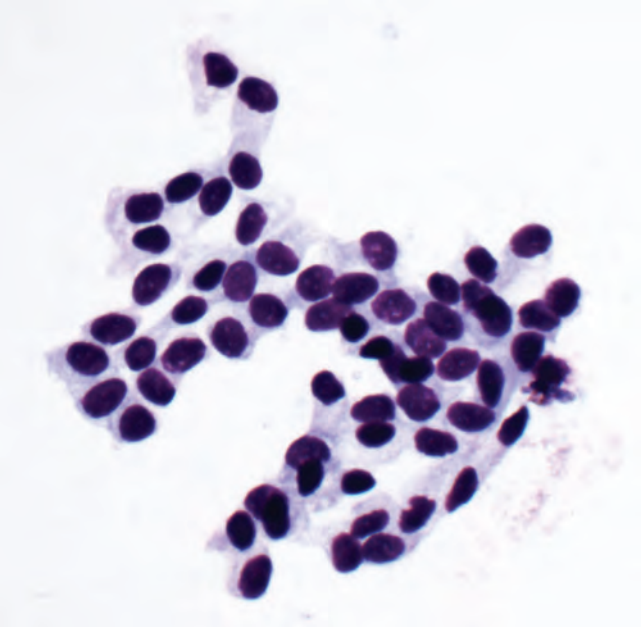

Figure 2.86 Normal air-sac cytology.

been used to determine origin of some metastastic tumors such as osteocalcin and osteonectin for osteosarcomas.

Air sacs

Cytology

As with the lung, air sacs are lined by simple squamous epithelium. Normal air-sac cytology preparations are poorly cellular, with only an occasional noncornified epithelial cell (Fig. 2.86).

Physical agents/trauma: ruptured air sacs

Focal to diffused subcutaneous pockets of air are most likely the result of a ruptured air sac. Rarely pneumocoelom may be recognized. This condition has been described as secondary to trauma or from an underlying air-sac infection. A specific infectious etiology is seldom identified. Air-sac rupture is more commonly described in Amazons, macaws, and cockatiels. The sites are usually around the head, ear, dorsal cervical region, and the flanks.

Urates may be deposited in air-sac membranes in birds with visceral gout.

Infectious disease

Bacterial infection

The same bacterial organisms that cause pneumonia can cause air sacculitis. Grossly there may be variable necrosis and yellow-white or gray exudate. Histologically the acute reaction is primarily heterophilic, with macrophages, lymphocytes, and giant cells increasing with chronicity.

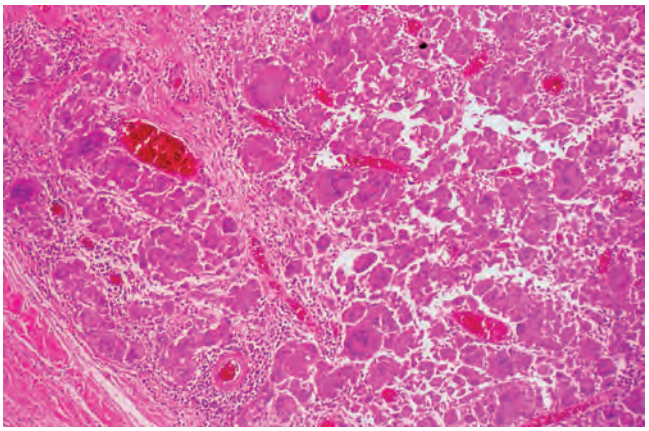

Figure 2.87 Chronic mycobacteriosis in an air sac. Plasma cells, macrophages, and giant cells are seen.

Mycobacterial infection

Air sacs can be involved in systemic mycobacteriosis. Air-sac disease is characterized grossly by yellow-white nodules and histologically by aggregates of macrophages with a foamy cytoplasm and small numbers of multinucleated giant cells that elevate as well as infiltrate and replace the respiratory epithelium (Fig. 2.87). Scattered plasma cells, lymphocytes, and rare heterophils will be seen in the connective tissue of the air sac.

Chlamydia infection

Chlamydiosis, also known as psittacosis, or parrot fever, and ornithosis in other bird species, is responsible for considerable morbidity, mortality, and production losses among pet birds. It is zoonotic and uncommonly causes a flulike condition and pneumonia in people. Chlamydiae are energy-dependent obligate intracellular parasitic agents. They are gram-negative, obligate intracellular bacteria that are susceptible to long-term tetracycline treatment.

Chlamydia psittaci infections of the air sacs produce a diffuse cloudy opacification of air-sac membranes. Occasionally tan-yellow plaques may be seen. The histologic lesion is a fibrinous air sacculitis. An accumulation of fibrin with an admixture of inflammatory cell debris thickens the air sacs (Fig. 2.88). The cells are primarily macrophages, lymphocytes, and plasma cells. Occasionally *Chlamydia* organisms can be recognized as punctate basophilic structures within the cytoplasm of macrophages. There are several stains available to identify the intracellular organisms. The differential diagnosis for the air-sac lesions can include chronic bacterial infections, mycoplasma, and mycotic air sacculitis.

Mycotic infection

The etiologic agents of mycotic air sacculitis are the same as those of mycotic sinusitis. *Aspergillus* spp. and Zygomycetes are the common organisms seen. These fungi can be identified because they grow as hyphae in tissue.

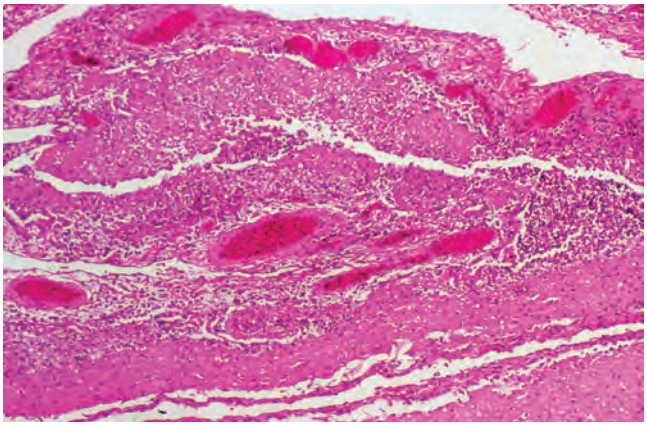

Figure 2.88 Congestion, fibrin deposition, and a diffused inflammatory infiltrate in an air sac from a bird with Chlamydiophila infection.

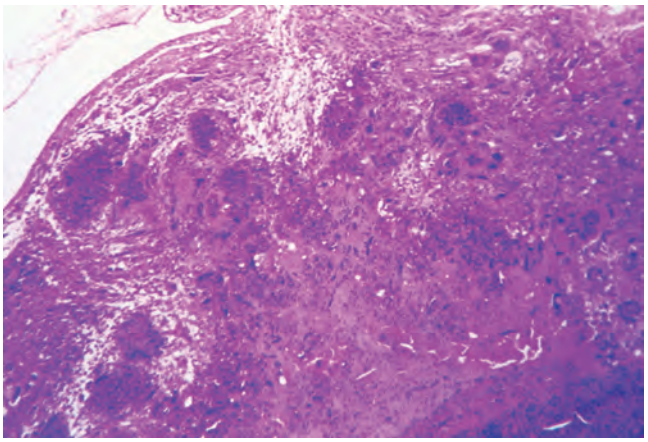

Figure 2.90 A thickened, necrotic air sac in aspergillosis.

The inflammation and growth of the fungi generally efface the air sacs (Fig. 2.89). Mats of the fungal hyphae are supported within necrotic debris, hemorrhage, fibrin deposition, edema, and mixed inflammation (Fig. 2.90). There are mixtures of heterophils, lymphocytes, and plasma cells. More chronic lesions will have perivascular clusters of lymphocytes and plasma cells. Fungal hyphae are associated with multinucleated giant cells and epithelioid macrophages. Conidiophores, the fruiting bodies of the fungal organisms, may occur on the air sacs and can be used to identify the organism (Fig. 2.91).

Parasitic infection

Nematodes can occasionally be found on the air sacs of birds (Fig. 2.92), most commonly in falcons but has also been reported in other genera: *Accipiter*, *Buteo*, *Haliaeetus*, *Aquila*, and *Gyps*. *Serratospiculum guttatum*, *Serratospiculum seurati*, *Serratospiculum tendo*, and *Serratospiculoides amaculata* are the best described. *Serratospiculum seurati* is the only species consistently identified in captive flacons of the Middle East. *Serratospiculoides amaculata* is found in North America falcons. The infections appear incidental in some birds, but it can be associated with pathology and clinically with decreased flight performance. The air sacs may be thickened and opaque. Nematodes may be seen adhered to the membranes. Histologically the thickening of the air sacs is due to fibrosis and chronic inflammation. Multiple perivascular heterophilic foci may be associated with nematode eggs, both in the air sac and into the lung.

Monopetalonema alcedinis, also a nematode of superfamily Diplotriaenoidea, can also be found within the air sacs of birds, especially belted Kingfishers (*Megaceryle alcyon*). Large numbers of the nematodes are associated with lesions. Grossly thickened and opaque air sacs support the nematodes. The lining epithelium of the air sac is hyperplastic and mixed inflammation expands the stroma. The first-stage larvae are ingested by an invertebrate host which is then consumed by a bird.

The family Syngaminae consists of *Syngamus*, *Cyathostoma*, and *Hovorkonema* which occur only in birds. The gapeworms *Cyathostoma* and *Syngamus* have a cosmopolitan distribution and may be found in many avian species. The adults and eggs of *Cyathostoma* spp. are primarily in waterfowl but have been associated with lesions found in air sacs, lungs, bronchi, and trachea of raptors in the Falconiformes and Strigiformes families.

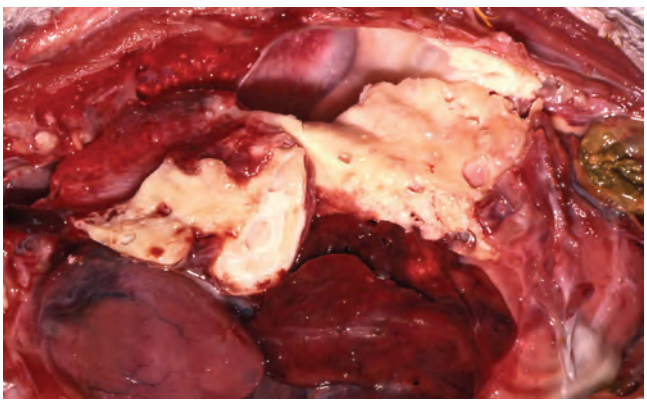

Figure 2.89 Severe caseous air sacculitis in a bird with aspergillosis.

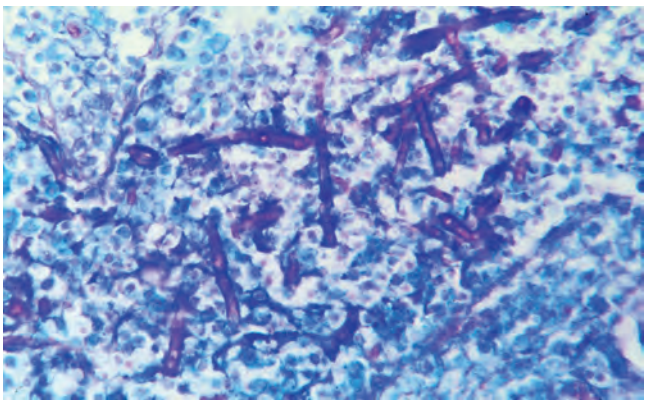

Figure 2.91 Air sacculitis due to fungus morphologically consistent with *Aspergillus* sp.

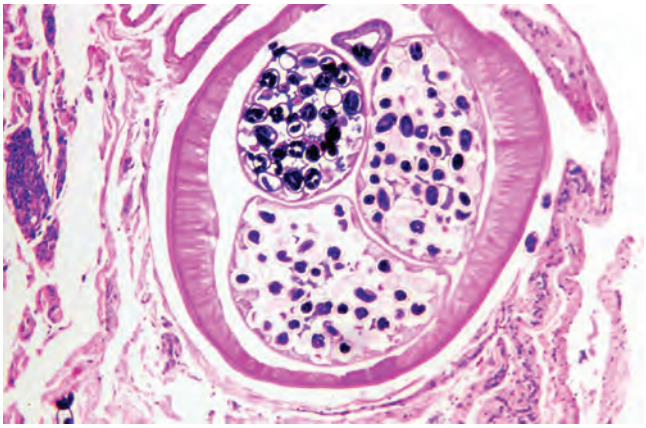

Figure 2.92 A portion of a nematode within an air sac.

The major pathologic changes include a diffuse pyogranulomatous air sacculitis, pneumonia, and bronchitis. Necrotic inflammatory cells may surround dead nematodes or eggs. Most infections are associated with a lymphoplasmocytic air sacculitis.

Trematodes are also occasionally found in the air sacs and into the airways of the lungs (Fig. 2.93). These have been described in barbets, mynahs, motmot, and other birds not identified. The trematodes were all identified to the family Cyclocoelidae and molecular genetic analysis further classifies them to *Circumvitellatrema* spp. Most are usually considered to be an incidental finding; however, some inflammatory exudates may accumulate on the respiratory surfaces admixed with the trematode eggs (Fig. 2.94). The trematode uses terrestrial snails as part of their life cycle.

Viral infection

Systemic poxvirus infection can lead to multifocal necrosis and variable inflammation in air sacs (Fig. 2.95).

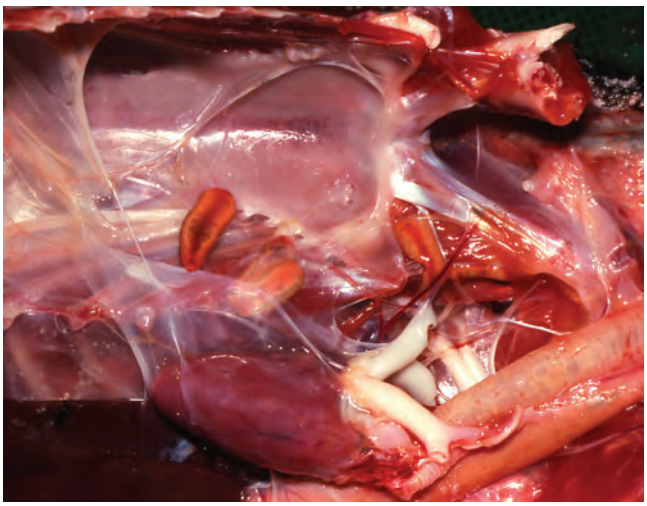

Figure 2.93 Air-sac flukes. There is often minimal gross reaction.

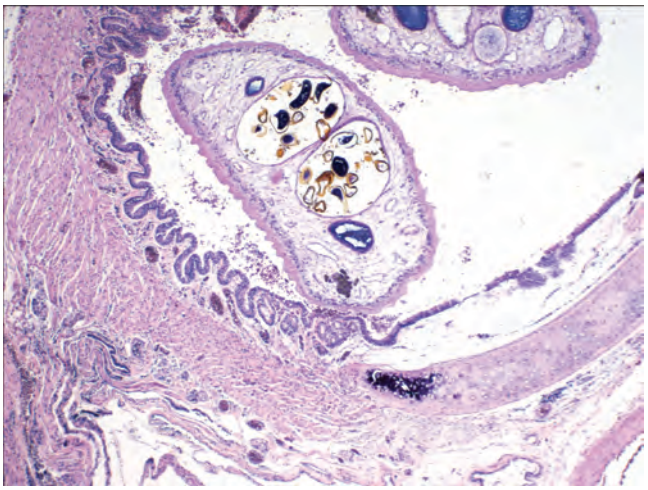

Figure 2.94 Trematodes in an airway. Little or no inflammation is seen.

Neoplastic disease

Air-sac carcinomas

These are rare tumors that are difficult to diagnose definitively as arising from the air sacs. The few cases described are in the large, mature psittacines. The initial presentation is of cystic masses or bony lesions primarily involving the right humerus (Fig. 2.96) and the birds may have a drooped wing or are reluctant to move the wing. The cystic masses are fluid filled and have intraluminal, large, friable, gray-brown, mottled polypoid masses. Radiographs of the humerus demonstrate deformed and proliferative new bone with areas of osteolysis. Aspiration cytology has not been diagnostic with these tumors. The tumors are poorly demarcated and nonencapsulated. They are comprised of variably sized acini, tubules, and papillary structures supported and separated by fine fibrous connective tissue. The neoplastic structures are lined by clumped cuboidal to short columnar epithelial cells. Rudimentary cilia may be identified on the apical pole of some cells (Fig. 2.97). Finding areas where the tumor is continuous with the air-sac reflection into the humerus and identifying

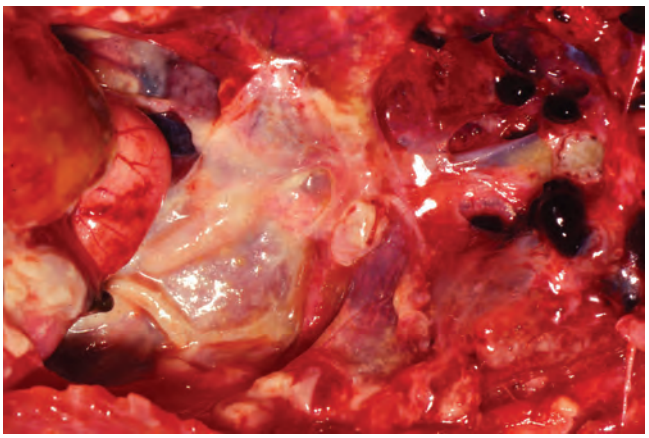

Figure 2.95 Poxvirus infection leading to air sacculitis. Air-sac membranes are thick and yellow-white.

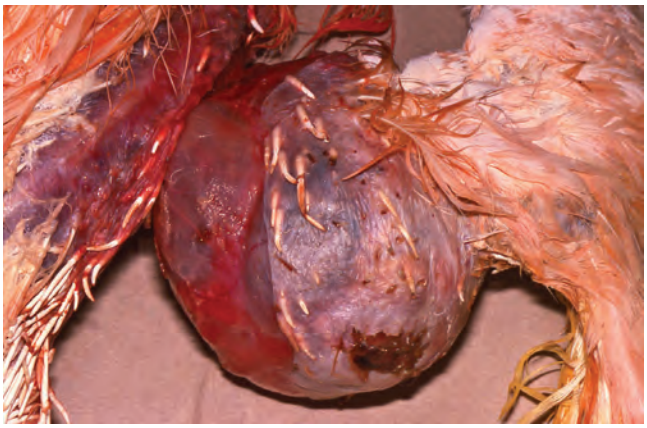

Figure 2.96 Air-sac carcinoma that has arisen in or extended to a pneumatized bone. This must be differentiated from synovial and other sarcomas.

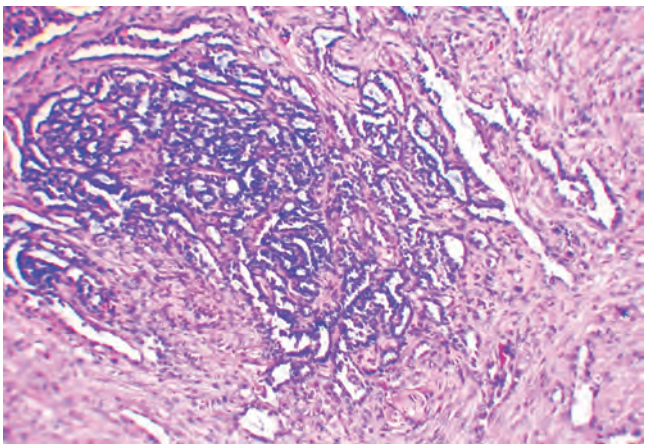

Figure 2.97 Infiltrative air-sac adenocarcinoma.

it within the pulmonary parenchyma helps determine the origin. Both enostosis and exostosis of the involved bone may be present.

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3 Gastrointestinal System and Pancreas

Normal structure

The beak

The anatomy of the beak in many respects resembles the anatomy of the hoof of a horse. A dense cornified epidermis—the rhinotheca (maxilla) and gnathotheca (mandible)—grows over the dermis and bones of the maxilla and mandible from a germinal layer at the junction of the beak with the skin. Damage to the germinal layer at the base of the beak will result in a defect extending the length of the beak. The toma (cutting edge) of the horny beak is the functional tooth structure.

Oral cavity and pharynx

In all birds, the oral and pharyngeal cavities form a common cavity called the oropharynx. Birds do not have a soft palate. The hard palate is divided caudally by the longitudinal v-shaped choanal fissure. The choanal fissure connects the oral and nasal cavities. Small caudally projecting papillae line the oral margins of the choanal fissure. Similar papillae are identified on the roof of the oropharynx as well as the infundibular cleft, tongue, and the laryngeal mound. Ridges run lateral and rostral to this choanal fissure and are used for holding seeds when removing husks. Caudal to the choana on the roof of the oral cavity is the infundibular fissure that connects the oral cavity with the middle ear. The cleft is the common opening of the auditory tubes and has abundant lymphatic tissue within the walls.

The shape of the tongue varies extensively according to the feeding habits of the bird. The tongue of the finches, canaries, and most commonly kept passerine birds is long, slender, flat, and cornified. Psittacine birds have a thick round and muscular tongue that is used for manipulating food. Their tongue is nonprotrusible, muscular, blunt, and dexterous. Psittacines have intrinsic muscles in the anterior regions of their tongues, independent of the hyoid apparatus that adds flexibility. The tongue of lories and lorikeets is densely covered with fimbria that evert when the tongue is protruded. These fimbria are used to gather pollen and nectar. Piscivores and carnivores which feed on relatively large, soft food items swallow the items with the aid of a nonprotrusible tongue with a rasp-like surface composed of keratinized papillae. Only a rudimentary tongue is present in species that swallow whole prey like the pelican. At the base of the tongue are the laryngeal mound and the glottis. Birds do not have an epiglottis.

Birds generally do not have large salivary glands; however, the salivary glands are better developed in birds with a relatively dry type of diet (insect or seed eaters). Most avian species have a diffuse layer of small compound tubular salivary glands present beneath the epithelium of the oropharynx. The oral cavity is lined by a stratified squamous epithelium. The rostral portion of the oral cavity including the tongue and the epithelium adjacent to the tongue may be heavily cornified depending on the species of bird.

Esophagus

The esophagus can be divided into the cervical esophagus, ingluvies (crop), and thoracic esophagus. Not all birds have a crop, such as ratites, most ramphastids, gulls, penguins, cracids, and a variety of raptor species. The cervical and thoracic esophagus is lined by a relatively thick stratified squamous epithelium. Beneath the epithelium are mucous producing glands that resemble salivary glands. These are, internal, surrounded by layers of the muscularis externa. The crop does contain mucous glands in the White-backed vulture, and probably other falconiforms. The cervical esophagus is on the right side of the neck.

In birds that have a crop, it dilates to become a sac-like, highly distensible structure. When fully distended, the crop is nearly transparent. The crop varies in size and shape according to the species of bird. The crop of the parrot first bulges to the right and then to the left across the midline and fills most of the space between the bones of the clavicle. The crop of nestling parrots is proportionately larger than that of the adult bird. The crop is well developed in pigeons, being bilobed or consisting of two, large lateral sacs. The crops of columbiformes are adapted to produce crop milk through desquamation of a large number of fat-filled stratified squamous epithelial cells lining the crop. Proliferation of these epithelial cells occurs in male and female birds in response to rising prolactin levels. The most unique crop is the highly muscular structure seen in the hoatzin (*Opisthocomus hoazin*). This structure mechanically grinds leaves and serves as the only known site of avian foregut fermentation.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

Proventriculus and ventriculus

The anatomy of the proventriculus and ventriculus vary considerably between species of birds. The following descriptions of the proventriculus and ventriculus apply to most psittacine birds, pigeons, doves, and the commonly kept passerines. Grossly, the proventriculus is a thick spindle-shaped organ. The wall is composed predominately of compound tubular glands. These glands contain a single round-to-cuboidal cell that produces both pepsinogen and hydrochloric acid. The glands connect to the lumen of the proventriculus through primary, secondary, and tertiary ducts. The cells lining the tertiary ducts and the mucosal epithelium are tall columnar. The proventricular glands are surrounded by a thin muscularis.

The ventriculus has a thick external muscularis that is necessary for grinding ingested pieces of food. It is wider in vertical cross section and thinner in the horizontal cross section. A tendon covers it caudally. The muscle layer of the caudal ventral aspect of the muscle coat thins, creating a slight outpouching of the ventriculus that grossly appears to be surrounded by the aponeurosis of this tendon alone. Histologically the muscularis contains three layers of smooth muscle, of which the middle layer is the thickest. The ventricular glands are tall, slender columns of cells surrounding a thin lamina propria. At the base of the crypts formed by these glands are simple tubular glands. The ventricular glands secrete a carbohydrate–protein complex called the koilin. Secreted koilin produces a dense, thick, serrated layer that completely lines the ventriculus. Microscopically the koilin emanating from the crypts of the ventricular glands stains more deeply eosinophilic than the koilin produced by the tips of the glands, giving the koilin a laminated appearance. The koilin from the crypts also appears to be softer and wears faster than the koilin from the gland tips, causing the surface of the koilin to be serrated.

The junction between the ventriculus and the proventriculus is the isthmus. This is a very short junction where there is a transition between the proventricular and ventricular glands. Koilin production is not present in the orad portion of this junction. Caudally a thin layer of koilin-like secretions is present at the transition to the ventriculus.

The need for a grinding stomach diminishes in species that feed predominantly on liquid or easily digested food, or in birds that eat whole prey. As a result, the ventriculus will either be thin walled, relatively small, or both in birds such as lories and lorikeets, hummingbirds, some insectivorous birds, and raptors. The size of the ventriculus not only varies with species but also can be altered in any bird by increasing the content of nondigestible fiber in the diet, with increasing amounts leading to a larger organ. This must be considered when determining the significance of ventricular size at necropsy.

Intestines

The intestines of most avian species are relatively simple. The intestines of the budgerigar contain five loops before becoming the colon, which itself is relatively short. The first loop of the intestine is the duodenal loop. Two shorter loops follow. In the middle of the second is the remnant of the yolk sac: the vitelline diverticulum. This is considered the junction between the jejunum and the ileum, although this is of little physiologic significance. The ileum then comprises two loops of similar length. Psittacine birds do not have ceca, which are poorly developed in commonly kept passerine birds. They are, however, important sites of disease in other species of birds. The microscopic structure of the intestines is very similar to that of mammals. One significant difference is that Brunner's glands are not found in the duodenum. Submucosal lymphoid tissue is found normally in many species of birds, particularly in the distal ileum and in the tips of the ceca. This tissue can significantly alter the shape of the villi.

Cloaca

The cloaca is the combined outflow tract of the digestive, urinary, and reproductive tracts. The colorectum enters into the coprodeum, the ventral aspect of the cloaca. Dorsally separated by a horizontal fold from the coprodeum is the urodeum into which the ureters empty. The oviduct in the female enters the urodeum from the left lateral wall. The deferent ducts enter the urodeum in the male. The urodeum and coprodeum open into the common chamber of the proctodeum. The cloaca is lined by a tall columnar epithelium. The villi of the coprodeum resemble those of the colon. Folds, but not villi, are present in the urodeum. Villi in the proctodeum diminish in height and contain few mucous-producing cells. At the skin-mucosal junction, the lining of the proctodeum becomes a stratified squamous epithelium. In many avian species the rectum and cloaca can reabsorb water from ureteral urine, and this may be particularly important for water consumption in desert dwelling birds.

Pancreas

The largest portion of the pancreas lies within the loop of the duodenum. This portion of the pancreas extends cranially and may come in contact with the spleen. A portion of the pancreas, in psittacine birds, parallels the abaxial side of the right duodenal loop. The normal pancreas is yellow to yellowish pink with a finely lobulated surface. Histologically it contains both exocrine and endocrine tissues that resemble its mammalian counterparts. Islets are not uniformly distributed in the pancreas of all birds, and sections from different portions of the pancreas must be collected if the islets are to be seen and evaluated. The pancreatic ducts generally drain into the distal part of the ascending duodenum. The enzymes secreted by the exocrines pancreas include amylase, lipase, proteolytic enzymes, and sodium bicarbonate.

Gastrointestinal disease

Beak

Anomalies

Deformities can be congenital or acquired. Genetically induced congenital deformities have been reported in budgerigars.

Figure 3.1 Beak malformation of unknown cause. Such malformations may be congenital or acquired.

Figure 3.2 Overgrown beak secondary to liver disease.

Variations in curvature and size are seen (Fig. 3.1). Congenital deformities of uncertain cause are also described. A normal structure at hatching is the egg tooth. This enlargement at the dorsal aspect of the end of the beak is normal and is lost in the few days after hatching.

A lateral deviation of the maxilla is a relatively common lesion in hand-fed nestling macaws and cockatoos. In these birds, the curvature of the maxilla is increased, causing the tip of the maxilla to rest on the oral surface of the mandible. Some of these birds appear to have an overly long mandible or possibly a foreshortened maxilla that may result in a decreased wear on the maxilla and may allow its increased curvature. The cause of these lesions in macaws and cockatoos is not known. Malocclusion may also be management related in raptors. Raptors fed a diet consisting exclusively of day-old chicks may show overgrowth of the rhinotheca. The use of a poorly fitting falconry hood can result in pressure necrosis lesions in the germinal tissue of the beak producing malocclusions.

Trauma. Beak trauma is common, and in psittacines it is most often the result of a bite wound from another bird. Male cockatoos are aggressive during the breeding season, and mate aggression is a common cause of crushed beaks and even more extensive injury to the face and head. If the underlying bone is ripped free, the beak will still heal but will only grow out to the point that it has bone to support it, or will grow in bizarre shapes. Psittacine birds are remarkable and can tolerate a considerable loss of much of their beak as long as their tongue remains uninjured. Trauma in other species is generally from flying into a vehicle or window or an attack by predators.

Nutrition

Malnutrition may cause softening and flaking of the beak. A report of the complete absence of vitamin A in the diet of nestling African grey parrots described transverse ridges in the rhinotheca of these birds. The beak grew out normally when the diet was replaced with one with adequate vitamin A.

Metabolic disease

Clinical observations suggest that one cause of overgrowth of the beak of parrots is liver disease especially in budgerigars and cockatiels (Fig. 3.2).

The lesions associated with beak deformities are usually obvious grossly and not examined histologically.

Infectious disease

The beak is a common target for a number of infectious disease processes.

Psittacine beak and feather disease virus (PBFDV) can affect a wide range of psittacine birds. There are many manifestations of this disease that vary with the species of bird. Beak lesions are common in sulfur-crested and Moluccan cockatoos, galahs, and the little corella. Gross lesions include hyperkeratosis, elongation, ulceration, necrosis, and fracturing of the keratin (Fig. 3.3). Separation of the palatine mucosa from the rhinotheca may occur, and eventually the distal beak may fracture, exposing the underlying bone.

Histologically there is necrosis of the epithelial cells in the basal and intermediate layers, the cornified layer may separate from the dermis, and there can be secondary bacterial or fungal infection with a pleocellular inflammatory infiltrate and organisms present. Intracytoplasmic inclusion bodies may be seen in macrophages infiltrating the epithelium, and intranuclear inclusions are occasionally present in epithelial cells.

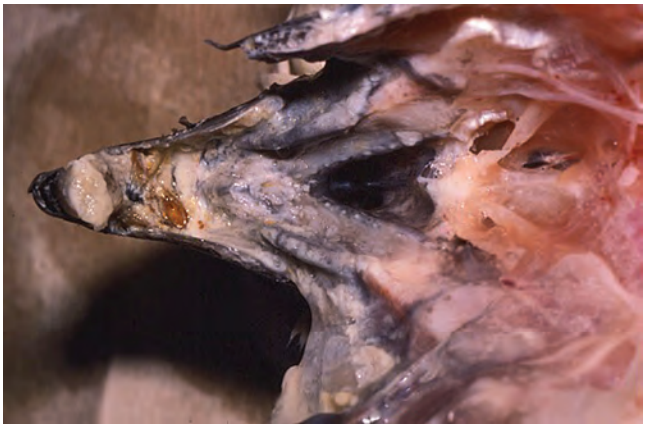

Figure 3.3 Beak necrosis due to circovirus infection.

Poxviruses can also affect the beak. Beak lesions are most commonly found in nonpsittacine birds but are occasionally seen in psittacine birds. Classically, poxvirus infection causes raised proliferative lesions that may or may not be necrotic and secondarily infected. These lesions are seen on the beak or at the beak–skin margin (Fig. 3.4). Occasionally there may be infection of the basal layers of the beak epidermis, with sloughing of the keratinized layers leading to the gross presentation of a beak with no keratinized structure. Histologically the diagnostic feature of poxvirus infection is swelling of epithelial cells and the formation of intracytoplasmic eosinophilic inclusion bodies (Bollinger bodies). These inclusions are so large as to cause the nucleus to be compressed into a crescent on the side of the cell.

There have been a few reports of polyomavirus infection of the beak germinal epithelium. Inflammation and necrosis were noted, as well as intranuclear inclusion bodies. Narrowing and elongation of the beak of finches, particularly Gouldian finches, is ascribed to infection with finch polyomavirus. Additional research is required to confirm this observation.

Figure 3.4 Poxvirus-induced lesion on a beak.

Primary bacterial and fungal infections of the beak may be associated with trauma. These lesions present as variable areas of necrosis, inflammation, and hemorrhage. The beak will often soften and become discolored. There may be hyperkeratosis and accumulation of necrotic debris. Histologically heterophils and macrophages predominate, and organisms may be found. Infections of the sinuses, pneumatized bone, or adjacent soft tissues can also result in beak disease that may first be noticed as an expansile lesion resulting in distortion and discoloration of the rhinotheca.

Mites such as *Knemidokoptes* sp. can cause inflammation and proliferation of the beak. The base of the affected beak is typically soft, and the surface has a fine honeycomb texture. In live birds, mites are abundant and can be readily found with a beak scraping. Histologically there is a pleocellular inflammatory reaction, proliferation of keratin, and intralesional fragments of mites.

Neoplastic disease

Several types of neoplasia have been reported to metastasize or locally infiltrate to the beak, but fibrosarcomas, squamous cell carcinomas, and malignant melanomas are the most common.

Fibrosarcoma is considered the most common primary beak tumor. Fibrosarcomas are most common in budgerigars and cockatiels and histologically comprise interlacing bundles of neoplastic cells with vesicular nuclei and fibrillar cytoplasm. Mitotic figures are usually abundant. Invasion into the nares, turbinates, and bone can result in deformation of the beak.

Squamous cell carcinomas are typical with moderately undifferentiated squamous cells forming infiltrative nests and cords. There is often secondary inflammation.

Malignant melanoma may also have the beak area as a primary site. Grossly, all tumors are proliferative black masses that distort the beak and surrounding soft tissue. There may be bone lysis (Fig. 3.5). Histologically these are infiltrative masses comprise tightly packed pleomorphic cells that vary from epithelioid to fusiform cells arranged in nests and sheets, supported on a delicate fibrous stroma. The cells have variably sized, round-to-oval nuclei, with coarsely clumped chromatin, variably prominent nucleoli, and moderate amounts of pale cytoplasm, supporting variable amounts of granular melanin pigment. The mitotic index can be moderate to high. The cells have negative S-100 immunoreactivity. Metastases are reported in many organs including the lung, liver, and spleen.

Oral cavity

Cytology

The normal cytology of the oral cavity is cornified squamous epithelium. The bacteria frequently occur on the surface of squamous epithelial cells. A large cocci, Sarcinia, can be confused with yeast organisms. One author (DRR) has observed that finches and canaries generally have very few bacterial organisms

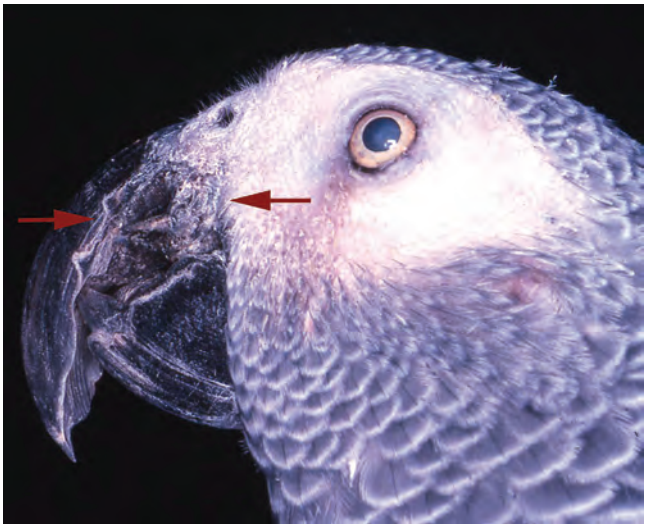

Figure 3.5 Destruction of the beak and surrounding area due to malignant melanoma.

in the oral cavity. The common oral lesions in birds that are frequently evaluated with cytology include septic stomatitis, candidiasis, trichomoniasis, and squamous cell hyperplasia.

Noninfectious disease

Noninfectious oral lesions include various types of trauma from foreign bodies to chemical or thermal burns. In psittacine birds, the potential insults to consider are of ingesting over-heated foods or other caustic substances including silver nitrate sticks and wood or plastic toys. Acute lesions present as lacerations or abrasions with variable hemorrhage. With chronicity there may be an inflammatory response, fibroplasia, and the formation of irregular thickenings in the affected area. In galliformes, ingestion of trichothecenes (T2) toxin produced by *Fusarium* spp. can cause caustic injury to the gastrointestinal tract mucosa producing erosive, exudative yellow plaques with underlying ulcers near salivary duct openings on the palate, tongue, and the oropharynx.

Foreign bodies (hooks, parts of toys, ingested bones, seed fragments) may penetrate the mucosa of the oral cavity and tongue and serve as a nidus for severe chronic inflammation and granuloma formation. These lesions must be differentiated from neoplasia histologically. In one case of a chronic seed hull granuloma in the tongue, circumscribed calcinosis and a secondary candida infection were identified. String foreign bodies can become wrapped around the lower beak or tongue resulting in extensive tissue necrosis and inflammation. This is more frequently described in pigeons and doves. One important noninfectious cause of oral disease reported primarily in large herbivorous Australian waterfowl is the development of an intermandibular skin pocket and possibly even submandibular lingual entrapment. The underlying cause may be access to unsuitable forage that forms a sublingual ball of grass. If these balls

Figure 3.6 Swelling of oral glands and mucosa associated with vitamin A deficiency.

of fibrous material are not dislodged, there will be stretching in the intermandibular skin, which then results in accumulation of more food and debris. In extreme or chronic cases, the intermandibular skin may stretch so much that the tongue slips ventrally and cannot be repositioned.

Vitamin A deficiency is becoming less common in cage birds with the development and use of pelleted diets. Historically, birds with vitamin A deficiency have been on an unsupplemented, all seed diet for many years. Vitamin A is essential for the integrity of mucous membranes and the epithelium. The absence of vitamin A results in squamous metaplasia of mucous glands, and the epithelium, in several organ systems. The small mucous glands in the oral cavity then fill with keratin and expand to form submucosal nodules that are filled with yellow-white and friable material (Fig. 3.6). These lesions can be severe resulting in obstruction of the choanal slit. Histologically, there is squamous metaplasia of oral glands with subsequent hyperkeratosis (Figs. 3.7 and 3.8). There may be

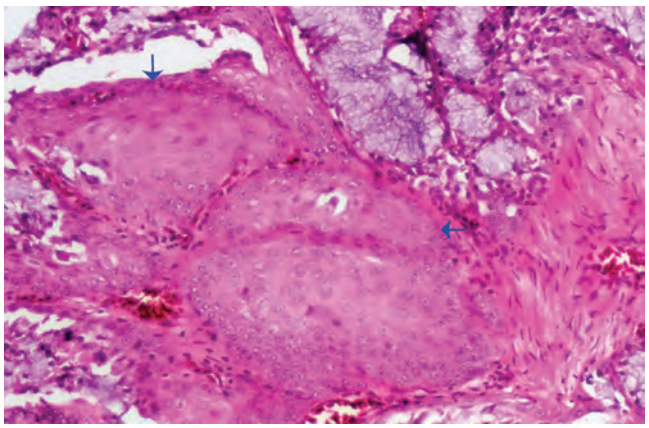

Figure 3.7 Vitamin A deficiency. Note the areas of glandular epithelial metaplasia (arrows) and hyperplasia.

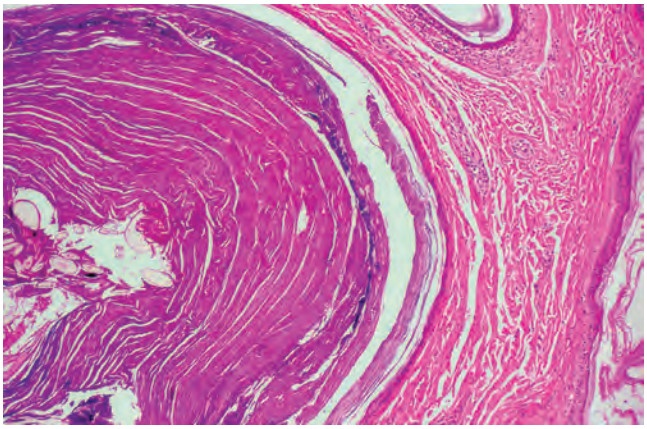

Figure 3.8 Advanced metaplasia of the oral glands in vitamin A deficiency.

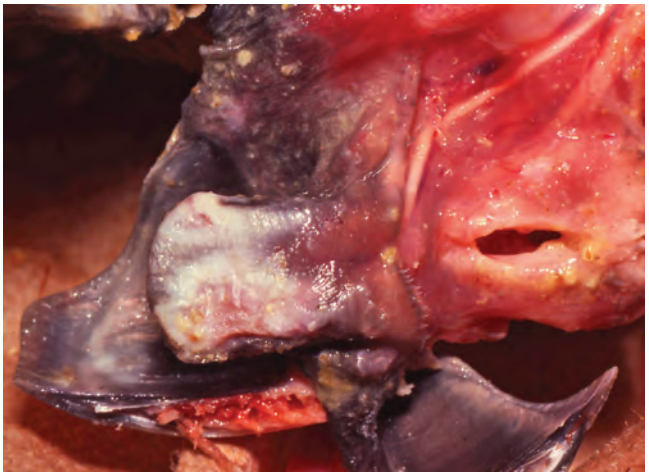

Figure 3.9 Poxvirus-induced glossitis. The gross appearance is not diagnostic.

secondary bacterial infections leading to necrosis and an inflammatory infiltrate that is primarily heterophilic. Blunting of the choanal papillae is a subtler lesion that is seen in birds with the early stages of vitamin A deficiency although other diseases can cause similar changes. On exfoliative cytology there will be sheets or aggregates of cornified squamous epithelial cells usually with little background debris until the condition progresses to a septic stage, with secondary bacterial infections.

Infectious disease

Infectious agents causing oral disease in psittacine birds include viruses, bacteria, fungi, flagellates, and nematodes.

Nearly every bird family or group has its own poxvirus that produces the typical skin and/or mucosa lesions. Agapornis (lovebird) pox produces lesions in the oral and nasal cavities, and on the palpebrae, axillae, shoulders, and/or abdomen. These lesions are dark, discolored areas of skin, and when secondary bacterial infections exist, they are very pruritic.

Amazona (neotropical) pox enjoys a wide host range in South American psittacine birds. Historically, this disease was a major problem in wild-caught blue-fronted Amazon parrots (*Amazona aestiva aestiva*) and pionus nestlings held in quarantine. The disease may present in either the dry (cutaneous) or wet (diphtheroid) forms. The cutaneous form involves the nonfeathered areas of skin with development of papules or raised scab-like lesions around eyes, beak, nares, tibiotarsus, and feet. Lesions will eventually desquamate, usually without leaving a scar. The wet form affects the mucous membranes and generally results in a high mortality rate. The associated lesion is a depigmented, raised plaque covered by a diphtheritic membrane and appears on conjunctiva, oral membranes, tracheal mucosa, and within bronchi (Figs. 3.9 and 3.10). Histologically mucosal epithelial cells are swollen with ballooning degeneration and contain the typical eosinophilic cytoplasmic inclusion bodies. Differential diagnoses for this lesion on mucosal membranes include vitamin A deficiency, bacterial infections, particularly with *Pseudomonas* sp., candidiasis, and trichomoniasis.

Avipoxvirus has been reported in a variety of free-living and captive raptors, including rare reports in owls. The oral and esophageal lesions are the typical diphtheritic form. These exudative lesions or plaques frequently support secondary bacterial and/or fungal infections resulting in the development of caseous plugs or swellings.

Pox viral infections in finches and canaries may produce lesions on the feet and legs, in oral the cavity, and in the upper respiratory tract. Early in a flock outbreak the initial cases die of a fulminating pneumonia. The diphtheritic form carries a higher mortality rate of up to 50%. Later the typical cutaneous manifestations of proliferative papules, pustules, and nodules appear. These lesions may ulcerate and then crust over.

Herpesvirus infections can cause acute necrosis and ulceration of the oral cavity. Pigeon herpesvirus (PHV-1) affects squabs or immunosuppressed young adults most severely. Ulcers and

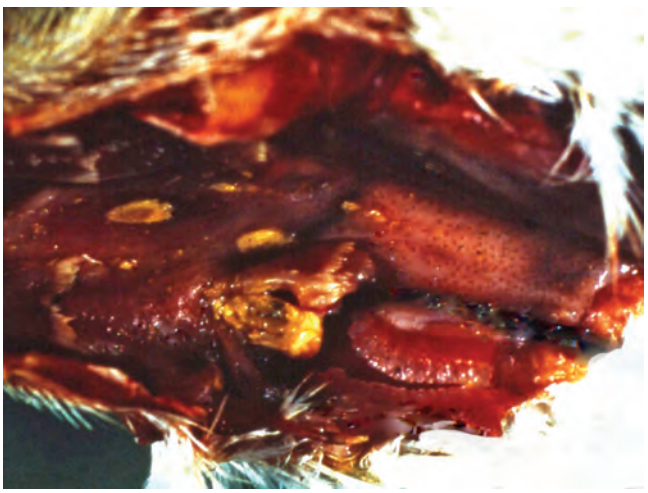

Figure 3.10 Multifocal oral lesions in a chicken with poxvirus infection.

diphtheritic plaques develop on the oropharynx, cere, rictus, and/or trachea as part of systemic infection. The gross change is not specific, and diagnosis is made histologically by finding intranuclear inclusion bodies in epithelial cells adjacent to the necrotic foci. Inclusion bodies are often rare and are often overlooked at necropsy due to the severity of the generalized disease process and/or association with concurrent infections such as trichomoniasis and bacterial colonization of the ulcerative lesions.

An important cause of oral lesions in all goose farming countries in Asia and Europe is goose parvovirus, also known as Derzsy's disease or goose hepatitis. Goose parvovirus infection is a highly contagious and fatal disease of gosling and Muscovy ducks. Fibrinous material on the tongue and diarrhea are seen as part of this systemic condition. Additional lesions include pericarditis, pulmonary edema, liver dystrophy, and catarrhal enteritis. Goose parvovirus has not been detected in the USA. A related parvovirus that has been shown to be antigenically similar is the Muscovy duck parvovirus. This has been isolated from an outbreak among Muscovy ducks in California. The lesions of this parvovirus are primarily of a degenerative skeletal muscle myopathy and myocarditis.

Polyomavirus infection can lead to oral hemorrhage and necrosis. The histologic lesion is characterized by finding karyomegalic nuclei and intranuclear inclusion bodies in epithelial or endothelial cells.

Bacterial infections can cause severe necrosis of the oral mucosa and glands (Fig. 3.11). These infections must be differentiated from poxvirus lesions and may be secondary to vitamin A deficiency. Acute infections may be hemorrhagic, but chronic infections with gram-negative bacteria or mycobacteria will lead to granuloma formation. Histologically, in bacterial infections, there is necrosis and an infiltrate of heterophils, macrophages, and plasma cells (Fig. 3.12). With chronicity a central necrotic core surrounded by macrophages and some giant cells is noted. Organisms may be seen, but special stains are necessary in some cases to demonstrate the organisms. Heterophils and macrophages characterize early mycobacterial infections. As the condition becomes chronic, macrophages with abundant cytoplasm form clumps and sheets. Acid-fast organisms are present in the cytoplasm. In some, but not all cases, necrotic foci and giant cells may be present.

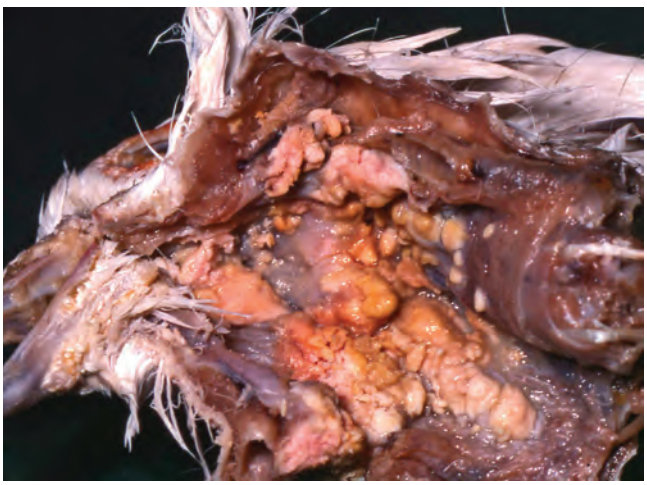

Figure 3.11 Severe chronic stomatitis due to bacteria. Differential diagnoses include poxvirus infection, vitamin A deficiency, and trichomoniasis, depending on the species affected.

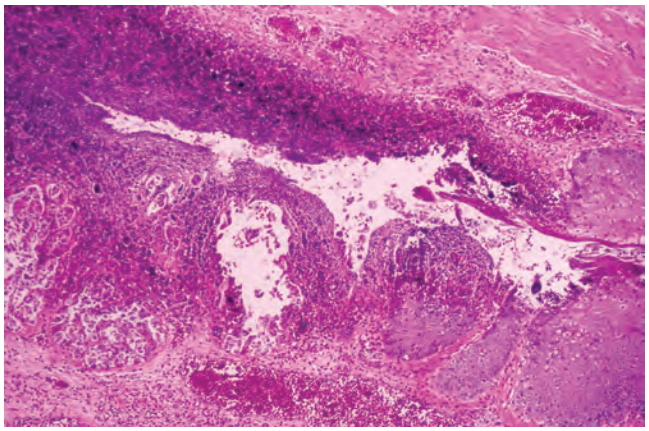

Figure 3.12 Bacterial stomatitis. Severe mucosal necrosis and a pleocellular infiltrate are seen.

Temporomandibular rigidity or 'lock jaw' primarily of young cockatiels is described in Chapter 2. The lesion starts as a sinusitis and the inflammation extends into the surrounding muscles. As the disease progresses, the birds are unable to open their beaks to eat or drink.

Bacterial stomatitis reported in falcons in the Middle East was due to *Pseudomonas aeruginosa* infections secondary to oral trichomoniasis lesions.

The primary mycotic infection of the oral cavity is by *Candida albicans*. The disease is usually secondary and represents the alteration of normal bacterial flora, changes in the integrity of the alimentary mucosa, or loss of immunocompetence that has permitted overgrowth (and possible dissemination) of resident yeast. Factors predisposing avian species to infection include prolonged antibiotic therapy, hypovitaminoses (especially Vitamin A), feeding spoiled, stale, or sour foods, a stressful environment with moist floors, dirty nests, and fecal contamination, malnutrition, and co-existing bacterial or viral infections. Possibly due to their immature immune systems, Candidiasis is more prevalent in young birds and may progress to a fatal systemic disease. This infection is most frequently seen in handfed psittacines and captive hummingbirds. Grossly the mucosa is thickened and there may be grey-white plaques. On exfoliative cytology, inflammatory cells and increased numbers of organisms (>1/hpf) are diagnostic for a candidal infection. *Candida* appears as a narrow-based budding yeast. Tissue invasion, which occurs with colonization and penetration of a disrupted epithelial surface, is indicated by the presence of mycelial forms

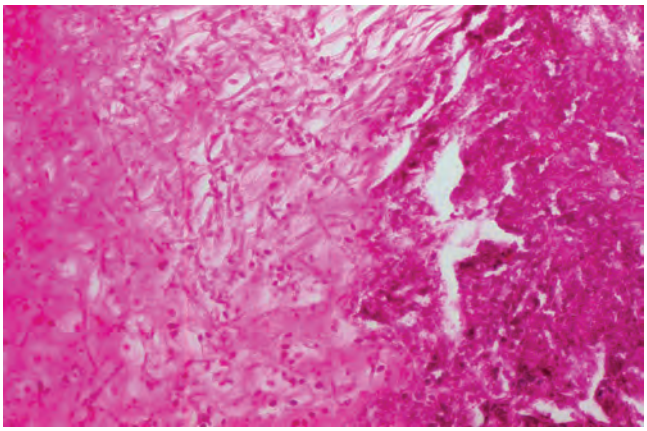

Figure 3.13 Proliferative stomatitis due to *Candida* sp.

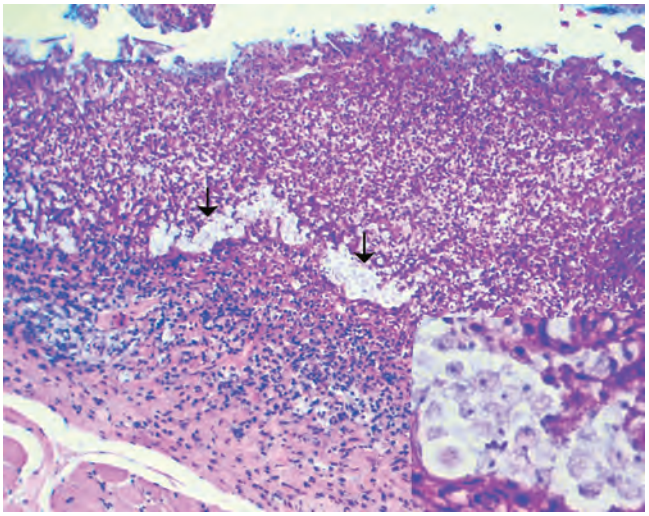

Figure 3.14 Oral trichomoniasis. There is mucosal proliferation and necrosis, and numerous organisms (arrows) are seen. Higher magnification of organisms (inset).

(Fig. 3.13). Histologically there may be excessive keratinization, and numerous organisms are present in the mucosa and keratin. Mucosal and submucosal inflammation is variable and primarily comprises lymphocytes, plasma cells, and macrophages.

Trichomoniasis is the most common infection in pigeons, finches, raptors (also known as frounce), and a variety of wild birds. *Trichomonas gallinae* is the most common isolate, although with expanding use of molecular characterization, other species are recognized. The oral form of the disease is rare in captive-raised psittacines and passerines species but common in young columbids. For raptors, exposure is by feeding freshly killed pigeons and doves that are often inapparent carriers of *Trichomonas* spp. Birds that normally feed on pigeons such as Northern goshawks and falcons are at increased risk. Raptors that do not normally eat pigeons, like eagles and large hawks, may be particularly susceptible when exposed to this organism. Grossly, yellow-white nodules and plaques characterize oral trichomoniasis. These plaques may extend into the esophagus, crop, and even the respiratory tract. The gross lesion may be similar to lesions seen with vitamin A deficiency, poxvirus infections, candidiasis, and bacterial infections. Histologically the mucosa may be moderately proliferative and there is some superficial necrosis. Macrophages and plasma cells are the predominate inflammatory response but when the organisms invade tissue there may be a marked heterophilic response. Organisms are present and must be distinguished from large pleomorphic macrophages (Fig. 3.14). They stain readily with silver stains. In the live bird, wet mount preparations have proven to be a more sensitive and specific means for diagnosis. They die rapidly after the bird's death. With Wright's stained smears Trichomonids may be observed as basophilic, piriform cells with flagella (Fig. 3.15).

Capillaria sp. may cause inflammation with hemorrhage and variable inflammation as will infections with the helminths *Spirurida* and *Ascaridia* spp. Histologically nematode fragments are found in the mucosa. In some cases gross changes are minimal or absent and the nematodes are an incidental finding at necropsy. Infections with this parasite are relatively rare in cage birds, with the exception of Australian grass parakeets and in other parrot species housed outdoors.

Cheilospirura gymnorhinis is a parasite of the Australian magpie. This parasite is found in large numbers protruding from the oral mucosa surrounding the tongue and glottis and the sides of the mouth in virtually all fledgling magpies. Infection occurs less commonly in magpie larks, black-faced cuckoo shrikes, currawongs, and butcherbirds.

Although few clinical signs are associated with the oral flukes, *Clinostomum complanatum* in pelicans, these can cause significant debilitation in related species (herons and egrets). Acute inflammation is found in the submucosa of the oral cavity and esophagus. Immature parasites were found to penetrate through the mucosal epithelium, but adults were seen attached to the oral cavity and the lumen side of the esophagus. Other helminthes

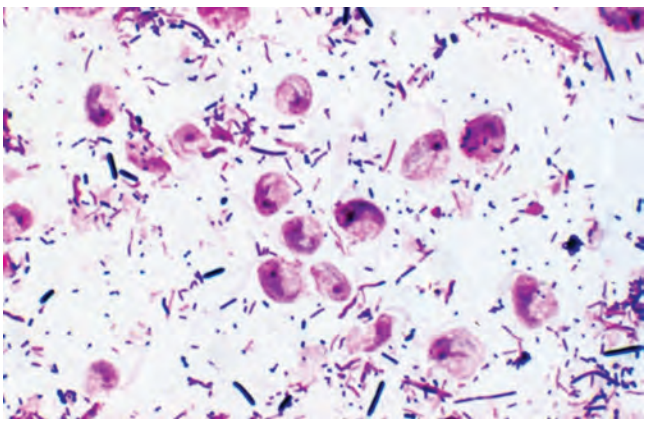

Figure 3.15 Trichomonads in a fecal preparation.

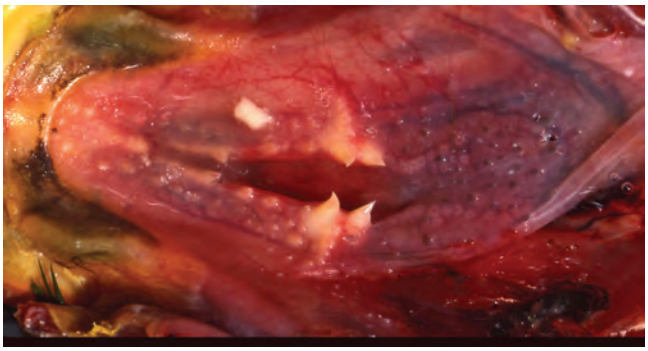

Figure 3.16 Multifocal hyperplasia of choanal papillae.

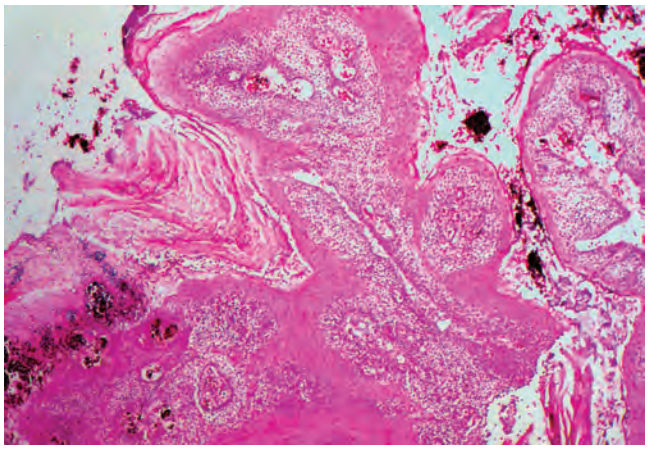

Figure 3.17 Typical histologic appearance of oral papilloma.

reported in pelecaniforms include *Capillaria* spp. and *Spirurida*. Contracaecum has been associated with severe stomatitis in young pelicans and other piscivores.

Neoplastic disease

Tumors of the oral cavity can be either of epithelial and mesenchymal origin. Choanal papillae may become hyperplastic (Fig. 3.16) and these lesions may be difficult to differentiate from neoplasia. The most common neoplasm of the oral cavity in New World psittacines is oral papillomatosis. This disease is most common in macaws, conures, Amazon parrots, and hawk-headed parrots. Oral lesions are particularly common in the larger macaws, but are relatively rare in Amazon parrots. Papillomas are most commonly located along the margins of the choanal fissure, at the base of the tongue, and on the glottis. Rarely, they may become large enough to cause obstruction of the airways. The papillomatous lesions are white to pink, raised, and focal to locally extensive. Most have the typical cauliflower-like appearance. These lesions wax and wane and smaller slightly raised discolored lesions that also represent this disease may be overlooked. Thickening of the choanal margin, discoloration of the choanal mucosa, and blunting of the choanal mucosa are also subtle changes that may be caused by this disease. Grossly the lesions are best observed in the live bird and are more difficult to see after death. Papillomas vary in size and may become secondarily infected, with hemorrhage and necrosis noted.

Histologically the papillary structures have a highly vascular connective tissue core and are covered by a proliferative mucosal epithelium (Fig. 3.17). Lymphoplasmacytic infiltration into the connective tissue core is a variable feature of this disease. Other reported sites of occurrence include the oropharynx, choanal cleft, conjunctiva, larynx, esophagus, crop, proventriculus, ventriculus, nasal mucosa, nasolacrimal duct, bile ducts, pancreatic ducts, intestines, and cloaca. Recent research links these tumors to a viral infection with PsHV genotypes 1, 2, and 3 (psittacid herpesvirus).

Squamous cell carcinomas will present as masses of the oral mucosa or tongue (Fig. 3.18). In some cases necrosis and hemorrhage are seen. The tumors are typical histologically. Grossly they occur as masses within the mucosa that also may be necrotic and hemorrhagic. Histologically they comprise infiltrative nests, acini, and cords of moderately undifferentiated to poorly differentiated epithelial cells with indistinct cytoplasmic boundaries and vesicular nuclei. There is moderate mitotic activity. These neoplasms are often locally invasive and destructive with a relatively high potential for local recurrence; however, they have a relatively low potential for metastasis. Severe secondary infections are common.

Sarcomas reported in the oral cavity include fibroma, fibrosarcoma, and lymphoma. Gross differentiation of these lesions from each other or from granulomas is difficult. Fibromas are composed of well-differentiated fibroblasts supported within a collagenous matrix. They are expansile and circumscribed. Fibromas are typically located in the skin and subcutaneous tissue of the extremities, sternum, neck, and head and are firm masses.

Histologically fibrosarcomas are similar to those seen in the beak. Lymphoma is usually lymphoblastic and comprised as a

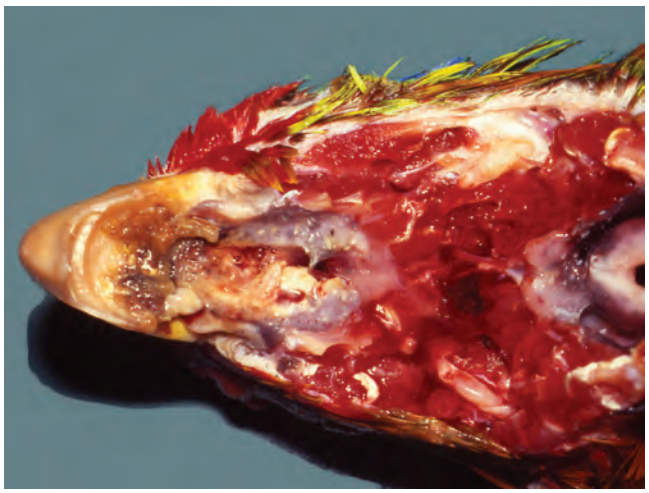

Figure 3.18 Squamous cell carcinoma of the oral cavity. Differential diagnoses would include severe poxvirus infection.

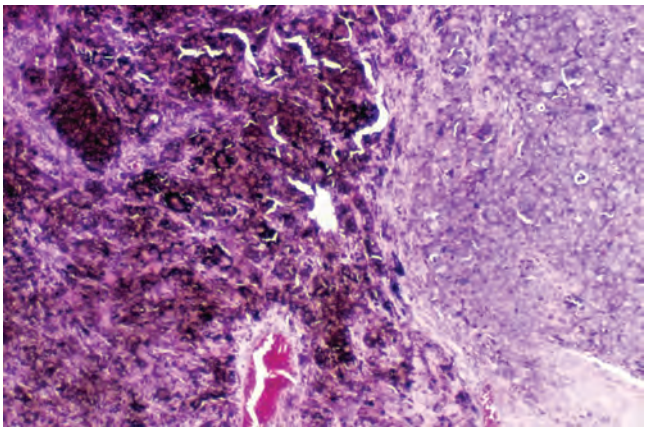

Figure 3.19 Oral malignant melanoma comprising poorly differentiated cells with abundant cytoplasmic pigment.

sheet of somewhat pleomorphic immature lymphoid cells. There is usually moderate mitotic activity and mild multifocal necrosis.

Oral malignant melanoma is unusual unless associated with melanoma of the beak. It is similar grossly and histologically to the tumors of the beak (Fig. 3.19).

Rare granular cell tumors have arisen on the tongue of psittacines. The other locations have been in the dermis on the head and over the ventral abdomen and more frequently on Amazon parrots and cockatiels. These have a benign behavior. The cell of origin remains elusive. Histologically these tumors appear to be of myoblastic origin though they exhibit features suggestive of neural origin as well. All tumors were discrete masses within the superficial dermis comprised primarily large cells with abundant eosinophilic, slightly granular cytoplasm, and were described as being present for weeks to months. The cells are PAS positive and acid-fast negative. They are variably vimentin and desmin immunoreactive, but negative S100 (Fig. 3.20).

Fibroepithelial polyp (skin tag) is a nonspecific and benign hyperplastic process that may occur secondarily to chronic trauma and/or irritation. Fibroepithelial polyps can arise bilaterally at the commissure of the beak. These appear more frequently in cockatiels. These fleshy growths histologically are fibrovascular cores covered by a benign squamous epithelium. They can interfere with eating and should be removed; however, regrowth is common (Fig. 3.21).

Esophagus and crop

Cytology

The esophagus and crop are lined with noncornified, stratified squamous epithelium (Fig. 3.22). It is normal to see extracellular bacteria, an occasional yeast organism, and starch crystals from food sources (Fig. 3.23). The bacteria frequently adhere to the surface of squamous epithelial cells. Alysiella filiformis can be confused with a pathogenic organism, as it appears in unbranched, ribbon-like chains. This is a normal gram-negative

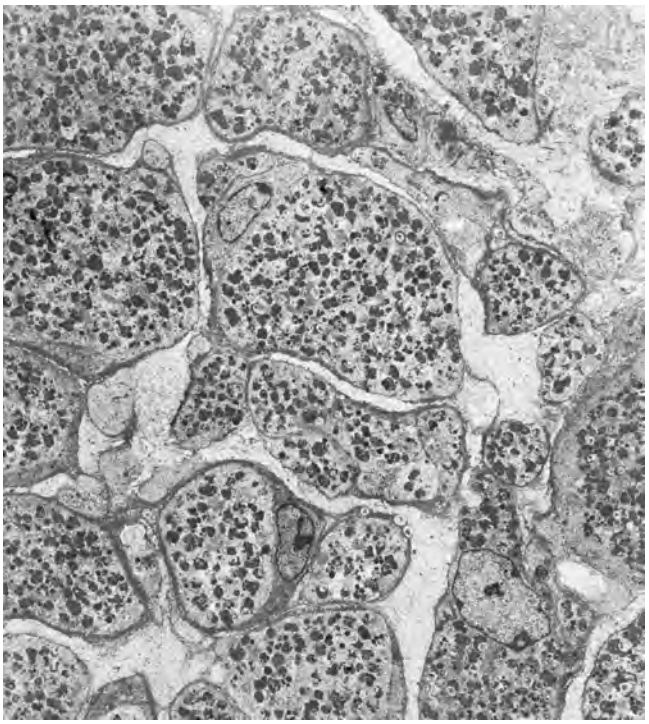

Figure 3.20 Ultrastructure of a granular cell tumor of the tongue.

bacterial inhabitant. A large cocci, *Sarcinia*, can be confused with yeast organisms.

The esophagus and crop can demonstrate many of the same conditions and changes as the oropharynx (see cytology above). In acute cases of ingluvitis, a fairly uniform population of bacteria will be found with few inflammatory cells (Fig. 3.24). The cytologic findings associated with a crop burn or trauma are similar to those of acute ingluvitis. Inflammatory cell populations can vary in these conditions. Capillaria eggs can be seen on

Figure 3.21 Fibroepithelial polyp that typically arises at the beak commissure. These are seen most commonly in cockatiels.

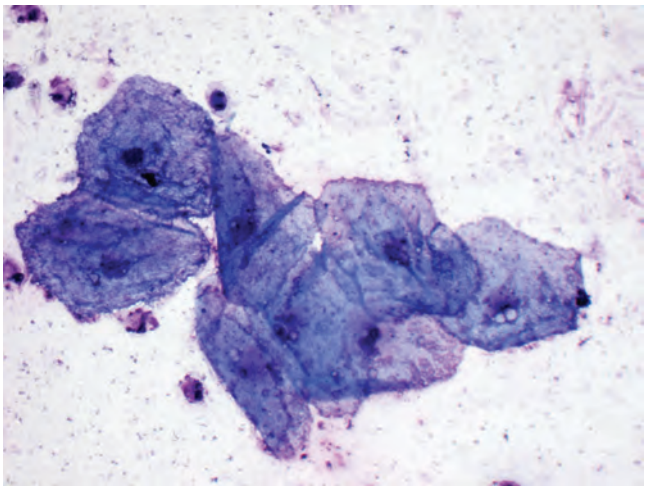

Figure 3.22 Normal crop cytology with noncornified squamous epithelial cells.

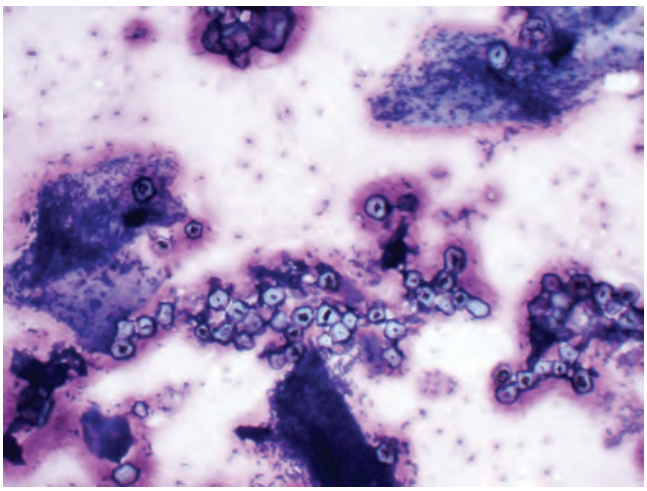

Figure 3.23 Minimal numbers of bacteria and starch granules noted in crop cytology. These are considered to be within normal limits.

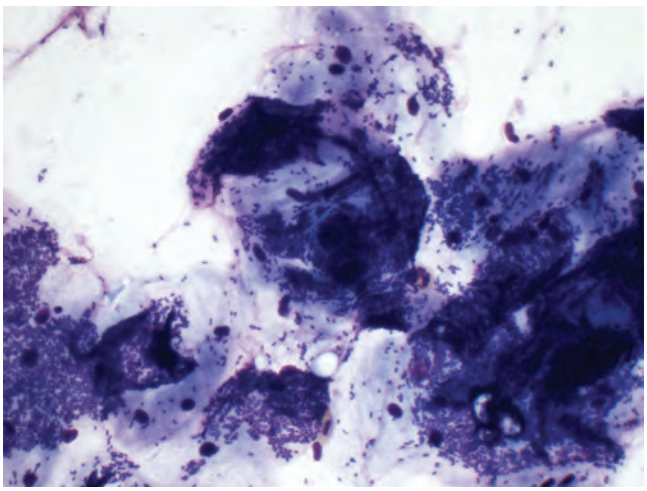

Figure 3.24 Crop cytology from a bird with bacterial ingluvitis.

samples from both crop flushes and swabs. Identification is based on the characteristic bipolar eggs. Megabacteria (*Macrorhabdus ornithogaster*) can be seen on crop cytology.

Congenital

Pharyngeal (branchial pouches) cysts

In the developing embryo four to five pharyngeal arches and pouches make up the pharyngeal apparatus. This is also known as the "branchial" apparatus although the current preferred term is "pharyngeal" for human and most veterinary species. In birds the arches are separated by four pharyngeal (or branchial) clefts laterally and four pharyngeal pouches medially. Each arch is composed of ectoderm, mesoderm, and endoderm. These pouches and clefts form parts of adult structures including jaw and muscles of mastication, hyoid apparatus and labial muscles, thymus, parathyroid glands, and middle and external ear. Abnormal regression of pharyngeal pouches or clefts can result in lesions of cysts, sinuses, and fistulae anywhere along the embryologic tracts. Most of the anomalies arise from the second arch. The development of these structures is uncommon in humans and domestic species and is rarely described in birds.

Although the cystic lesions are present at birth, they may not be clinical evident until adulthood as they slowly enlarge, most filling with fluid and compressing adjacent structures (Fig. 3.25). They can be multilocular. Fluid aspiration cytology from avian branchial cleft cysts may contain lymphocytes, erythrocytes, heterophils, and macrophages. Histologically the cystic structures may be lined by any combination of pseudostratified columnar, partially ciliated epithelium or focally squamous, cuboidal to attenuated epithelium (Fig. 3.26). The lining epithelium is positive on CK immunohistochemistry staining. Lymphoid follicular aggregates or thymic lobules may be within the fibrous connective tissues wall and in rare cases an associated in situ carcinoma. One possible differential for the cysts is of thyroglossal duct cysts which are lined by multilayered

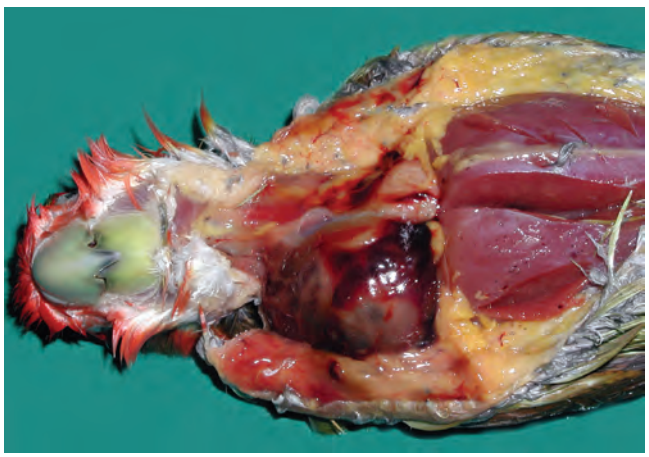

Figure 3.25 Branchial cyst compressing adjacent tissue. The lesion is not grossly specific.

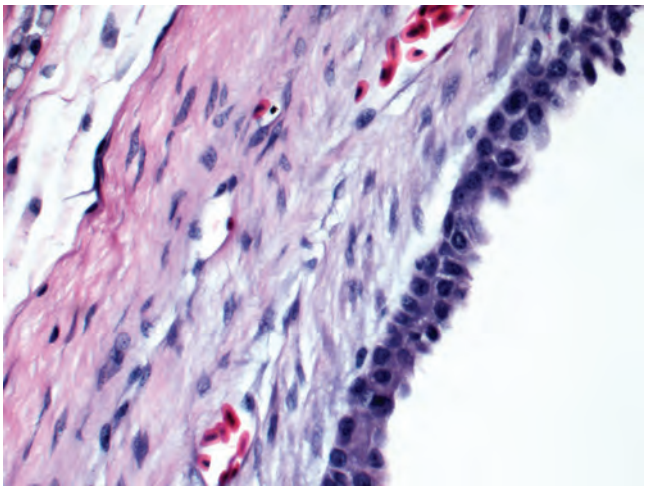

Figure 3.26 Typical histologic structure of a branchial cyst.

thyroidogenic epithelium and lie midline on the ventral neck. In mammals the thyroglossal duct cysts are remnants of the descent of the thyroid primordium from the pharynx near the base of the tongue to its adult position in the neck. These have not been identified in birds.

Noninfectious disease

Primary noninfectious lesions of the crop include crop burns, foreign-body penetration, and vitamin A deficiency. Burns are secondary to hand feeding of overheated food and are usually found in the cranial-ventral portion of the crop. Grossly there may be reddening and edema. Blistering or necrosis occurs in severe cases. Histologically, coagulative necrosis of the crop wall is present and associated with a peripheral inflammatory reaction comprises heterophils and macrophages.

Foreign bodies may penetrate the wall of the crop, leading to necrosis and loss of food that migrates in the subcutis of the neck, resulting in widespread inflammation and necrosis. Crop perforation is most common in birds that are being tube fed as nestlings or in the hospital. In these birds, the instrument being used for tubing may accidentally perforate the crop or the esophagus, and large boluses of food may then be injected subcutaneously. Histologically there is a pyogranulomatous reaction, comprises primarily heterophils, initially. Subsequently macrophages and giant cells are seen if the lesion becomes chronic. There may be a secondary bacterial infection resulting in septicemia.

Vitamin A deficiency results in squamous metaplasia of esophageal glands and proliferation of crop mucosa, often with secondary infections. Histologic changes are similar to those seen in the oral cavity.

Thickening of the crop epithelium is a common finding in birds that are not eating.

Ingluvoliths have been described in budgerigars. In those composed of urates, it is speculated that the calculi originated from the ingestion of excreta and seed husks. Other ingluvioliths have been found to contain potassium phosphate, oxalate, and cysteine.

Lymphangiectasis leading to grossly noted fluid-filled spaces in the submucosa is occasionally seen, but the cause is usually not determined.

Salivary mucoceles develop when saliva leaks from the duct or gland. The saliva will incite an inflammatory reaction that can range from acute heterophilic infiltrates to more chronic granulation tissue and variable fibrous encapsulation. These masses are painless, soft, and fluid-filled anywhere along the esophagus. The fluid is generally clear, colorless to yellow, and viscous with a variable number and type of inflammatory cells. Histologically they are multilocular cysts filled with mucus-rich fluid and lined by cuboidal to columnar epithelial cells. These appear similar to pharyngeal cysts.

Infectious disease

Poxvirus infection can lead to proliferative and necrotic lesions similar to those described in the oral cavity (Fig. 3.27). Herpesvirus infection results in mucosal necrosis and hemorrhage. Histologically, intranuclear inclusion bodies are present in mucosal epithelial cells (Fig. 3.28).

In cases of proventricular dilatation disease (PDD), myenteric ganglia may have lymphoplasmacytic inflammatory infiltrates. Biopsy of the crop is a commonly used antemortem morphologic diagnostic tool for PDD because of the ease of access of the crop. Histologic lesions, however, are not as consistently found in the crop as they are in the proventriculus and ventriculus. Therefore the absence of lesions in the myenteric ganglia of the crop does not rule out PDD.

Bacterial infections of the crop and esophagus can be primary or secondary. In immunosuppressed birds, there may be bacterial colonization and overgrowth in the mucosa. This overgrowth is not observable grossly, and little or no inflammatory response is seen histologically. Bacterial and yeast overgrowth

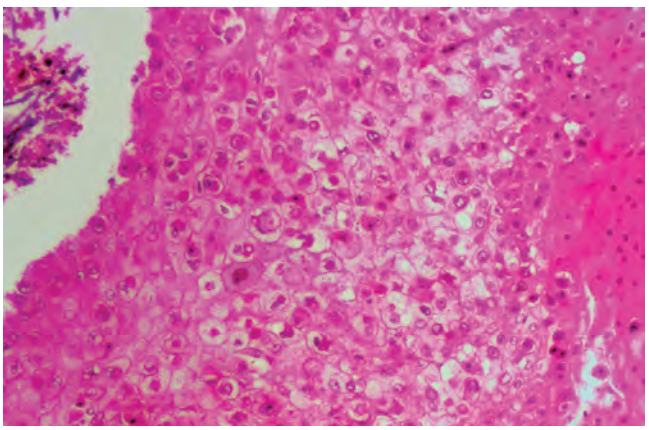

Figure 3.27 Poxvirus infection of the crop. A proliferative epithelium with ballooning degeneration and intracytoplasmic inclusion bodies are seen.

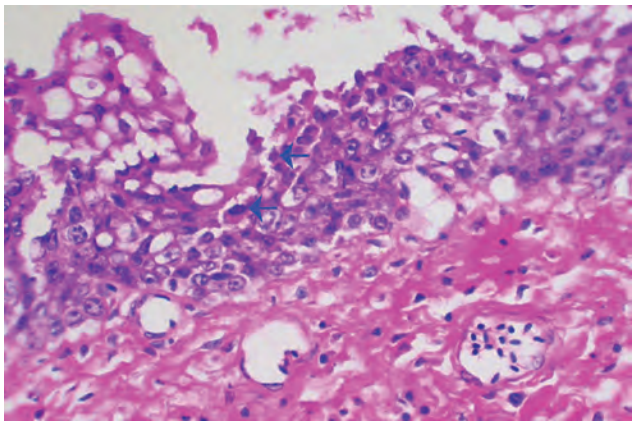

Figure 3.28 Esophageal lesion in herpesvirus infection. There are mucosal hyperplasia and focal necrosis, and intranuclear inclusion body formation can be seen in some pyknotic nuclei (arrows).

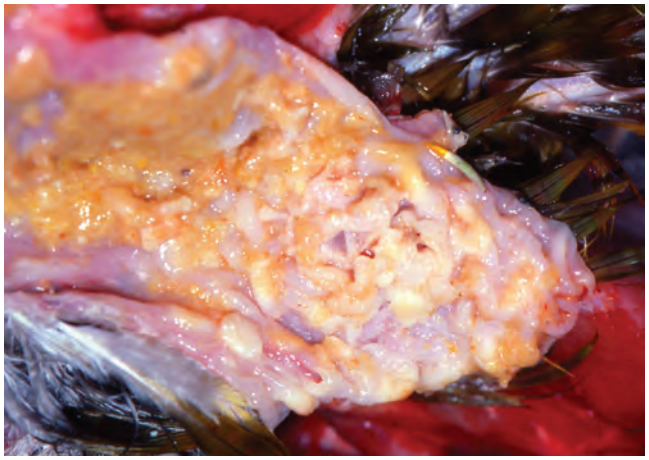

Figure 3.29 Severe ingluvitis due to *Candida* sp.

of the crop are also common in nestling birds with crop stasis. Failure of the crop to empty is a nonspecific sign and may be secondary to many digestive and systemic disorders. In severe infections of the crop, yellow-white nodules and plaques, hemorrhage, necrosis, and a variable fibrinopurulent exudate affect the mucosal surface. Histologically the presence of bacteria associated with necrosis and a predominantly heterophilic infiltrate is diagnostic. In chronic infection, heterophils, macrophages, and giant cells surround bacterial colonies and necrotic debris. *Pasteurella multocida* has been associated with unique oropharyngeal and esophageal granulomas reported in Buteos hawks. *Pasteurella multocida* is not part of the normal flora in the pharynx, choana, or cloaca, but was isolated from raptors with these lesions. The lesions grossly are indistinguishable from the plaques of hypovitaminosis A, trichomoniasis, and yeast infections. Pasteurellosis has also been described in barn owls (*Tyto alba*) and Hawaiian owls (*Asio flammeus sandwichensis*).

Yeast infection of the crop can appear to be a primary problem in some birds, particularly cockatiels, lovebirds, and finches. Human error (overfilling the crop or feeding formula at an improper temperature) can predispose to crop stasis and candidal overgrowth in handfed psittacines. Gross changes are similar to those seen in the oral cavity, with necrosis and a grey to yellow-white exudate on the mucosal surface (Fig. 3.29). Often the crop wall appears significantly thickened and is thrown into broad folds. Histologically there is proliferation of mucosal epithelium and variable hyperkeratosis. A mononuclear inflammatory response may be seen, and organisms are present in the mucosal epithelium (Figs. 3.30 and 3.31).

Mixed bacterial and yeast infections are occasionally found with the organisms noted histologically.

Trichomoniasis causes lesions of the crop in budgerigars and thoracic esophagus in the cockatiels. The disease affects adult birds primarily and causes a proliferative lesion that can be caseous. Histologically the lesion is similar to that seen in the oral cavity. Differential gross diagnoses include poxvirus and

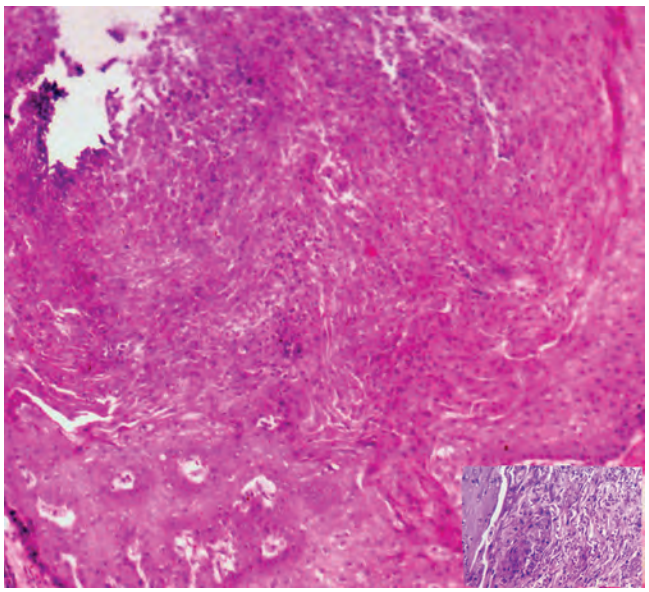

Figure 3.30 Candidiasis of the crop. There is marked mucosal proliferation associated with pseudohyphae and spores (inset).

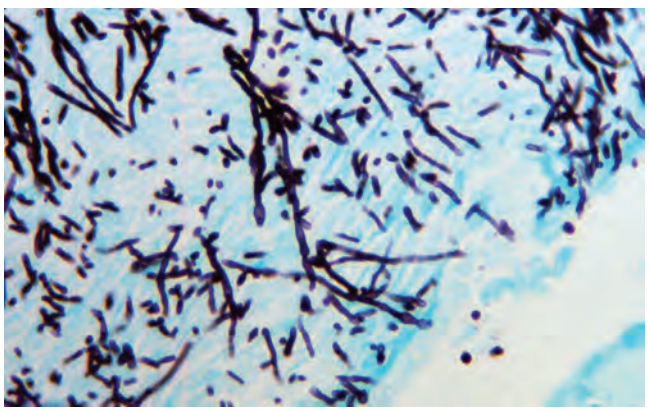

Figure 3.31 Silver stain illustrating the *Candida* organisms in the crop mucosa.

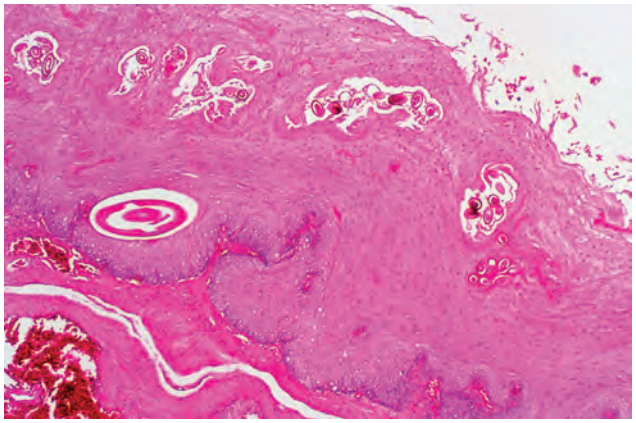

Figure 3.32 Eggs of *Capillaria* sp. within the crop mucosa.

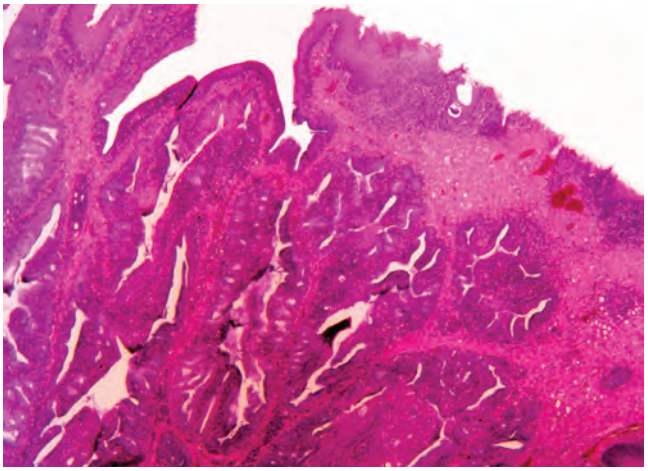

Figure 3.33 Papilloma of the crop. Multiple papillary projections are seen.

bacterial infections, as well as vitamin A deficiency. Finding the organism in the lesion is necessary for a positive etiologic diagnosis. Pigeons, doves, and mockingbirds occasionally develop a form of trichomoniasis resulting in invasion of the tissues of the face, throat, and neck. Grossly the lesions are soft swellings that are red and highly vascular. Histologically the trichomonads induce a marked heterophilic response and locally extensive necrosis.

As in the oral cavity, intraepithelial nematodes or nematode eggs may be found, usually as an incidental histologic lesion (Fig. 3.32). Capillariasis of the esophagus is common in pheasants and is of particular concern in the vulturine guinea fowl where it is associated with high mortality. It is also a significant infection of raptors. The life cycle is direct or indirect with an earthworm intermediate host depending on the species. The thread-like adult worms burrow into mucosa of the oropharynx, esophagus, crop, and intestines of the avian host. Severe infections produce diphtheritic membranes. In young raptors the esophageal wall may be palpably thickened. Capillaria eggs may be detected in fecal samples, egested pellets, or in cytologic samples from the oropharynx and esophagus.

Neoplastic disease

Neoplasms of the esophagus and crop include papillomas and carcinomas. Papillomas are proliferative masses that project into the lumen of the esophagus or crop. Mucosal papillomas of the crop and the esophagus are most common in green-winged, scarlet, military, and blue and gold macaws. These birds typically also have oral and cloacal lesions. Amazon parrots can also have esophageal or crop papillomas, but far less commonly than macaws. These mucosal papillomas of New World psittacines are associated with PsHV genotypes 1, 2, and 3 (psittacid herpesvirus). Histologically there are numerous papillary projections covered by large epithelial cells (Fig. 3.33).

Squamous cell carcinomas are also found in the esophagus and crop. Carcinomas are both proliferative and invasive. Secondary infections of the diseased tissue are common. They present as variably sized masses that may contain areas of necrosis and hemorrhage. Histologically they comprise nests and cords of neoplastic epithelial cells and variable stroma.

Carcinomas of the submucosal glands occur, but do not appear to have been previously reported. These lesions are often large and involve much of the wall of the esophagus/crop with extension into surrounding tissue (Fig. 3.34). They can be necrotic and hemorrhagic. Histologically they comprise moderately undifferentiated to poorly differentiated epithelial cells forming nests, acini, and trabeculae that infiltrate into surrounding tissue. There is usually minimal to moderate stroma.

Tumors of smooth muscle origin result in large space-occupying masses that may become necrotic and hemorrhage, although they can be asymptomatic when small. Microscopically they are characterized by interlacing bundles of fusiform cells with moderate amounts of cytoplasm. Differentiation between leiomyomas and leiomyosarcomas is done histologically based on characteristics such as degree of anaplasia, mitotic index, and other typical parameters.

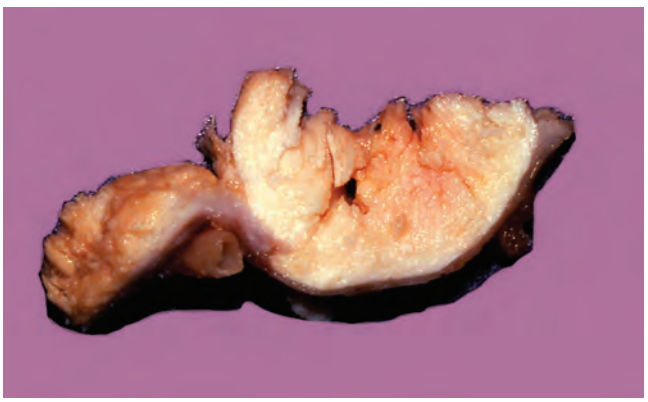

Figure 3.34 Squamous cell carcinoma of the esophagus that has obliterated the lumen.

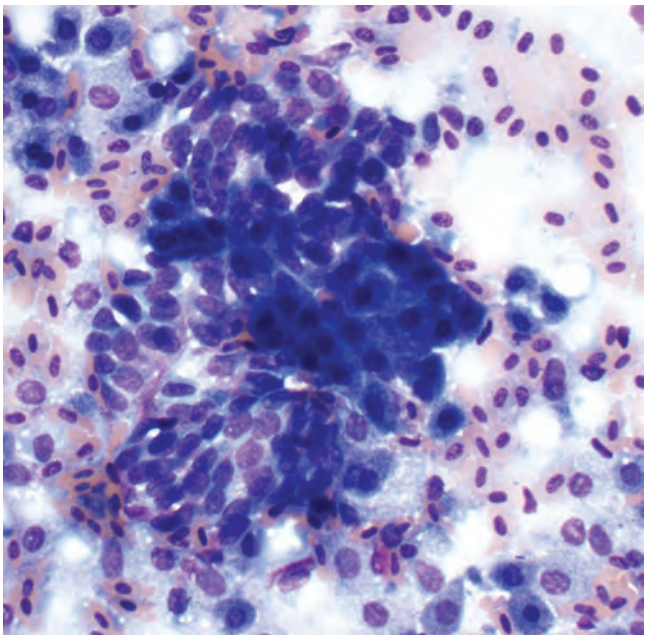

Figure 3.35 Brush preparation of normal proventricular mucosa.

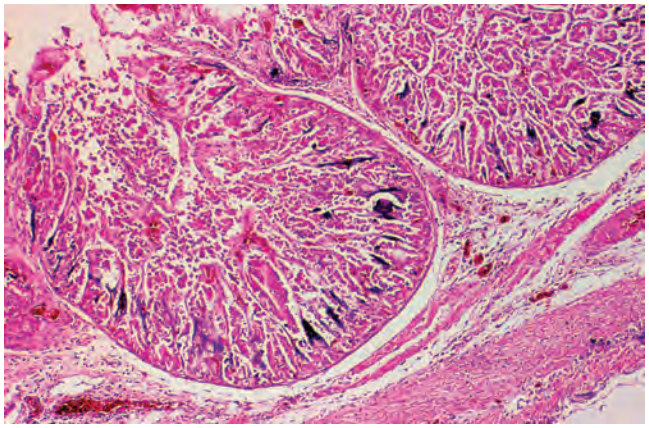

Figure 3.36 Mineralization of proventricular glands. Note the diffuse involvement of basement membranes.

Proventriculus

Cytology

Cytology collection for the proventriculus and ventriculus is generally of endoscopic brush preparations. These types of preparations generally are of the surface material with mucus, food particles, and rarely some variety of microbes. Preparations at postmortem examinations will contain some of the mucosal epithelial cells and fragments of the koilin (Fig. 3.35).

Noninfectious disease

Gastric impactions that sometimes result in perforation are most common in young psittacines that ingest foreign material. Affected birds have proventricular dilatation, and the proventricular wall is flaccid. Perforation or rupture is characterized by hemorrhage and accumulation of ingesta in and around the affected area.

Birds with severe vitamin A deficiency may have metaplasia of the proventricular glands, leading to gross thickening and accumulation of excessive keratin, which must be differentiated from caseous material due to inflammation/infection.

Mineralization of the proventricular mucosa is seen in birds and is believed to be secondary to excessive dietary calcium and/or excessive vitamin D_3. The lesion may not be noticeable grossly but histologically proventricular glands are variably affected (Fig. 3.36). This lesion seems to be more common in macaws, particularly the blue and gold macaw and cockatiels possibly due to dietary imbalances of vitamin D. Exposure to cholecalciferol rodenticides will also lead to soft tissue mineralization. Renal failure can be associated with soft tissue mineralization especially of the proventricular glands and lungs.

Infectious disease

Infectious diseases affecting the proventriculus include viral, bacterial, mycobacterial, fungal, and parasitic.

PDD is a disease of the central and peripheral nervous systems. It will be discussed in this section because one of the most common lesions associated with this disease occurs in the proventriculus. The disease has also been called neuropathic gastric dilatation, myenteric ganglioneuritis, and splanchnic neuropathy. It is reported in many species of psittacine birds and may also occur in other species of birds ranging from red-tailed hawks to Canada geese. African grey parrots, macaws, Amazon parrots, conures, and cockatoos are the most commonly affected psittacine species. PDD is defined by lymphoplasmacytic inflammatory infiltrates within the peripheral and/or central nervous system. A viral etiology is associated with PDD (bornavirus by two research groups in 2008); however, the mode of transmission, incubation, and disease development is unknown. Recent research has identified multiple avian bornavirus genotypes involved in the development of the disease.

Many birds develop a complete ileus of the digestive tract and as a result are severely wasted and have no body fat by the time that they die. The primary gross lesions seen in PDD are flaccidity and dilatation of any portion of the gastrointestinal tract with the proventriculus, ventriculus, and crop being most commonly affected (Fig. 3.37). The proventriculus may be so dilated as to fill much of the left side of the celomic cavity and to displace the ventriculus to the right and cranially. If the bird has been on a seed diet, the proventriculus and ventriculus will be packed with seeds. Atrophy of the muscles of the ventriculus and thinning of the proventriculus mucosa are common. Multifocal ulceration of the proventricular mucosa also occurs. Some birds will be present for necropsy with no gross change in the digestive system.

Histologic lesions are characterized by a lymphoplasmacytic infiltrate of the myenteric plexus of any part of the esophagus, crop, or gastrointestinal tract. These infiltrates may vary in

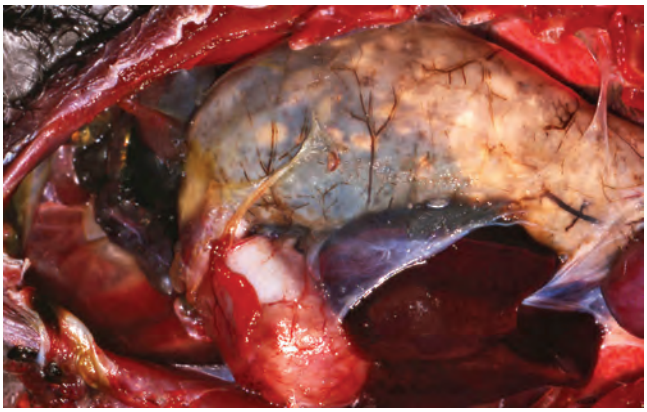

Figure 3.37 Grossly dilated and flaccid proventriculus typical of severe proventricular dilatation disease.

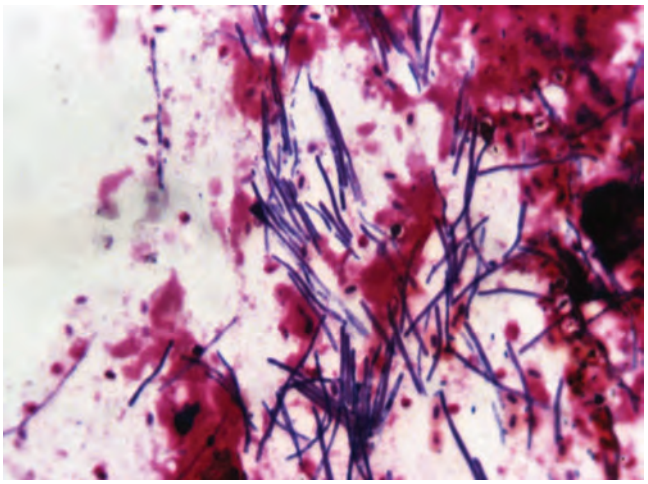

Figure 3.39 Gram stain of *Macrorhabdus* [avian gastric yeast] from a smear of the proventriculus.

severity (Fig. 3.38). The inflammatory infiltrate may also affect the smooth muscle. Crop biopsy has been reported to be an effective method of antemortem diagnosis in 76% of affected birds, provided a large biopsy sample and a visible blood vessel are included in the sample. Routine sampling in a diagnostic pathology practice has been less effective (30–35% positive).

Proventricular dilation is not pathognomonic for PDD. Any disease that causes partial or complete obstruction of the intestines will result in proventricular dilation. The differentials for gastric dilation can include any number of infectious disease agents including clostridial infections, gastric mycobacteriosis, fungal gastritis, peritonitis and/or serositis, and ulcerative or erosive gastritis. Proventricular dilation is also a common lesion in geese that are poisoned by lead. Although infrequently seen, internal poxvirus infection and Pacheco's disease can lead to proventricular lesions grossly and histologically similar to those previously described.

Bacterial infections of the proventriculus can be primary or secondary. Gram-negative bacterial infections will present grossly as focal to diffuse hyperemia, with variable necrosis and hemorrhage of the mucosa. Fibrin may be present. In severe cases, the proventriculus can be perforated. Histologically the reaction is primarily heterophilic, with variable numbers of macrophages and plasma cells. Finding the organism is necessary for confirmation of the etiology.

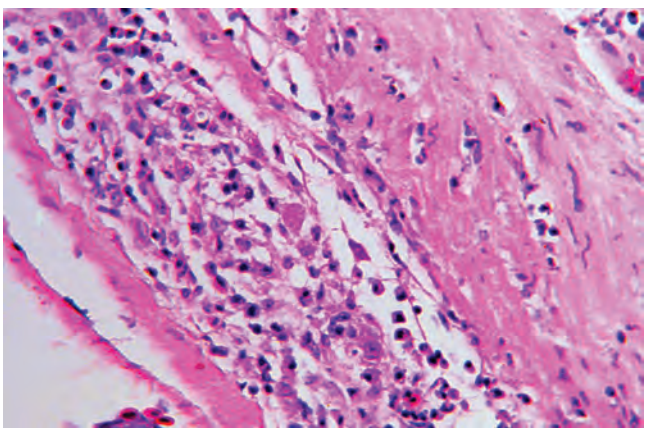

Figure 3.38 Lymphoplasmacytic infiltrate typical of proventricular dilatation disease in nerves and nerve ganglia of the proventriculus.

Mycobacteriosis has been reported in the proventriculus of passerine birds and is also seen in psittacine birds. Mycobacterial disease of the small intestine, which is far more common, is discussed in detail in the section on small and large intestine.

An organism that is frequently referred to as "megabacteria" or "avian gastric yeast" is commonly found on the mucosal surface of the isthmus of budgerigars, canaries, finches, parrotlets, ostriches, a lesser sulfur-crested cockatoo, and less frequently poultry (chickens, turkeys, quail, and gray partridges (*Perdix perdix*)). Phylogenetic research identifies this organism as a previously undescribed anamorphic ascomycetous yeast representing a new genus, *Macrorhabdus ornithogaster*. The organisms are relatively large (2 × 20–40 μm), gram positive, PAS positive, and stain strongly with Calcaflour White MR2 (a chitin stain). They are densely packed, resembling a log jam, on the surface of the isthmus and often penetrate down between the glands of the isthmus. They may also extend into the ventriculus and penetrate deeply into the koilin. They can be seen on cytologic scrapings from the affected area (Fig. 3.39).

It is widely accepted by clinicians that this organism is pathogenic and associated with a chronic wasting disease. It must be noted, however, that many birds infected with this organism do not have clinical signs or histologic lesions. Therefore, the presence of this organism in a necropsy specimen without concurrent gross or histologic disease is not conclusive evidence that it contributed to the bird's death.

The primary gross lesion associated with this infection is excessive mucus production. Histologically there is goblet cell hyperplasia and a variable mononuclear inflammatory infiltrate in the mucosa (Figs. 3.40 and 3.41). Although some

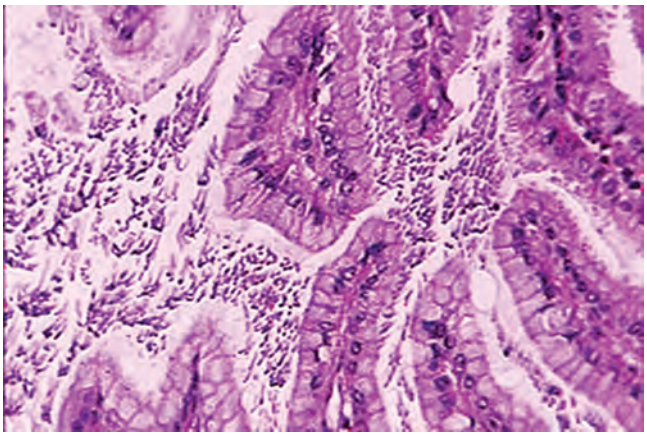

Figure 3.40 Avian gastric yeast infection of the proventriculus. Note the goblet cell hypertrophy/hyperplasia and excessive surface mucus. Minimal necrotic debris is present.

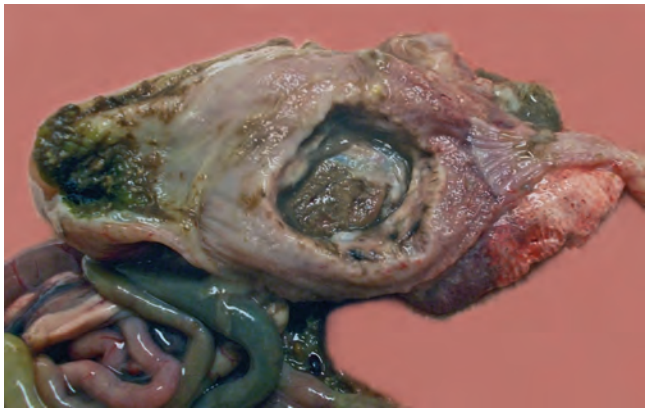

Figure 3.42 Proventricular ulcer following infection by a zygomycete fungus.

underlying stress may be necessary for the infection to become clinical, proventriculitis associated with avian gastric yeast is often the only postmortem change in chronically ill birds with severe weight loss. Mild to moderate lymphoplasmacytic infiltrates have also been observed by one of us (DLP) in the lamina propria of the proventriculus of budgerigars that were raised in isolation and were free of this organism; therefore, these changes may not always be attributable to the organism.

Zygomycete fungi are a cause of proventriculitis as well as ventriculitis in several avian species. The morphology these fungal organisms are suggestive of *Mucor*, *Absidia*, or *Rhizopus* fungal groups although tissue cultures or chromosomal analysis would be necessary for specific identification. It is unknown what initiates this type of fungal infection; however, this disease entity has proven difficult to diagnose antemortem and treatments are not described. The majority of cases are in young (<1 year) large psittacines and older birds with multiple disease conditions and general debilitation. Gross lesions are similar to bacterial infections and erosions or ulcers are common (Fig. 3.42). Histologically there is necrosis and hemorrhage with a pleocellular inflammatory response and intralesional fungal hyphae which are seen throughout the proventricular wall and within blood vessels (Fig. 3.43).

Cryptosporidiosis of the proventriculus is seen in a variety of psittacine and small passerine birds. Clinically these birds may present with gastrointestinal signs including weight loss and chronic vomiting. Often no gross lesion is reported, but there may be excessive mucus production and variable mucosal hypertrophy. Histopathologically, the typical lesion is an extensive hyperplasia of the ductal epithelium of the proventricular glands resulting in some distortion of the glandular architecture due to the hyperplastic changes. Variable numbers of oval to round amphophilic protozoa-like organisms closely adhere to the lining of ductal and surface epithelial cells (Fig. 3.44). A

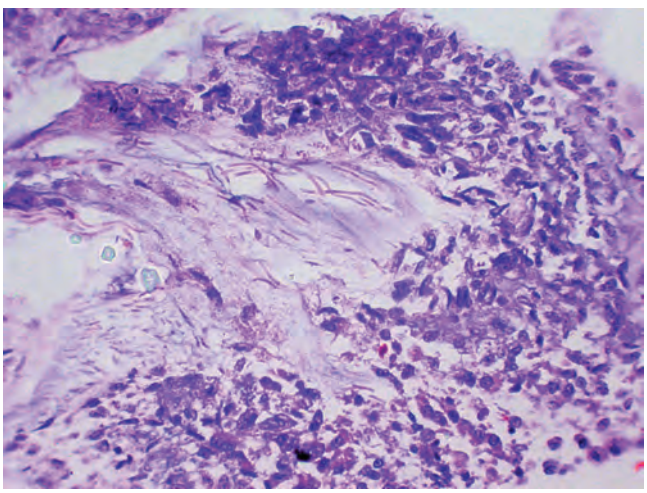

Figure 3.41 Detail of avian gastric yeast infection of the proventriculus with excessive mucus and numberous organisms.

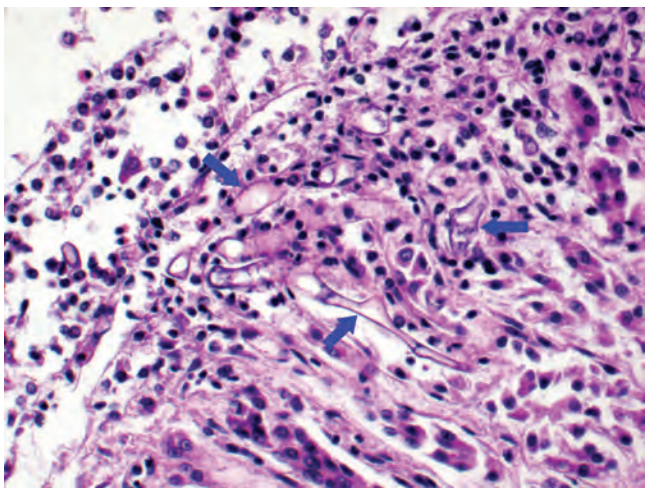

Figure 3.43 Proventriculitis associated with zygomycete fungal infection.

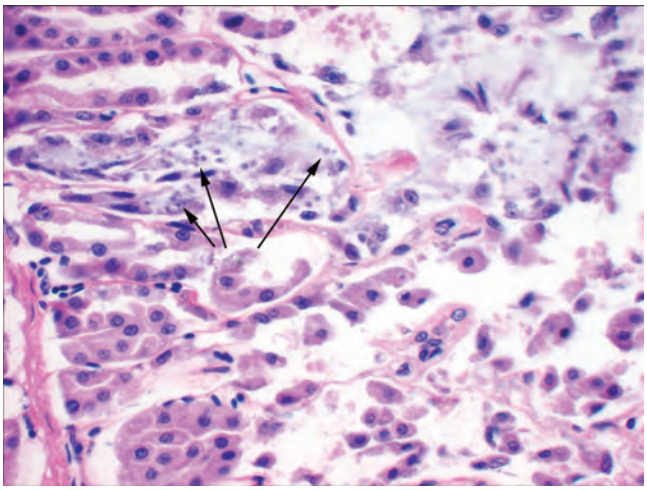

Figure 3.44 *Cryptosporidia* (arrows) on the surface of proventricular mucosal cells.

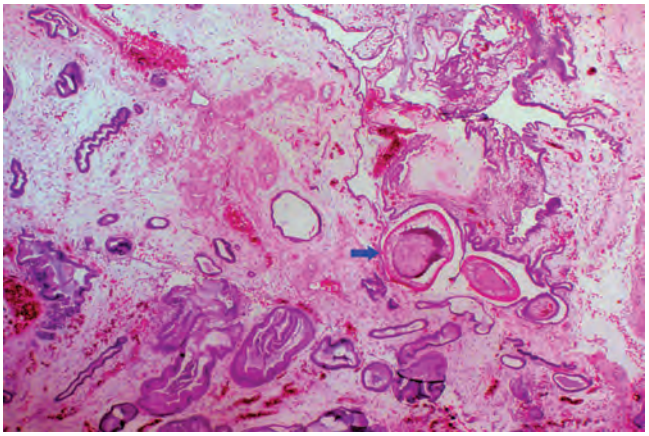

Figure 3.46 Proliferative proventricular glands with edema and inflammation. Nematode fragments (arrow) are seen in the deep mucosa.

variable mononuclear inflammatory response may be present. The cryptosporidia identified in a series of cockatiels and lovebirds by PCR is of an unnamed *Cryptosporidium* sp. as avian genotype III. Crytosporidiosis is a one possible complication of PBFDV infection of cockatoos.

Spiruids, including *Spiroptera* sp. and *Dyspharynx* sp., can colonize the proventriculus. They require an intermediate arthropod host and thus are primarily seen in birds kept outdoors. In minimal infections, there is no gross change, and the parasites are seen histologically. In severe chronic infections, the wall of the proventriculus, particularly the mucosa, will be thickened, and the proventriculus may be distended. Hemorrhage is seen in severe cases, and nematodes may be found in the lumen (Fig. 3.45). Histologically there is mucosal hyperplasia, excess mucus production, and an inflammatory infiltrate of varying severity that includes heterophils, lymphocytes, and macrophages. Parasite fragments may be present in the mucosa and the lumen (Fig. 3.46). Perforation of the proventriculus may occur, but it is uncommon. Doves and pigeons are commonly infected with *Tetrameres* sp. These large roundworms cause the wall of the proventriculus to have a red, beaded appearance grossly (Fig. 3.47).

Neoplastic disease

Proventricular papillomas are morphologically similar to those previously described. They are an uncommon lesion and are most likely to occur in macaws, particularly the green-winged macaw. These birds generally have lesions of the esophagus and crop and often are chronically debilitated.

Adenomas arising from the mucosa of the proventriculus are rare in birds. These generally present as nodular, expansile masses that obstruct the lumen of the proventriculus. The tumor comprises irregular glandular acini formed by well-differentiated glandular epithelial cells. The cells are simple

Figure 3.45 Proventricular nematodes (*Contracecum* sp.). Note the thickened mucosa.

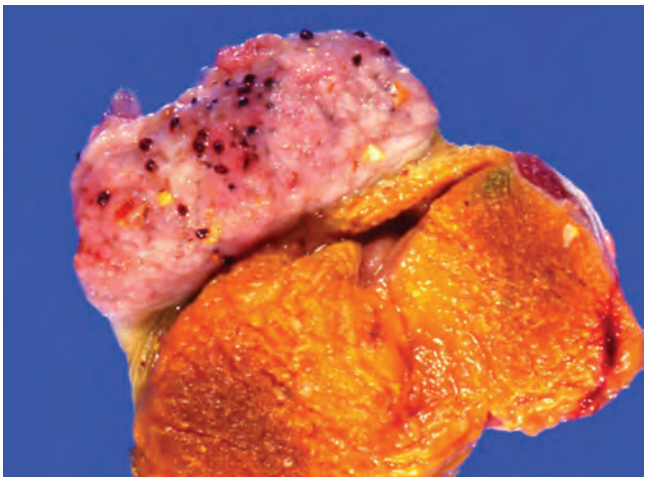

Figure 3.47 Tetrameres infection of the proventriculus in a pigeon. The multiple dark red foci represent dilated and possibly inflamed proventricular glands.

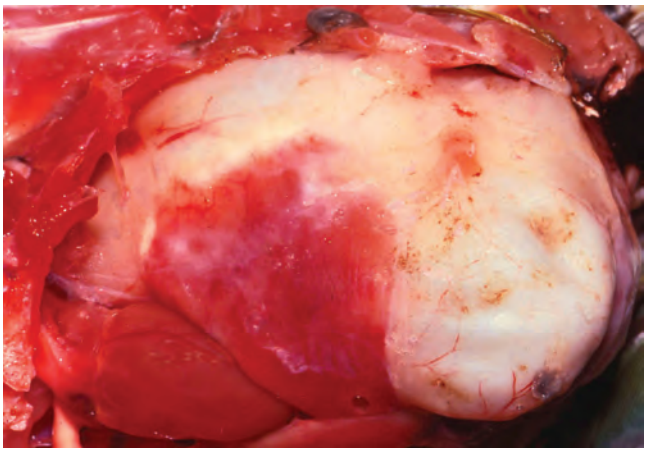

Figure 3.48 Thickened, irregular proventricular wall with adhesions secondary to proventricular carcinoma.

columnar epithelial cells with a centrally located nuclei. The neoplastic cells and adjacent are immunoreactive positive for pancytokeratin. Ki67 IHC used to verify mitotic activity is negative.

Proventricular carcinomas and adenocarcinomas are reported in several species of birds, but in pet birds they are most common in budgerigars, grey-cheeked parakeets, lovebirds, cockatiels, and Amazon parrots. Proventricular carcinomas are often found at the proventricular–ventricular junction and may be difficult to distinguish grossly in some cases. These lesions are generally flat rather than nodular. If they extend to the serosal surface, there may be peritonitis, fibrin deposition, and adhesion to the liver or other organs (Fig. 3.48). If nodular proliferation is noted in the lumen (Fig. 3.49), there may be lumenal hemorrhage associated with ulceration of the tumor.

Histologically carcinomas comprise poorly differentiated cells, including goblet cells, and there may be mucin production. Tumor cells are moderately undifferentiated and tend to form infiltrative nests, tubules, and cords, but may be individualized. There is moderate mitotic activity and stromal proliferation. They extend through the muscularis and may proliferate

Figure 3.49 Proventricular carcinoma presenting as a large, irregular mass that is replacing normal tissue and filling the lumen.

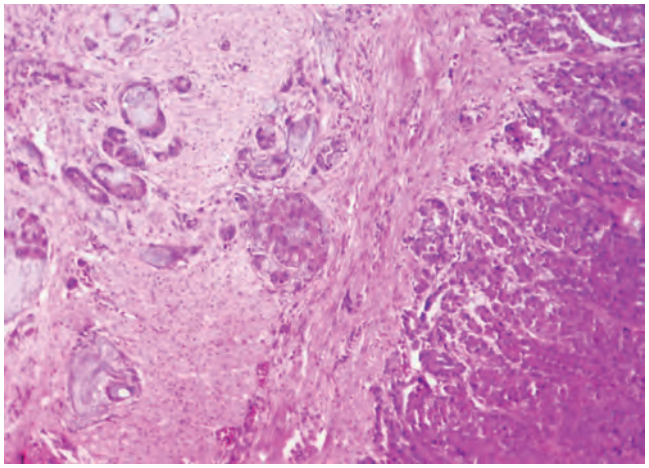

Figure 3.50 Infiltrative nests of cells in the muscularis of a bird with proventricular carcinoma. Note the loss of polarity and disorganization of the mucosa.

laterally into the ventricular wall and through the serosa. Stromal production is variable (Fig. 3.50). These tumors metastasize infrequently.

Smooth muscle tumors are rare. Grossly and histologically they are similar to those previously described.

Ventriculus

Noninfectious disease

Trauma to the ventricular koilin and mucosa may be secondary to ingested foreign bodies. This can include chewed toys given to psittacines, feathers, substrate such as crushed granite or sand, phytobezoars, nails, keys, coins, and other material from the housing. Depending on the species and thickness of the ventricular wall, there may be associated perforation. Grossly erosions, ulcers, and hemorrhage are noted, and foreign material may be identifiable in the lesion (Fig. 3.51). Histologically there is also a pleocellular inflammatory response and the lesion may become secondarily infected by bacteria or fungi.

Grit is small stones that are intentionally fed to birds for the stated purpose of assisting in digestion. Most cage birds do not need grit. When birds are fed grit, they occasionally consume too much, and it will interfere with digestion, causing erosion of the ventriculus and may result in starvation.

Mineralization, possibly associated with excessive dietary calcium, is usually not noted grossly. Histologically the mineral is deposited in the superficial mucosa and the koilin (Fig. 3.52).

A common manifestation of zinc poisoning is an erosive ventriculitis. Histologically the koilin layer is disrupted; there is ulceration of the underlying mucosa and dysplasia of the ventricular glands.

Xanthomatosis is a rare finding in the ventricular musculature. If the lesion is large enough, there is a nodular irregularity to the ventricular wall. Microscopically the xanthoma is similar

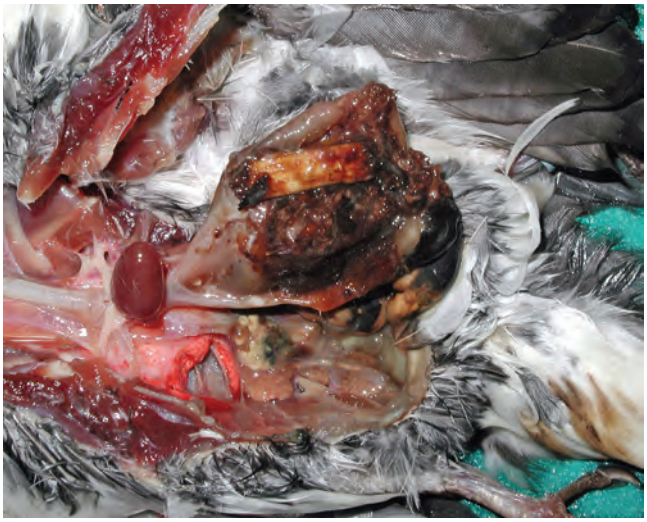

Figure 3.51 Ventriculitis associated with foreign body ingestion.

to that seen in the skin and subcutis, with numerous large, foamy macrophages surrounding cholesterol clefts (Fig. 3.53).

In some fruit-eating pigeons the ventriculus has rows of projections that aid in crushing hard fruit. Occasionally portions of the koilin in these birds become hyperplastic and form horn-like structures that protrude into the lumen (Fig. 3.54).

In cases of vitamin E deficiency, there may be degeneration of the ventricular musculature that is grossly (Fig. 3.55) and histologically similar to what is seen in other organs.

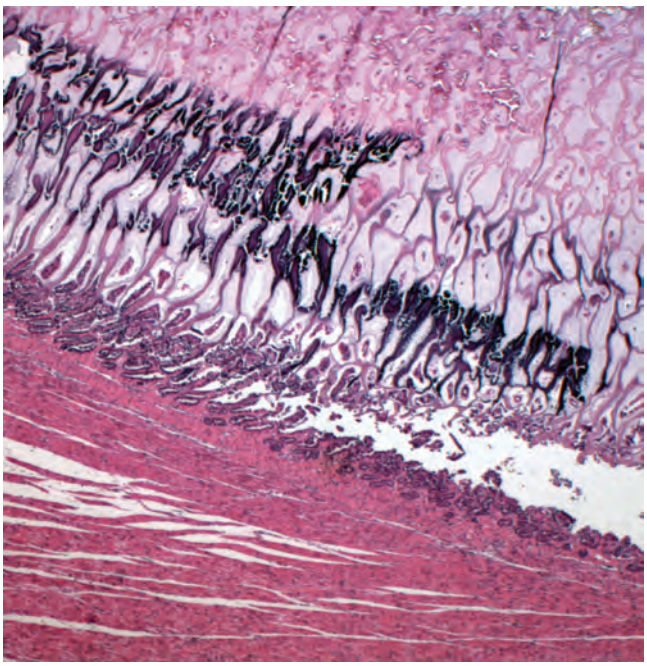

Figure 3.52 Mineralization in the superficial mucosa and koilin of the ventriculus.

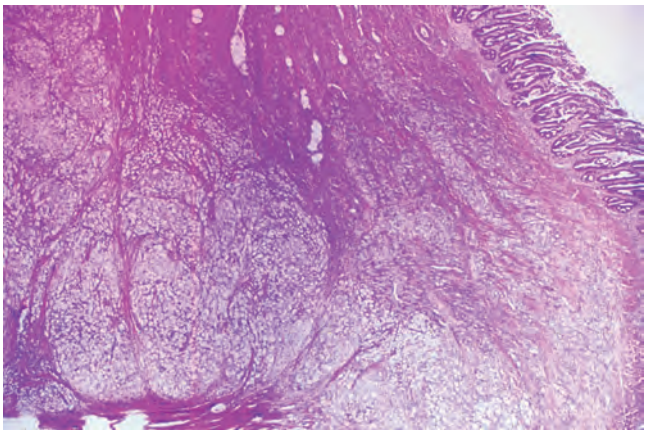

Figure 3.53 Xanthoma within the wall of the ventriculus. Multiple expansile masses are seen.

Melanosis of the ventriculus is occasionally seen and should not be considered a lesion (Fig. 3.56).

Infectious disease

PDD commonly affects the ventriculus. Typically the ventriculus is dilated and has a thin wall. Nerves on the serosal surface of the ventriculus may be enlarged. Histologic lesions for PDD of the ventriculus are similar to those described for the proventriculus and can be severe (Fig. 3.57).

Adenovirus infections are typically multisystemic, but ventricular lesions are the only lesions noted in some birds. Grossly, small areas of necrosis and ulceration of the koilin and mucosa are noted. Histologically, necrosis, hemorrhage, and a mononuclear inflammatory infiltrate are noted. Intranuclear inclusion bodies are seen in mucosal epithelial cells (Fig. 3.58).

Bacterial infections may be primary or secondary and result in loss of koilin, necrosis, and ulceration of the underlying mucosa and hemorrhage. A fibrinous exudate may cover an underlying ulcer. Histologically a pleocellular inflammatory response

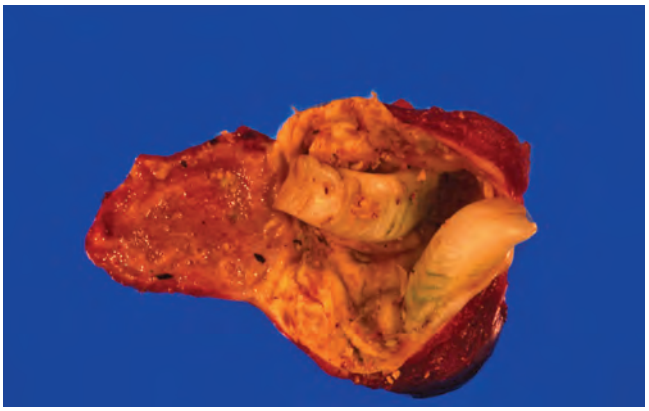

Figure 3.54 Hyperplastic koilin forming "horns" in the ventriculus of a fruit-eating pigeon. This is a sporadic finding and the cause is not known.

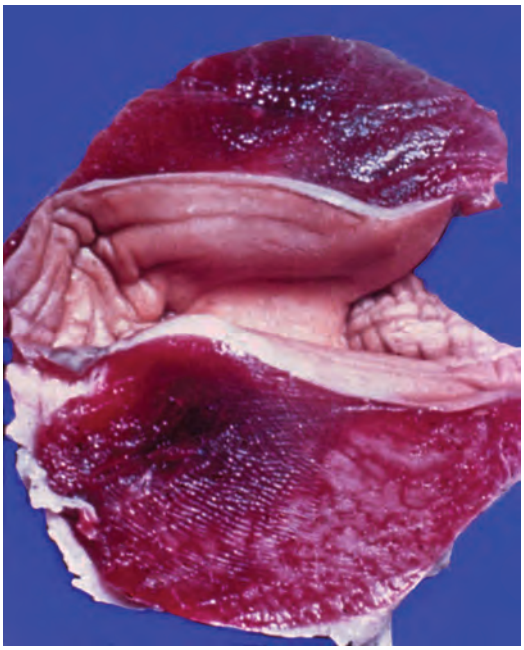

Figure 3.55 Pale foci and streaks in the ventricular musculature of a bird with vitamin E deficiency. This is more common in fish-eating waterfowl, but has been seen in many avian species.

is seen, and organisms must be present to make a positive etiologic diagnosis. Immunosuppressed birds may have bacterial colonization of the ventricular koilin, with no associated inflammation.

Ventricular mycosis is seen in a variety of pet birds and is especially common in finches.

Endoventicular mycosis is a condition in which fungal organisms (usually *Candida* sp.) may be found in the koilin layer and occasionally in the mucosa. Gross changes are not often seen, but the mucosa may be slightly nodular and discolored (Fig. 3.59).

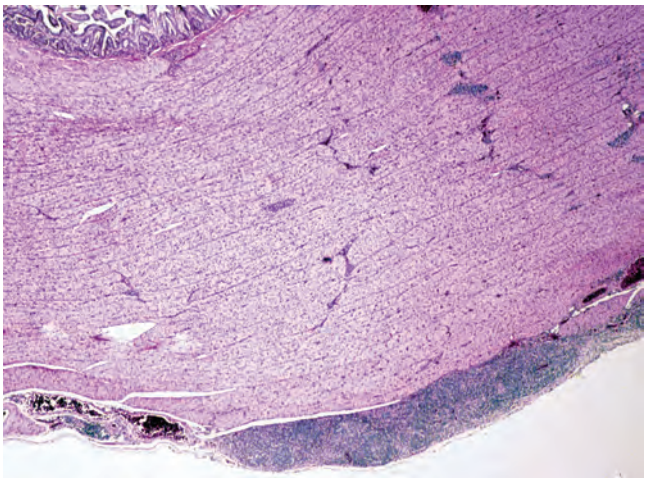

Figure 3.57 Severe ganglionitis of the ventriculus in a bird with bornavirus (PDD) infection.

Histologically variable numbers of spores and pseudohyphae may be present (Fig. 3.60). The extent of the infection may be better appreciated with special stains (Fig. 3.61). Inflammation is usually mild, and gross changes are rarely seen. Destruction of the koilin and ulceration of the underlying mucosa are uncommon manifestations of yeast infections of the ventriculus. These lesions, like those of bacterial infections of the koilin, may bleed, causing anemia or rarely a fatal blood loss. Zygomycete fungi are a cause of necrotizing ventriculitis invading beneath the koilin layer. The morphology these fungal organisms is suggestive of *Mucor*, *Absidia*, or *Rhizopus* fungal groups, although tissue cultures or chromosomal analysis would be necessary for specific identification. Gross lesions are of nodular, irregular thickening of the koilin with discoloration. Edema and congestion may be noted along the serosa. Histologic findings are of diffuse transmural necrosis and hemorrhage with diffuse edema and

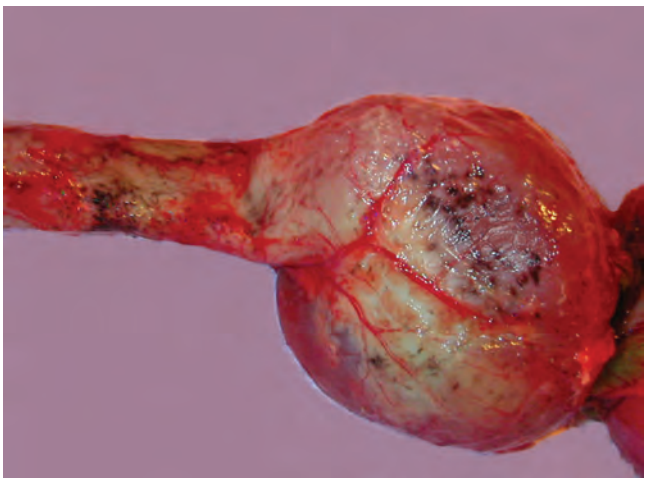

Figure 3.56 Melanosis of the ventriculus in a cockatoo. Cockatoos may have melanin deposits in a wide variety of tissues.

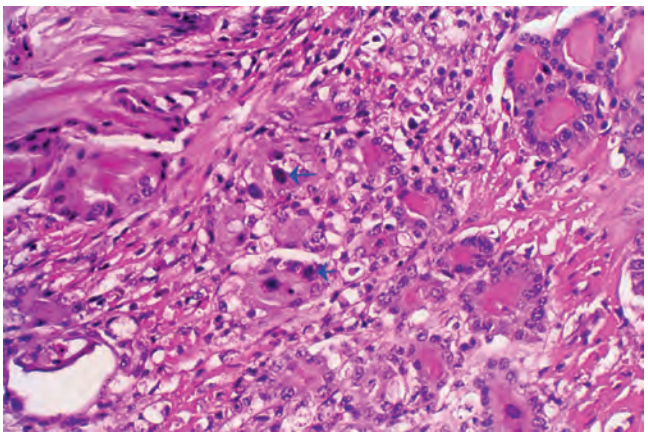

Figure 3.58 Adenoviral infection of the ventriculus. Note the large intranuclear inclusion bodies (arrows).

Figure 3.59 Endoventricular mycosis. In mild infections there may be little or no gross change.

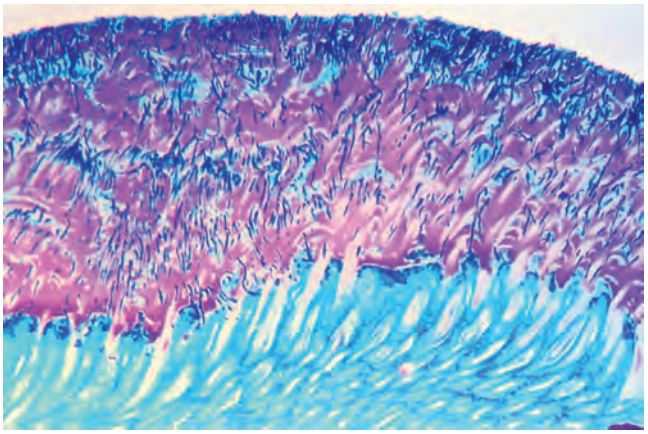

Figure 3.61 Periodic-acid-Schiff stain to illustrating fungal organisms in the ventricular koilin.

moderate to marked infiltration of mixed inflammation (heterophils, lymphocytes, macrophages). Large numbers of fungal hyphae with nonparallel walls will be present in the lesions. It is unknown what initiates this type of fungal infection; however, this disease entity has proven difficult to diagnose antemortem as these birds rapidly deteriorate. The majority of cases is in young (<1 year) or stressed large psittacines (Fig. 3.62).

Metazoan infections of the ventriculus can lead to necrosis of the mucosa and koilin with numerous worms seen (Fig. 3.63), or be essentially incidental with little or no gross change, and small nematodes may not be seen at necropsy. Histologically fragments of nematodes are noted in the lumen and mucosa.

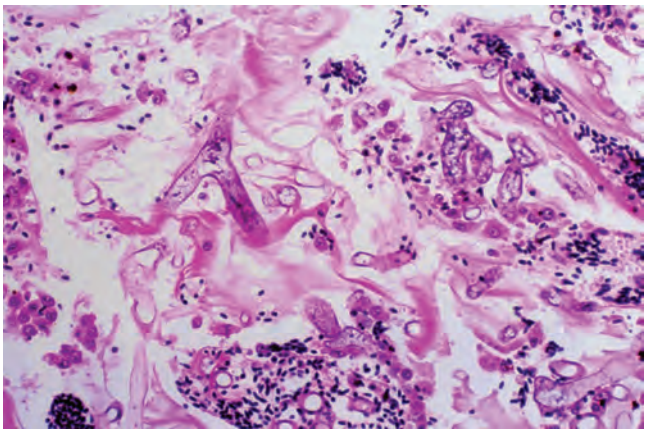

Figure 3.62 Ventricular infection by zygomycete fungi. Large, irregular hyphae are seen in an area of necrosis and hemorrhage.

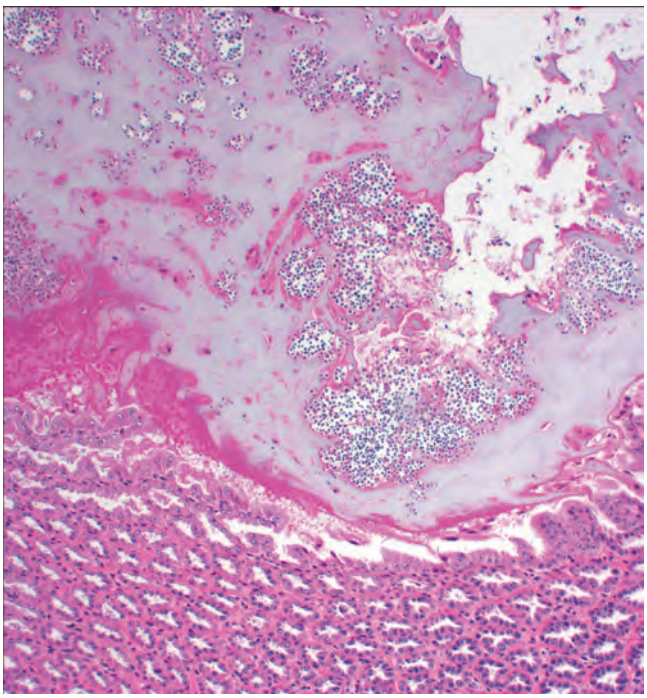

Figure 3.60 Ventricular candidiasis. Organisms are present throughout the koilin. There is usually no inflammatory response.

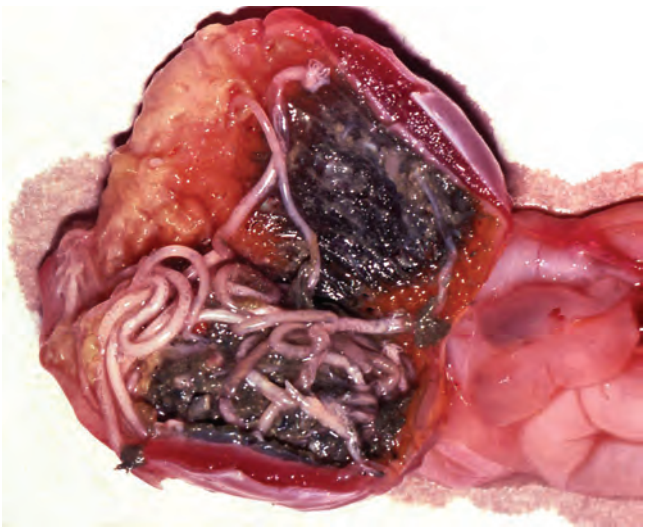

Figure 3.63 Severe ventricular nematodiasis.

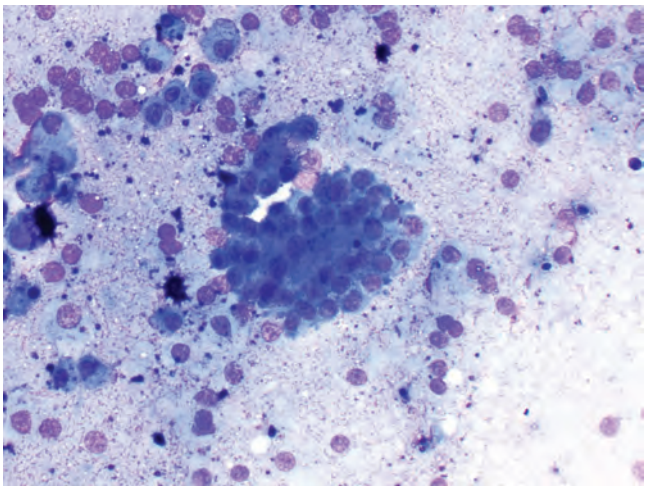

Figure 3.64 Cytology of normal intestinal epithelial cells.

Neoplastic disease

Papillomas and carcinomas are reported and are morphologically similar to those of the proventriculus. Carcinomas are usually at the proventricular junction, and the exact site of origin may be difficult to determine in extensive tumors. These neoplasms may infiltrate into the ventricular muscle and extend laterally some distance from the primary site.

Small and large intestines

Cytology

Intestinal samples are generally only available from necropsy specimens although aspirations collected during surgical evaluation have been described (Fig. 3.64). Duodenal aspiration may be helpful in identifying occult parasitic (*Giardia* spp. and *Strongyloides* spp.) and *Mycobacteria* spp. infections and small intestinal bacterial overgrowth.

Noninfectious disease

Noninfectious diseases of the intestinal tract of pet birds include trauma secondary to foreign bodies, infrequently torsion or intussusception, atresia, and ingested toxins. Trauma and torsion are usually obvious at necropsy, but histologic examination of affected tissue may be necessary to rule out underlying disease. Torsion leads to distension of a portion of the intestine, and edema fluid may be present in the lumen. The intestinal wall is edematous and congested, and histologically there is an infiltrate of heterophils and macrophages. True intussusception must be differentiated from agonal telescoping of a portion of the intestine. In true intussusception, there is edema and congestion, with subsequent inflammation and fibrin deposition and adhesion formation.

Foreign material enteritis is rare in birds as most materials are unlikely to pass from the ventriculus into the small intestine. Impaction of the intestines is usually the result of improper diet, ingestion of foreign material, and, in some cases, dehydration. Impactions can occur with proliferation of nematodes or accumulation of necrotic material. The impacted section is dilated and firm, and foreign material and ingesta are present in the lumen. Because the ventriculus is designed to hold ingested items until they are small enough to be digested by the intestines, intestinal foreign bodies are rare in birds.

Atresia or stenosis of the intestinal tract is uncommon in mammalian species and rarely reported in avian species. Atresia is the complete occlusion of the lumen and stenosis implies incomplete occlusion. Atresia is further classified as membrane atresia, in which the obstruction is formed by a simple membrane; cord atresia where the blind ends of the intestine are joined by a cord of connective tissues; and blind end atresia that has a completely missing segment of intestine and possibly the mesentery. Segmental ischemia from a mechanical lesion of the blood supply (ischemia) such as from a volvulus, intussusception, or malrotation is purported to be the primary cause. In a series of helmeted guineafowl hatchlings, where control of the population was by physically addling the eggs, several chicks had segmental intestinal atresia at various levels. The foci were noted between the ventriculus and intestine and at the level of the cloaca (see below).

Several benzimidazoles such as fenbendazole and albendazole result in a marked heteropenia followed by a progressive anemia, bone marrow suppression, and an enteritis. This occurs even at published dosages for birds (pigeons, doves, vultures, storks, psittacines). The inhibition of microtubule polymerization is suspected of interfering with mitosis in rapidly dividing cells of the bone marrow and mucosa of the gastrointestinal tract (Fig. 3.65). Both the immunosuppression from the bone marrow damage and the epithelial necrosis of the intestines result in secondary septicemias several days to weeks after therapy. The lesions include fibrinonecrotic enteritis with crypt cell necrosis, splenitis, and portal hepatitis with centrilobular necrosis. In cockatiels, the most significant finding is the submassive hepatic necrosis.

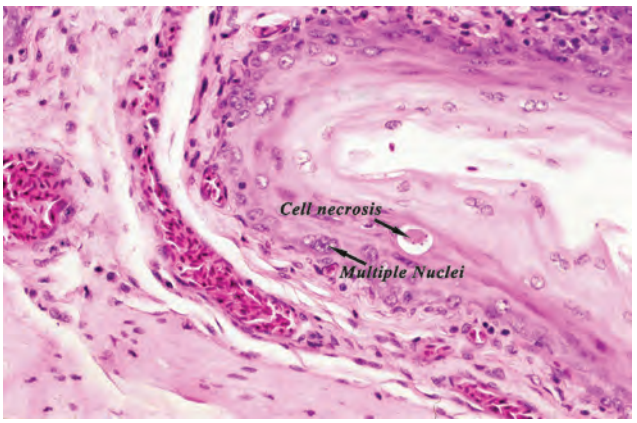

Figure 3.65 Changes in the GI (crop) mucosa associated with benzimidazole toxicity.

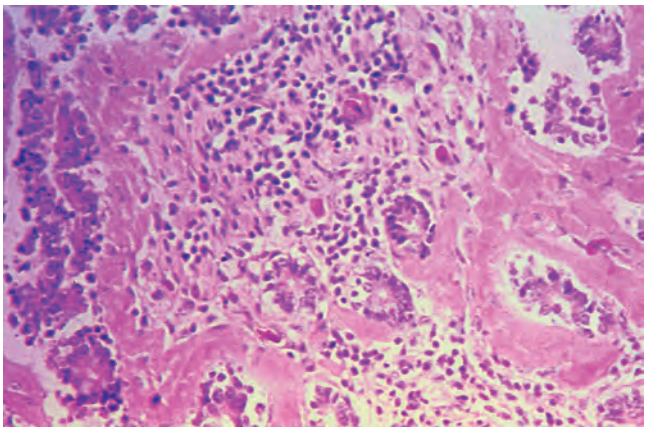

Figure 3.66 Amyloid deposition in the basement membranes of the small intestine.

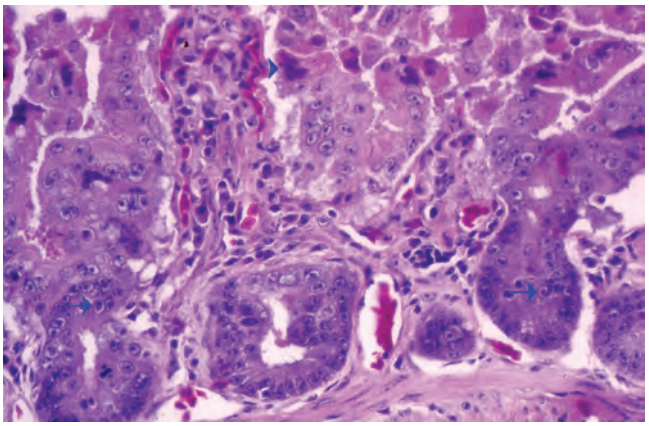

Figure 3.68 Herpesvirus-induced necrosis in the small intestine. There is early syncytial cell formation (arrowhead) and intranuclear inclusion bodies are seen in some enterocytes (arrows).

Amyloidosis and mineralization may occur in the intestinal tract, usually with no gross change noted. Mineral is found most frequently in vascular walls and amyloid in vessel walls and the lamina propria (Fig. 3.66).

Hyperplasia of all layers of the smooth muscle of the small intestine is rarely seen in birds, and the cause is not known. The intestinal wall is thickened and intestinal villi are enlarged due to proliferation of smooth muscle in the lamina propria.

Infectious disease

Numerous infectious agents affect the large and small intestines. Enteritis, to some degree, occurs in approximately 30% of birds, with disease caused by psittacid herpesvirus (Pacheco's disease virus). The lesions are generally mild, but severe enteric necrosis and hemorrhage that is seen grossly on the mucosal and serosal surfaces may occur (Fig. 3.67). Enterocyte necrosis, variable mononuclear inflammatory infiltrates, and intranuclear inclusion bodies are seen in the mucosa (Fig. 3.68).

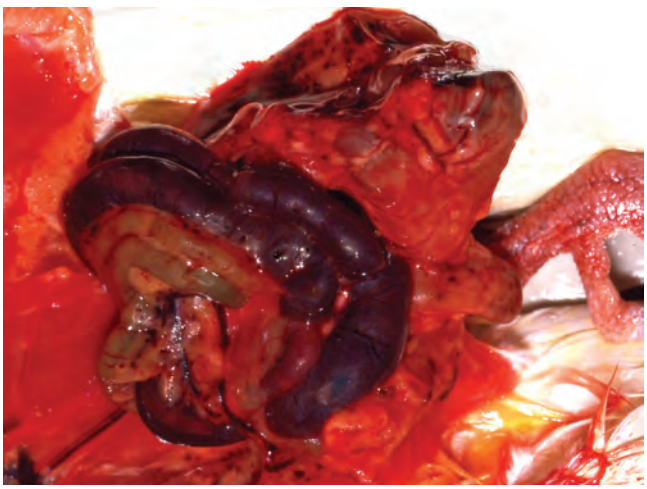

Figure 3.67 Severe intestinal hemorrhage due to herpesvirus infection. Both mucosal hemorrhage and serosal hemorrhage are seen.

Gross dilation of the intestines is an uncommon finding in birds with PDD. Histologically, segmental inflammation of intestinal smooth muscle, nerves, and ganglia is seen in PDD. The degree of gross dilatation will be variable, and histologic changes are similar to those previously described.

Paramyxovirus 1 (exotic Newcastle disease) can potentially infect many species of pet birds. Lesions are variable, but gross hemorrhage and necrosis are present in the intestines of some birds. Histologically the lesions are due to a vasculitis of the intestinal wall and necrosis of submucosal lymphoid tissue. Fibrinoid degeneration and a mononuclear inflammatory infiltrate characterize the vasculitis. In raptors PMV-1 outbreaks are generally traced back to contact with wild birds, pigeons, and poultry (alive or as food).

Adenovirus also causes hemorrhagic enteritis in psittacines, pigeons, and raptors (captive American kestrels (*Falco sparverius*)). Gross necrosis and hemorrhage are noted. Histologically there is variable inflammation, thrombi in intestinal capillaries and large basophilic intranuclear inclusion bodies in enterocytes.

Reovirus, coronavirus, and rotavirus have been implicated as causes of avian viral enteritis, but their occurrence in pet birds is poorly documented. Gross lesions are nonspecific, with edema and possible mucosal necrosis seen. Blunting and fusion of villi are described in cases of coronavirus infection and, in cases of suspected rotavirus, there is atrophy of villi (Fig. 3.69).

A variety of bacteria cause enteritis in psittacine birds. Gram-negative pathogens can be primary or secondary invaders. Historically, in psittacine birds, any finding of gram-negative bacteria has been considered by some to indicate disease; however, organisms such as *Escherichia coli* have been found in surveys of psittacine birds without clinical signs or lesions indicative of intestinal disease. Therefore the culture of *E. coli* from the intestine without associated gross and microscopic evidence of

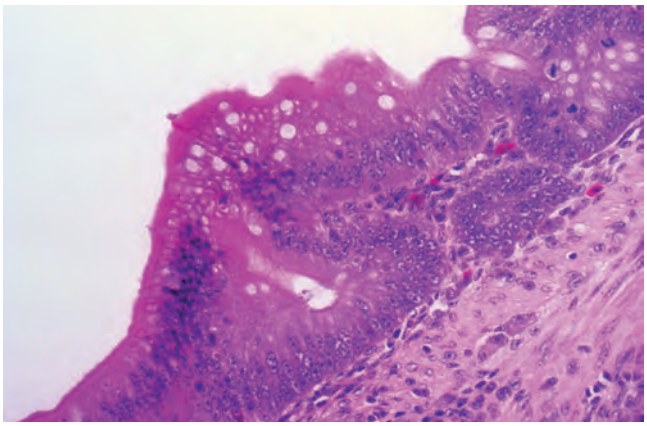

Figure 3.69 Intestinal mucosal atrophy that could be due to rotavirus infection.

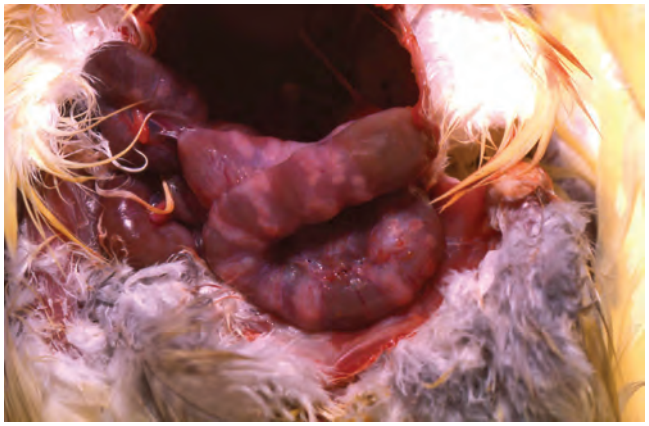

Figure 3.71 Severe necrotizing enteritis in a bird with Yersiniosis.

disease is insufficient proof that the organism was associated with the bird's death. Salmonellosis is a problem in all bird species. The disease in pet birds was a significant problem among wild-caught birds that were closely confined in quarantine stations. Currently it is more likely to be seen in birds from aviaries that have a significant rodent infestation. *Salmonella* sp. and most pathogenic enteric bacteria generally are invasive, resulting in significant lesions outside of the intestinal tract.

The gross lesions of a bacterial enteritis include redness, exudation, and, in some cases, ulceration of the mucosa. Gas or fluid may distend the intestine (Figs. 3.70 and 3.71). Diphtheretic membranes can be seen in some severe cases. Generally there is fecal soiling of the feathers of the vent, a lesion consistent with diarrhea. Histologically necrosis, fibrin deposition, and an infiltrate that is primarily heterophilic characterize the lesion. There may be extension into the submucosa muscularis, and crypt dilatation and abscess formation can be seen. Bacteria may not be present in all lesions (Figs. 3.72 and 3.73). The gram-negative, anaerobe, spiral-shaped bacteria,

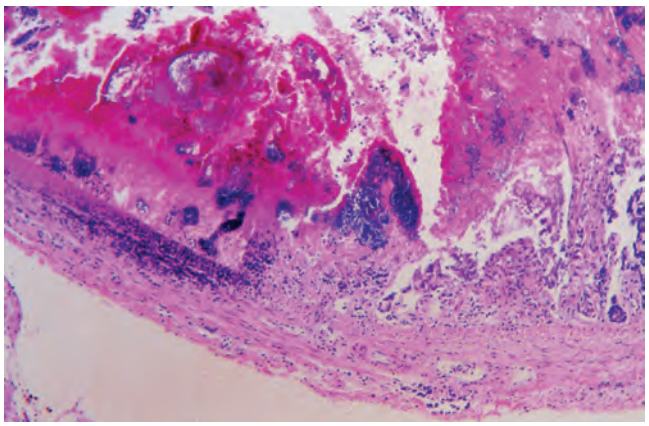

Figure 3.72 Bacterial enteritis. There is severe focal necrosis and inflammation extending into the muscularis.

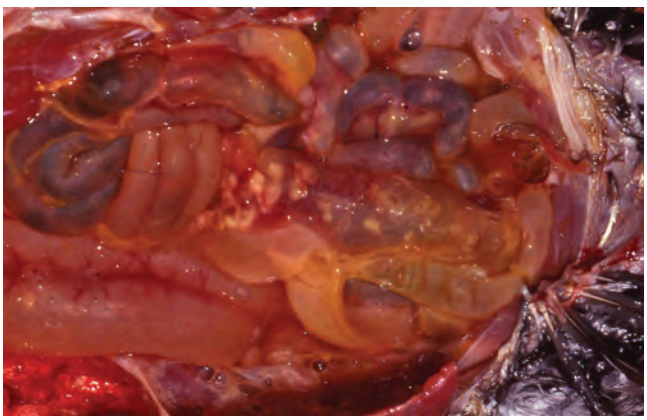

Figure 3.70 Distended, thin-walled intestines in a bird with bacterial enteritis. Necrotic material and exudate can be seen through the dilated walls.

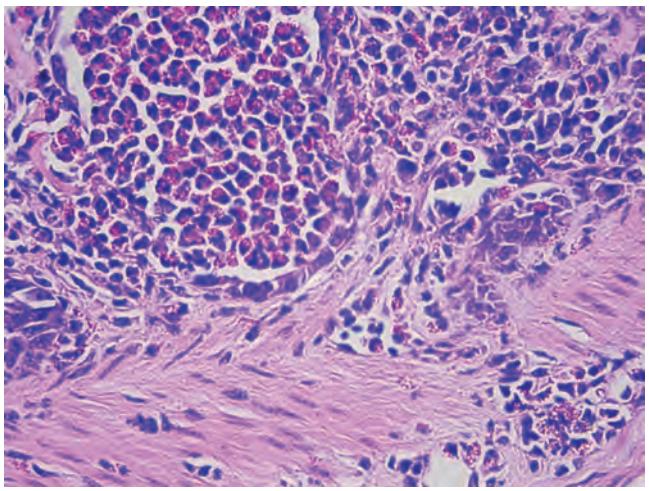

Figure 3.73 Bacterial enteritis. Note the crypt dilatation and infiltration by the heterophils and macrophages.

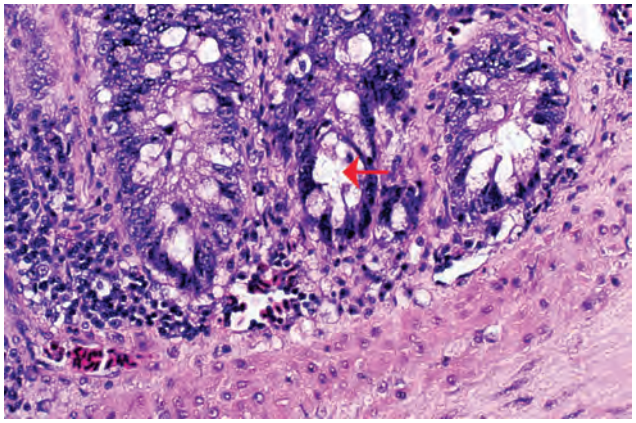

Figure 3.74 Enterotoxemia. Note the mild inflammatory infiltrate and clumps of large, spore-bearing, rod-shaped bacteria in the mucosa (arrow). This may be the only microscopic change in some cases.

Figure 3.75 Intestinal mycobacterial infection. There are variably sized thickened areas as the result of infiltration and distortion of the intestinal villi.

Brachyspira hyodysenteriae and *Brachyspira Pilosícoli*, are associated with a fibrinonecrotic typhlocolitis in ducks of all ages. The lamina propria is infiltrated lymphocytes, heterophils, and histiocytes with hemorrhages.

Gram-positive bacteria also cause enteric disease. Enteritis and septicemia due to *Enterococcus hirae* have been reported in 10 psittacine species. This organism, however, is found in the feces of normal birds and may be a part of the normal flora.

Clostridial overgrowth of the intestines may result in fatal enteritis. Lesions are more severe in the small intestine and vary from focal to diffuse hemorrhage, necrosis, and fibrin deposition. Although severe hemorrhage may be present, no other histologic changes are noted in some cases. Numerous large, gram-positive, spore-forming, rod-shaped bacteria are seen in the lumen and mucosa of affected birds (Fig. 3.74). The lack of histologic lesions may be due to acute death from systemic enterotoxemia. *Clostridium tertium* has been reported in a cockatoo with megacolon. At necropsy, there was severe dilatation of the colon, and a severe lymphoplasmacytic inflammatory reaction was noted histologically.

Mycobacterial infections occur sporadically in many species of pet birds and generally results in a chronic wasting disease. Amazon parrots, brotogerids, Pionus, and finches/canaries are more commonly infected. Infection is usually oral through ingestion of the organism. Clinically with the intestinal form, muscle wasting and emaciation is the usual presentation, along with eventual decrease in appetite. The primary site of infection for the *M. avium*/intracellulare complex and *M. genavense*, the two most common causes of mycobacteriosis in birds, is the intestinal tract. Gross lesions include diffuse and/or nodular thickening and opacification of the intestinal wall (Fig. 3.75). Impression smears of the lesions will contain large macrophages with poorly defined organisms in their cytoplasms (Fig. 3.76).

Histologically the common pattern is a diffuse infiltration of the lamina propria by large macrophages that have abundant amphophilic cytoplasm. These cells contain acid-fast bacteria; however, the abundance of the organism will vary from case to case. In severe cases, the infiltrate may extend through the intestinal wall to the serosa. A variable amount of necrosis and scattered accumulations of small macrophages, lymphoid cells, and heterophils may also be present (Figs. 3.77, 3.78, and 3.79). In some birds, multiple granulomas are seen in the submucosa and muscularis (Fig. 3.80).

Chlamydial infections can lead to diffuse mucosal necrosis and a moderate mixed mononuclear inflammatory infiltrate.

Primary mycotic infections of the intestines are rarely reported. Secondary infections, particularly by *Candida* sp. or zygomycete fungi, are occasionally seen, and the lesions are similar to those described in the upper gastrointestinal tract. Finding the organism histologically is necessary for a definitive diagnosis.

Encephalitozoon hellem is an obligate intracellular single-celled microsporidial parasite. Birds may be the primary host

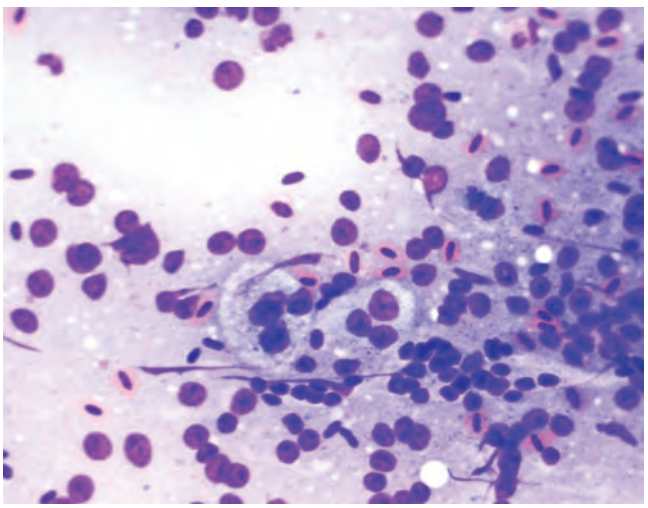

Figure 3.76 Cytology of the intestinal tract from a bird with mycobacteriosis. The large macrophages contain poorly defined bacteria.

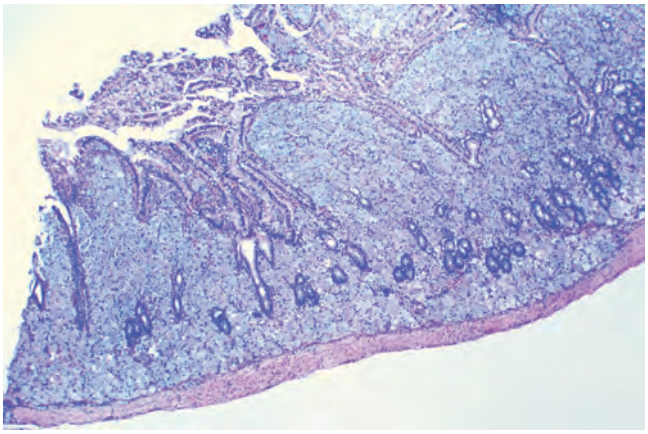

Figure 3.77 Intestinal mycobacteriosis. There is diffuse thickening of the villi due to infiltration of large macrophages with abundant, pale cytoplasm.

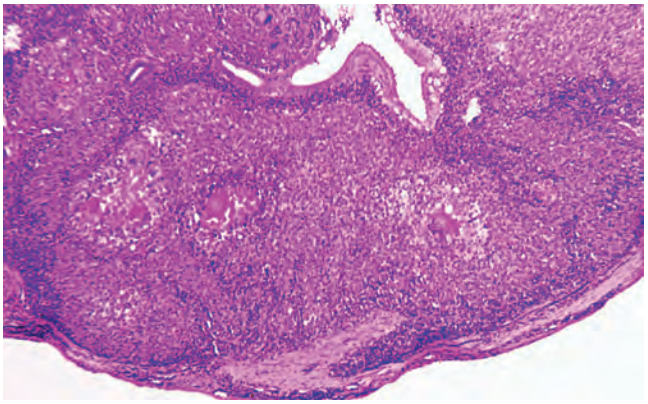

Figure 3.80 Multiple intestinal submucosal granulomas due to mycobacterial infection.

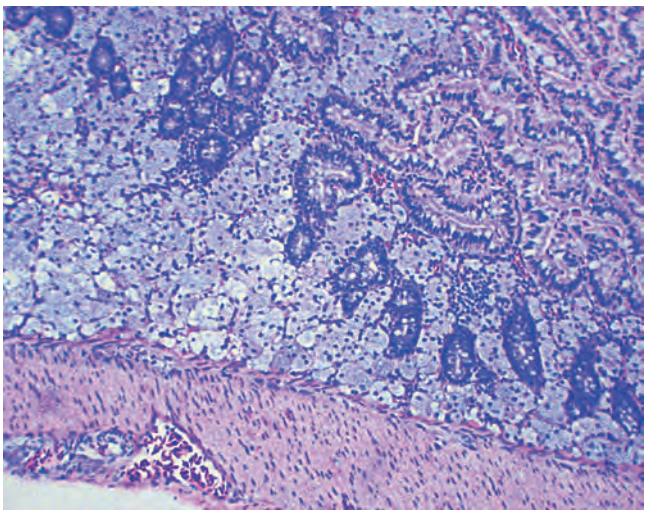

Figure 3.78 Detail of Figure 3.44 illustrating diffuse macrophage infiltration.

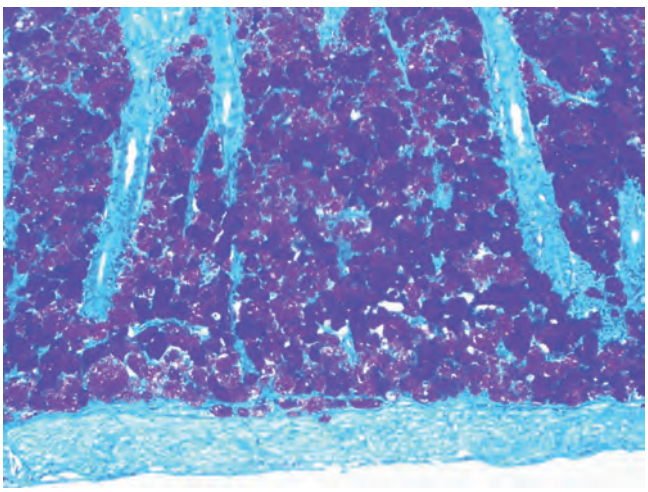

Figure 3.79 Mycobacterial organisms in macrophages demonstrated by acid-fast staining.

for *E. hellem* and most infections are self-limiting and inapparent. Columbids also appear to be a carrier of microsporidiosis. There appears to be an association between feral urban pigeons and human-virulent microsporidian species, particularly *Enterocytozoon bieneusi*. Immunosuppression or poor husbandry, especially with lovebirds and budgerigars, can result in clinical disease. Psittacine Beak and Feather Disease is a common associated infection in lovebirds. Budgerigars may have multiple infections caused by *Polyomavirus*, *Cryptosporidia*, *Giardia*, *Macrorhabdus ornithogaster* (Megabacterium), and *Chlamydia*. Disease has been documented in a wide range of companion birds including parrots and finches, in an ostrich, and in hummingbirds within a rehabilitation facility. Lesions are primarily found in the eye, intestines, liver, and kidney. The intestines may be distended with fluid and/or gas. Irregular pale foci may be present in the liver and kidney. Histologically there is a subacute hepatitis and a lymphoplasmacytic interstitial nephritis. The microbes will cluster within the cytoplasm of infected cells, generally renal tubular and collecting duct epithelium, hepatocytes, and intestinal epithelial cells, resulting in cytoplasmic expansion and rupturing of the cell. Additionally the microbes may be found in the spleen, the lamina propria of the intestines, and ocular conjunctiva. *Encephalitozoon hellem* stains poorly with H&E (Fig. 3.81), but are gram positive and can be visualized with modified trichrome and calcoflour white M2R staining.

Giardia and *Hexamita* are two flagellates that are considered as intestinal pathogens. These organisms may cause minimal gross change. Excessive fluid and mucus as well as mucosal hyperemia are seen in some birds. Histologically there may be villar atrophy and a mononuclear inflammatory infiltrate or no lesions at all. Organisms are usually found in intestinal crypts but (Fig. 3.82), at least in the case of *Giardia*, will extend the entire length of the villi. Histologically these organisms can be differentiated morphologically in some cases. *Hexamita* is a rod-shaped organism, whereas *Giardia* is a flattened, pear-shaped organism. Flagellates disappear from the intestine rapidly if the intestines are not immediately preserved. Therefore, wet mounts of intestinal,

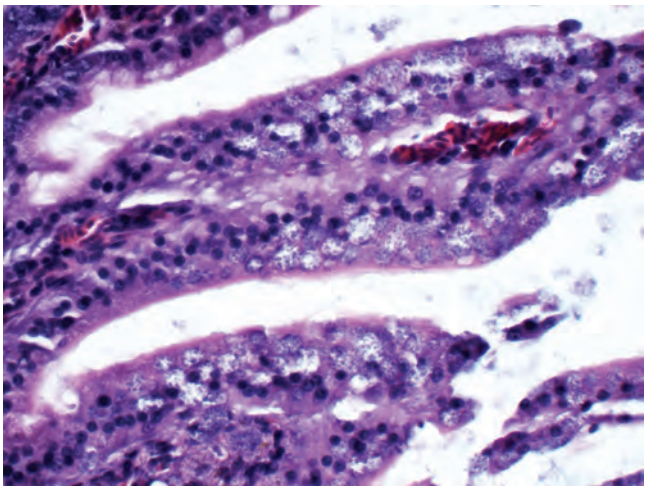

Figure 3.81 *Microsporidia* (*Encephalitozoon*) in the intestinal mucosa.

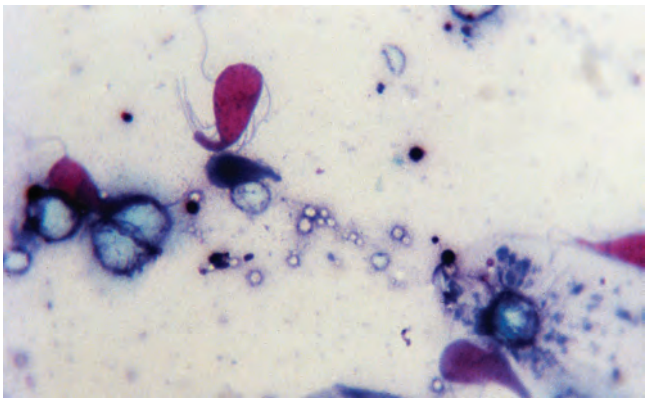

Figure 3.83 Cytologic smear illustrating *Giardia*, which has been considered to be a cause of feather picking in cockatiels.

particularly duodenal, scrapings from a bird that has just died are the most sensitive means of finding these organisms. Cytologic preparations of intestinal contents may contain the organism (Fig. 3.83). Each of these organisms has characteristic shapes and movements, making the wet mount an excellent means of differentiating them. It is also important to note that giardiasis is extremely common in budgerigars, yet most infected budgerigars are asymptomatic. Infection is also common in cockatiels, although disease is confined predominantly to nestlings that are near weaning age.

Two species of *Eimeria* (*E. dunsingi* and *E. haematodi*) and one species of *Isospora* (*I. psittaculae*) have been described in psittacine birds. The coccidium of canaries is *I. canaria*. These four organisms complete their life cycle in the intestine. Coccidia also infect many other species of birds, including cranes, waterfowl, and poultry. Coccidiosis in psittacine birds is rarely seen because current avicultural practices interrupt the infection cycle.

Coccidial infections may be inapparent or result in disease. When disease occurs, gross lesions varying from excessive fluid in the intestinal lumen to dilation of the intestine and gray-yellow foci are visible on the serosal surface (Fig. 3.84). A fibrinonecrotic enteritis occurs in severe cases. Histologically organisms will be present in enterocytes. Different species of coccidia have different trophisms for different portions of the intestinal tracts. In some cases, finding organisms in the enterocytes may be the only change (Fig. 3.85). In more severe infections, there is a variable nonsuppurative inflammatory response and there may be necrosis.

Cryptosporidiosis is reported in a wide range of birds, including ducks, chickens, psittacine birds, and ostriches. Infection

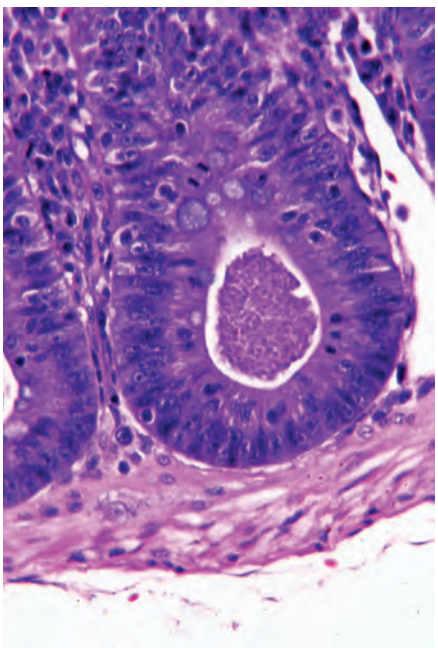

Figure 3.82 *Giardia* in intestinal crypts. No inflammatory reaction is seen.

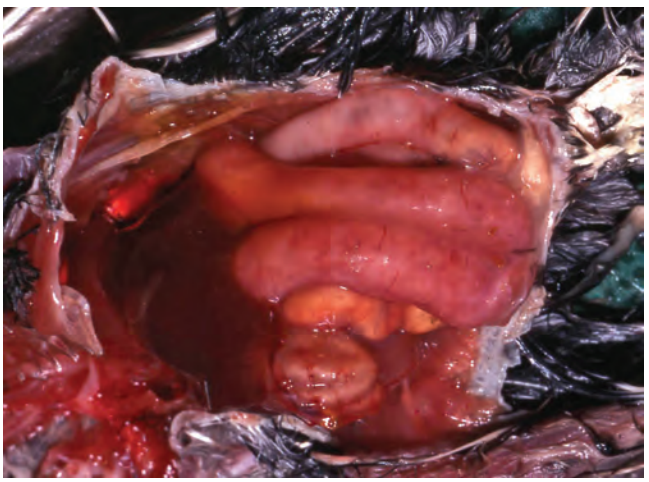

Figure 3.84 Enlarged and discolored intestines in a bird with clinical coccidiosis.

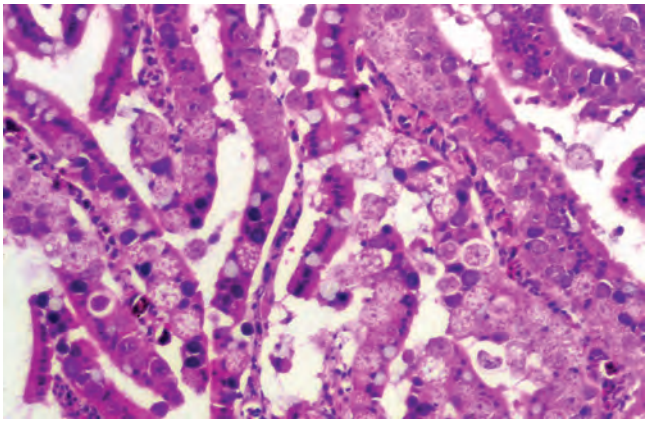

Figure 3.85 Coccidial organisms in enterocytes. Minimal necrosis is seen, but there is essentially no inflammation.

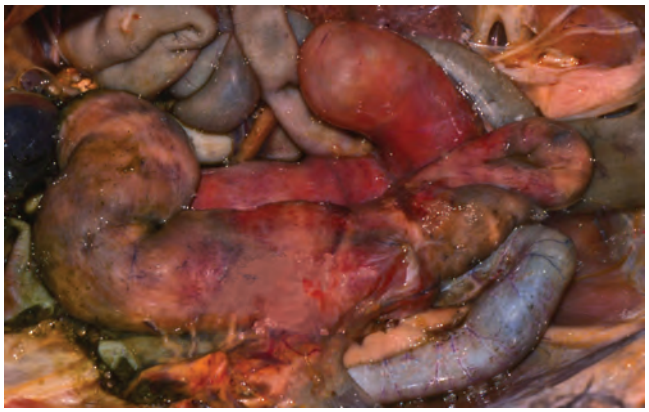

Figure 3.87 Enlarged, discolored cecum in a chicken with histomoniasis.

is not always associated with disease. Disease, in companion birds, is often secondary to another immunosuppressive disorder, but *Cryptosporidia* may also be the primary pathogen. Cryptosporidiosis is characterized grossly by mucosal thickening and excessive mucus production. Histologically, variable mucosal hyperplasia, mucus production, and a lymphoplasmacytic and histiocytic inflammatory response are seen. Villi may be misshapen and thickened. Atrophic villi are also seen in some cases. Small organisms are found in the microvillus border of enterocytes and in the surface mucus (Fig. 3.86).

Toxoplasmosis, is uncommon in pet birds, but has been reported in passerine birds, including canaries, and in lories, a regent parrot, a superb parrot, and a crimson rosella. It causes a systemic disease. Intestinal lesions may or may not occur. The intestines may be dilated, and there may be pasting of the vent, suggesting diarrhea. Multifocal to locally extensive necrohemorrhagic enteritis, with intralesional organisms, that may result in a transmural lesion and peritonitis is reported, but is not a consistent lesion.

Although not seen in common pet species, *Histomonas* is a cause of typhlitis, particularly in Galliformes. In turkeys, peafowl, quail, and uncommonly guinea fowl, histomoniasis can result in significant fatal disease. This particular protozoan parasite, *Histomonas meleagridis*, is transmitted through the embryonated eggs of the cecal nematode *Heterakis gallinarum*, harbored in earthworms. Birds given access to the ground and earthworms can be expected to be exposed to the *Histomonas* protozoa through its interesting lifecycle. Many healthy chickens will carry these infected cecal worms. So mixing of species, particularly chickens and turkeys, is discouraged and again can provide a differential with turkeys that are dying of the disease and are in contact with chickens. The gross lesions are of enlargement of the ceca, mottling of the cecal wall, and a caseous exudate in the lumen (Fig. 3.87). Histologically diffuse severe transmural necrosis extends are seen (Fig. 3.88). Organ-

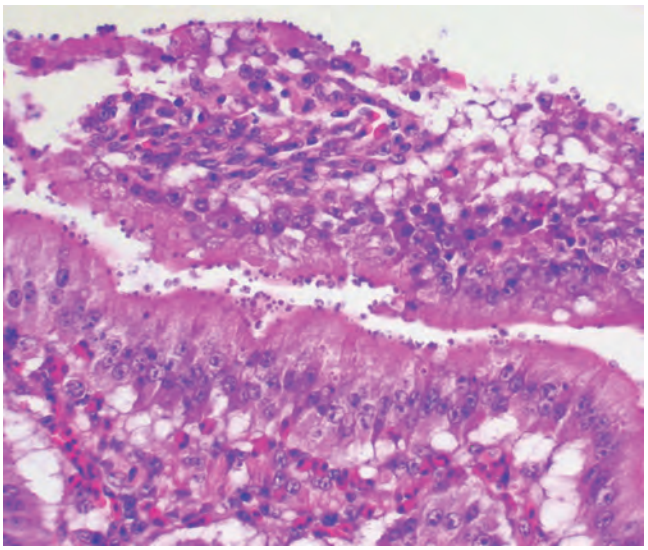

Figure 3.86 Intestinal cryptosporidiosis. The mucosa is variably proliferative and irregular. Organisms are present on the apical surfaces of enterocytes.

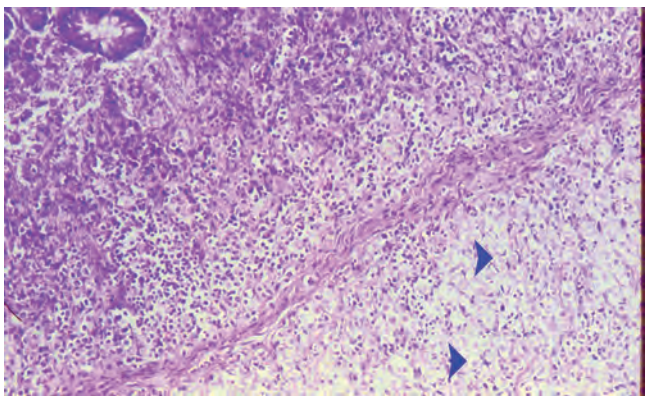

Figure 3.88 Severe transmural necrosis and inflammation of the cecum in histomoniasis. A few faintly staining organisms are present (arrowheads).

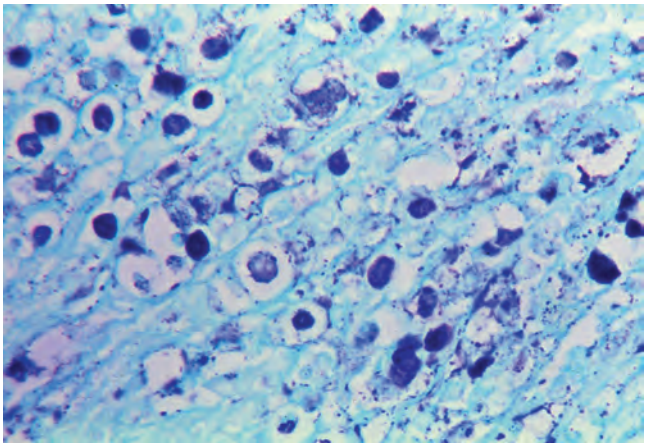

Figure 3.89 Silver-stained section to demonstrate *Histomonas* in necrotic tissue.

isms may be difficult to see unless special stains (PAS) are used (Fig. 3.89).

Metazoan parasites are infrequent causes of clinical disease in well-managed aviaries or in household pets. Cestodes are occasionally diagnosed at necropsy. There is usually no associated gross or histologic lesion (Fig. 3.90). Cestodes are particularly common in Australian finches and wild-caught African grey parrots and cockatoos. These parasites will survive in their hosts for many years and have the potential for causing intestinal obstruction in rare cases.

Birds with schistosomiasis may have scattered granulomas in the submucosa and muscularis. Egg fragments are usually seen in the lesions.

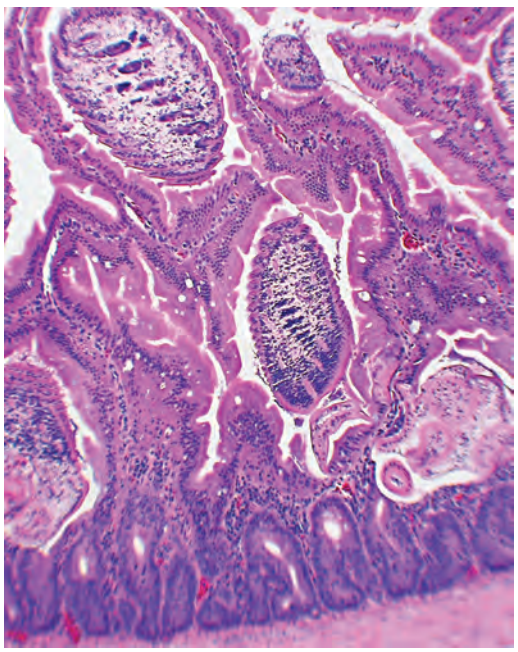

Figure 3.90 Cestode found incidentally at necropsy. No reaction is seen.

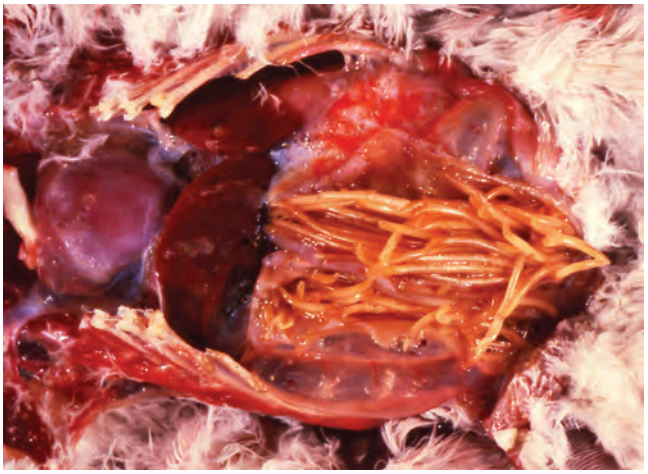

Figure 3.91 Ascarid infestation of the small intestine. The intestinal lumen was occluded, and numerous worms are seen.

A number of nematodes have been reported in cage birds. Ascarid infestations generally result in weight loss, anorexia, diarrhea, and death. Numerous parasites maybe found in the intestinal lumen in severe cases, and blockage of the intestine may occur (Fig. 3.91). Of particular concern are the roundworms of the genus *Ascaridia*. Roundworms are particularly common in Australian grass parakeets (*Neophema* sp.) and cockatiels that are raised in cages that reach the ground. Recently, roundworms of wild bird origin have been observed to cause intestinal disease in a macaw, Amazon, and cockatoos housed outdoors. Worms obstructed the intestinal tract of these birds and were also present in the bile and pancreatic ducts. Histologic lesions may be minimal and are usually characterized by an excessive accumulation of mononuclear inflammatory cells within the lamina propria of the intestine. Fragments of adults, larvae, and eggs can be found in the mucosa and the lumen. In some cases, invasion of the mucosa results in necrosis, severe inflammation, and occasional perforation of the intestinal wall. Rare reports in psittacines describe tissue migration of ascarid adult and/or larvae.

Acanthocephalids are rarely found in birds. As in mammals, they penetrate into the intestinal wall, and gross nodules are seen on the serosal surface. In addition to necrosis, there is a pleocellular inflammatory response.

Neoplastic disease

Primary neoplasms of the intestine include papillomas, carcinoma, and several types of sarcoma. Papillomas may be associated with psittacine herpesvirus infection, and birds with intestinal papillomas may also have similar lesions in the choana and/or cloaca, as well as proliferative changes in the bile ducts and pancreatic ducts. They can be multiple and are usually fairly well differentiated (Fig. 3.92). Carcinomas are infrequent. They present as variably sized masses that may be ulcerated on the

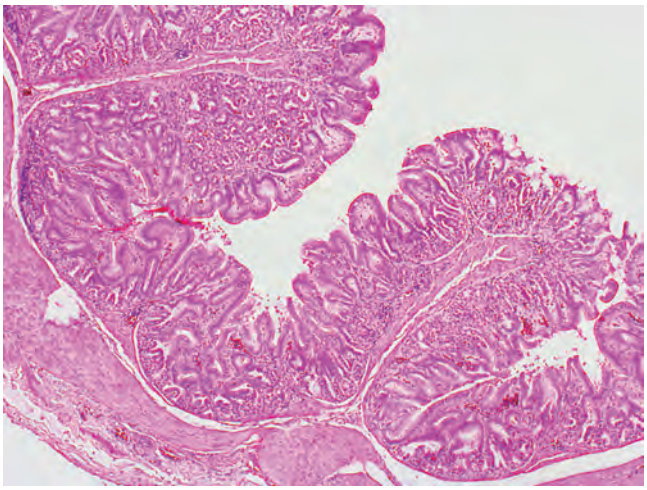

Figure 3.92 Multiple well-differentiated papillomas in the intestine.

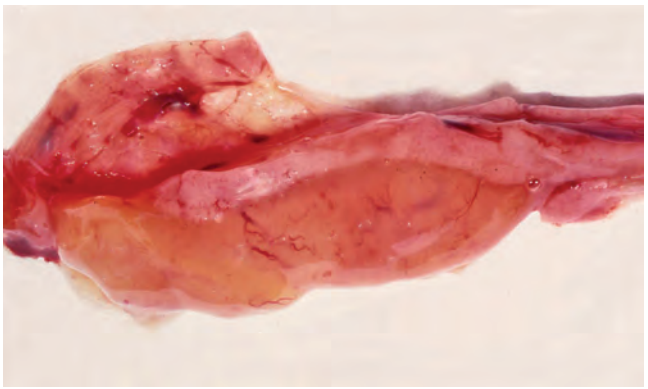

Figure 3.94 Myxosarcoma arising in the wall of the small intestine. Although not grossly conclusive, note the mucoid appearance of the tumor.

mucosal surface. Histologically they comprise poorly differentiated epithelial cells that form infiltrative nests and cords separated by minimal to moderate amounts of stroma (Fig. 3.93). Tumors metastasis has been identified in the lungs, heart, kidney, and adrenal glands. In one poorly differentiated intestinal carcinoma, the neoplastic cells were strongly positive for pancytokeratin and cytokeratin 8 and 18 and only partly positive for E-cadherin antibodies. The neoplastic cells were not immunoreactive to CD3 and NSE.

Sarcomas present as masses within the intestinal wall that vary from firm and red-brown to gray-white or yellow. Myxosarcoma (Fig. 3.94) will have a shiny myxoid appearance grossly and comprises anaplastic cells with fibrillar cytoplasm surrounded by myxoid ground substance. Fibrosaromas can arise within the muscular tunics. These tumors are nonencapsulated, invasive, and composed of densely cellular sheets, streams, and bundles of large, closely packed spindle-shaped cells with fine fibrillar cytoplasm. The high mitotic index is generally high. Fibrosarcoma with myxoid degeneration is also seen in pet birds and may have a similar gross and histologic appearance.

Leiomyomas and leiomyosarcomas comprise interlacing bundles of cells with fibrillar cytoplasm and vesicular nuclei. Differentiation between leiomyoma and leiomyosarcoma depends on mitotic activity and the degree of cellular anaplasia.

Lymphoma and histiocytic sarcoma of the intestinal tract usually present as a diffuse or nodular thickenings that must be differentiated from conditions such as mycobacteriosis (Fig. 3.95). Grossly the adjacent mesenteries may be involved. Neoplastic cells may extend from the mucosa to the serosa, usually effacing the normal architecture of the intestinal wall (Fig. 3.96).

In birds that are chronically infected by *Heterakis* sp., sarcomas can develop. Histologically these appear to be fibrosarcomas.

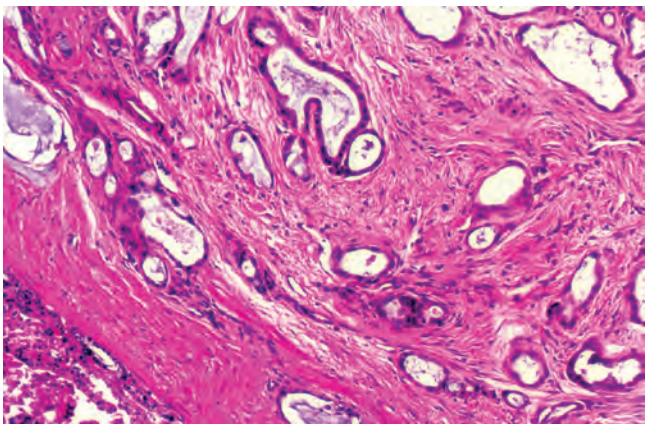

Figure 3.93 Infiltrative tubular structures in intestinal carcinoma. Neoplastic structures extend through the wall and elicit a variable amount of stromal proliferation.

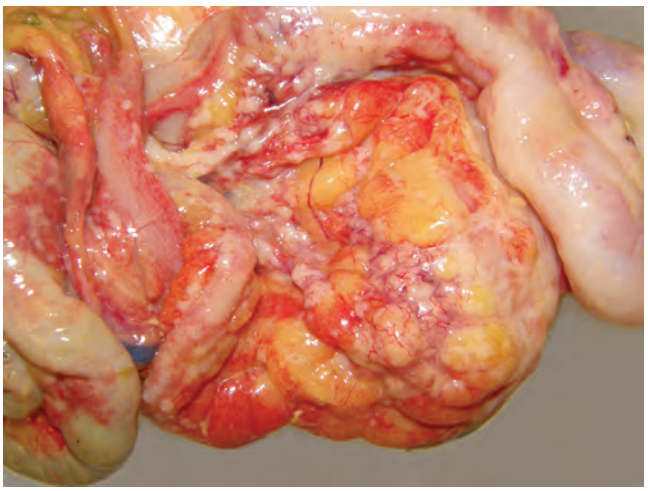

Figure 3.95 Malignant lymphoma involving much of the intestinal tract and adjacent mesentery.

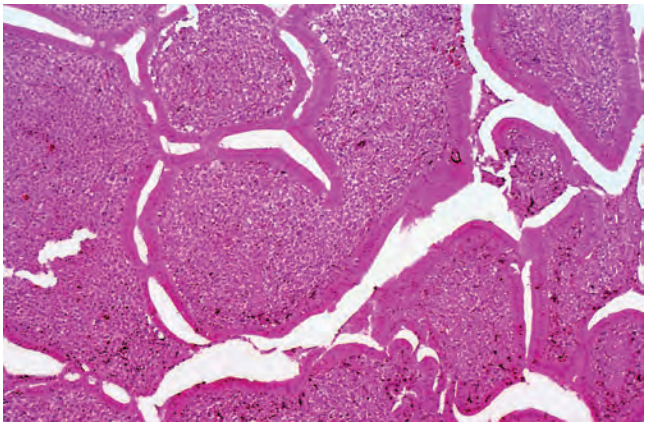

Figure 3.96 Effacement of the intestinal mucosa by a sheet of neoplastic histiocytic cells.

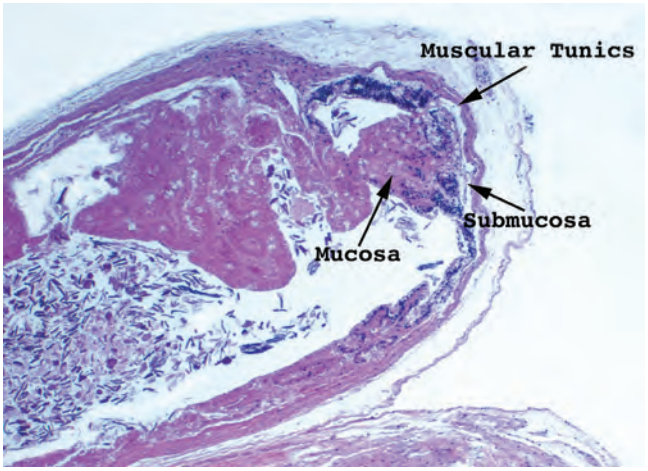

Figure 3.98 GI tract atresia. The large intestinal blind end near the cloaca was lined with mucosal epithelium, submucosa, and attenuated muscularis (arrows).

Cloaca

Noninfectious disease

Congenital anomalies include the atresia described in the series of helmeted guineafowl hatchlings mentioned previously. Grossly there was no connection between the end of the large intestine to the cloaca. Within the cloaca the closure was close to the level of the vent (coprodeum) (Fig. 3.97). Histologically the large intestinal blind end into the cloaca was lined with mucosal epithelium and submucosal tissue (Fig. 3.98). One lesion was suggestive of cord atresia, with a connection from the cloaca to the vent by a thin remnant of muscular tunic connecting the coprodeum and the proctodeum.

Impaction of the cloaca can result from a variety of causes, including failure to pass an egg, intrinsic disease of the cloacal wall, and loss of muscle tone due to virus-induced ganglioneuritis (PDD). Grossly there is dilatation of the cloacal wall, and it may be irregularly thickened (Fig. 3.99). The lumen may contain an egg, impacted fecal material, or products of inflammatory disease. Abscesses of the cloacal wall may partially obstruct the cloaca or rupture into the lumen of the cloaca.

There are a variety of causes of cloacal prolapse. The prolapsed mucosa will appear nodular or proliferative, and there may be areas of necrosis and hemorrhage. Histologic examination may be necessary to differentiate prolapse and associated inflammation from cloacal papillomatosis. The prolapsed mucosa will be somewhat thickened and inflamed, but mucosal epithelial cells will not be markedly hypertrophied, and papillary structures are not seen. A variable pleomorphic inflammatory infiltrate is usually present, and, if there is a primary or secondary infection, microorganisms may be seen. Cloacal prolapse is especially common in tame cockatoos and African grey parrots. It is speculated that behavioral factors and not disease cause the prolapse to occur. Cloacal prolapse is also a common condition in young male ostriches. In ostriches, infection with histomoniosis can lead to cloacal prolapse in young birds. The prolapsed tissues are congested and edematous. The ceca are distended with watery, brown material. Into the cloacal mucosa there are infiltrates of

Figure 3.97 Congenital atrestia of the GI tract leading to lack of a vent opening.

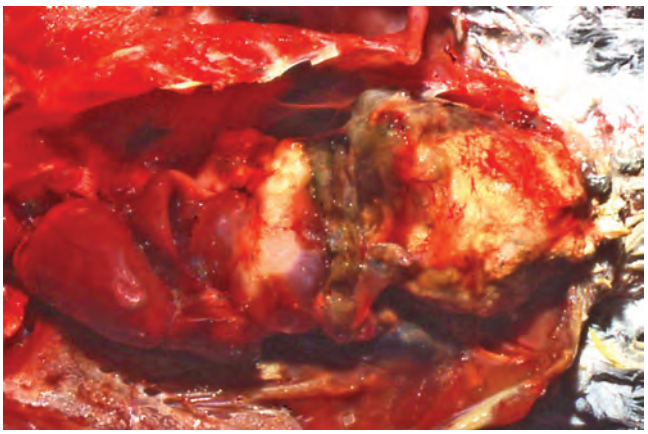

Figure 3.99 Dilated impacted cloaca. This appearance can be the end result of a variety of causes.

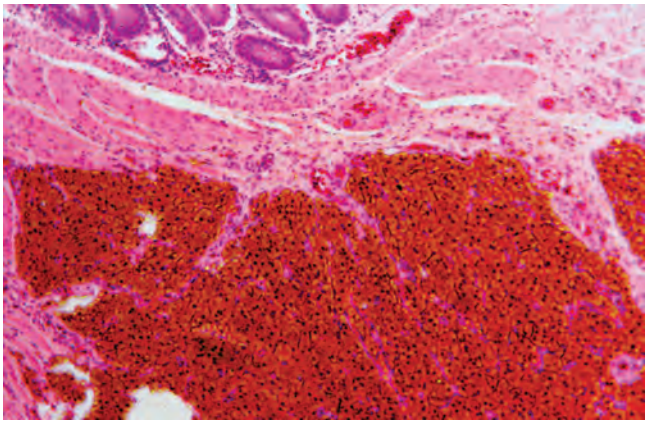

Figure 3.100 Phagocytosed barium being taken into the wall of the cloaca. Note the accompanying fibroplasia.

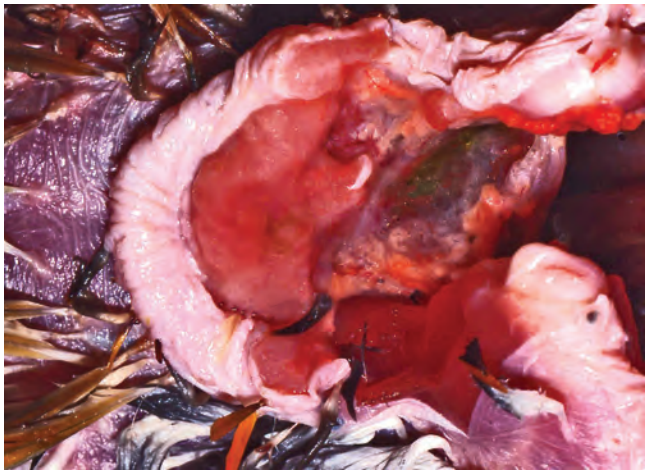

Figure 3.101 Typical appearance of cloacal papillomatosis.

lymphocytes and macrophages. Trophozoites of *H. meleagridis* can be identified in the feces.

The use of barium in radiologic diagnosis can lead to a lesion that is occasionally encountered at necropsy. The barium will be taken up by the mucosa of the large intestine and cloaca and is seen diffusely in the submucosa and muscularis. A slight discoloration of the cloacal wall may be seen grossly. Microscopically, free and phagocytosed barium is present as a brown crystalline material (Fig. 3.100), and there may be mild fibroplasia.

Infectious disease

Infections affecting the cloaca are the same as those seen in the upper intestinal tract, and the gross and histologic features are similar.

Neoplastic disease

Papilloma is the most common cloacal neoplasm. They are more common in New World parrots, particularly Amazon parrots and macaws, and occur in the cloacal mucosa near the junction with the skin but may extend into the cloaca for some distance (Fig. 3.101). Lesions may be focal or diffuse. When the papillomas are large, they prolapse and ulcerate. Chronic soiling of the surrounding skin leads to inflammation, fibrosis, and stricture of the vent. If repeated surgical removal of the cloacal papillomas is performed, strictures of the cloaca develop.

Histologically they are typical papillomas covered by a layer of stratified cuboidal to pseudostratified columnar epithelial cells (Fig. 3.102). The thickness of the epithelial layer can vary considerably, depending on where in the cloacal mucosa the lesion originates. A fibrovascular core supports the epithelium. Lymphoplasmacytic infiltration of the fibrovascular core is a common, but inconsistent, finding. In some birds, there is an apparent correlation between the occurrence of cloacal papillomas and proliferative biliary, pancreatic, or upper intestinal lesions, and these changes should be ruled out in affected birds. The etiology of this lesion in New World parrots is felt to be PsHV's, identical or closely related to those that cause Pacheco's disease. Mucosal papillomas have developed in some parrots that survived the acute PSHV infection (Pacheco's disease). No herpesvirus or papillomavirus has been identified in the cloacal papillomas of cockatoos or cockatiels.

Cloacal carcinoma is an infiltrative tumor that leads to thickening of the cloacal wall (Fig. 3.103). Carcinomas are usually firm and gray-white. They comprise moderately undifferentiated to poorly differentiated epithelial cells that form infiltrative cords and nests. There is usually moderate to abundant scirrhous stroma, and necrosis and hemorrhage are seen (Fig. 3.104).

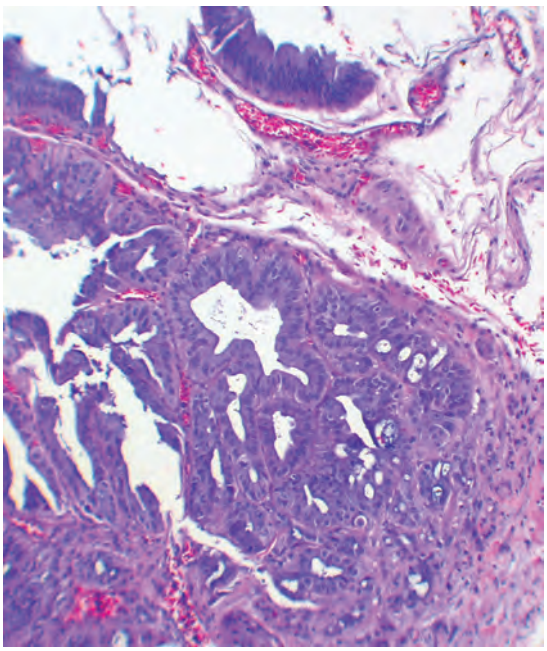

Figure 3.102 Multiple papillary structures in cloacal papillomatosis. Vascular stroma are covered by hypertrophied epithelial cells.

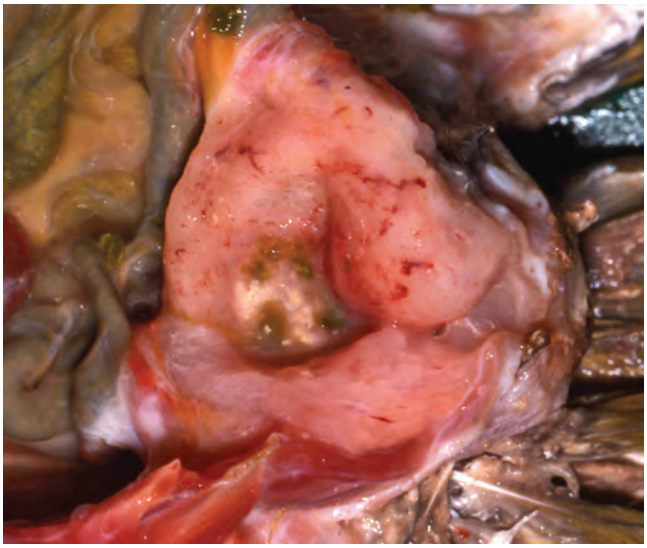

Figure 3.103 Typical presentation of cloacal carcinoma which involves almost the entire circumference of the cloaca.

Smooth muscle tumors and fibrosarcomas are infrequently reported. They present as thickened, firm lesions of the cloacal wall or may protrude from the vent. Histologically the smooth muscle tumors are typical and differentiation between benign and malignant varieties must be done by established cytologic criteria. Fibrosarcomas composed of interlacing bundles of pleomorphic spindle cells with numerous mitotic figures. In one canary, the neoplastic cells were positive for vimentin and negative for desmin and actin. The ultrastructural features included dilated stacks of rough endoplasmic reticulum, intermediate filaments, rare collagen secretion granules, and lacked external lamina typical of fibroblasts. The cell nuclei were irregular with prominent nucleoli and frequently had irregular invaginations with pseudoinclusion formations.

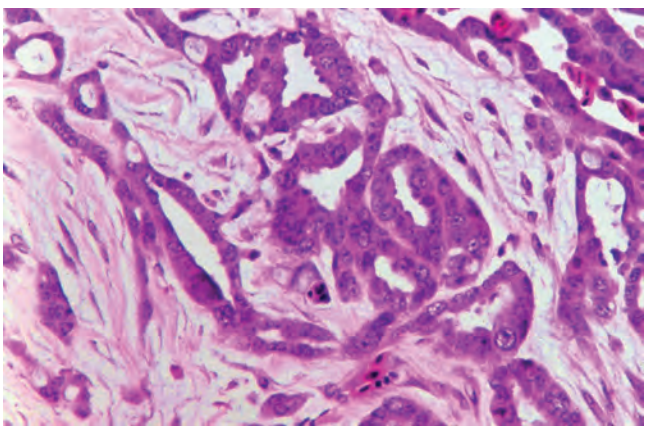

Figure 3.104 Cloacal carcinoma. Tubular and trabecular structures are infiltrative into a dense fibrous stroma.

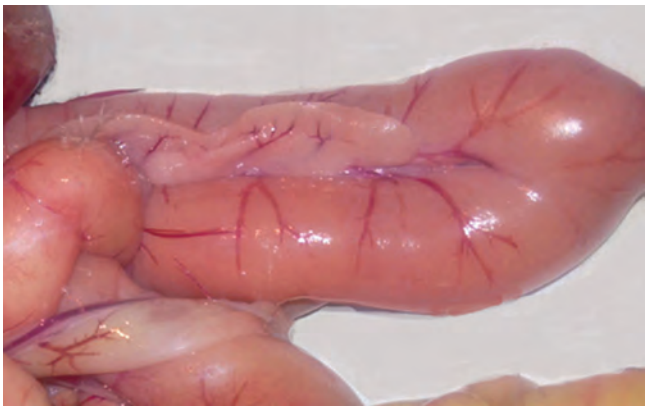

Figure 3.105 Atrophic pancreas. These can be either congenital or acquired.

Exocrine pancreas

Diseases affecting the exocrine pancreas may also affect the islets of Langerhans. Specific diseases of the endocrine pancreas are covered in Chapter 10.

Noninfectious disease

Prolonged caloric deficiency in birds will lead to pancreatic atrophy. Grossly the panacreas may be small (Fig. 3.105), or the change may not be visible, but histologically there is acinar epithelial atrophy (Fig. 3.106) associated with a normal islets of Langerhans.

The pancreas is the target organ in cases of zinc toxicity. Gross lesions may not be noticeable, but parenchymal mottling is occasionally seen (Fig. 3.107). The primary microscopic lesion is vacuolation and degranulation of acinar cells (Fig. 3.108). Necrosis of individual cells may also be present. Minimal mononuclear inflammatory infiltrates may be seen.

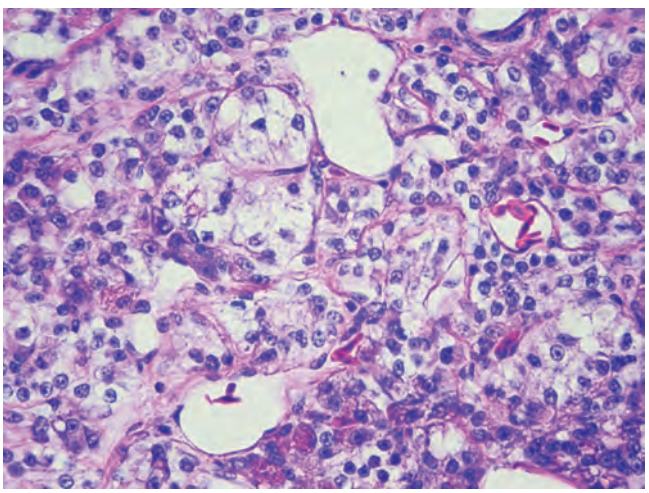

Figure 3.106 Atrophic pancreas with small acini comprised of cells with no zymogen.

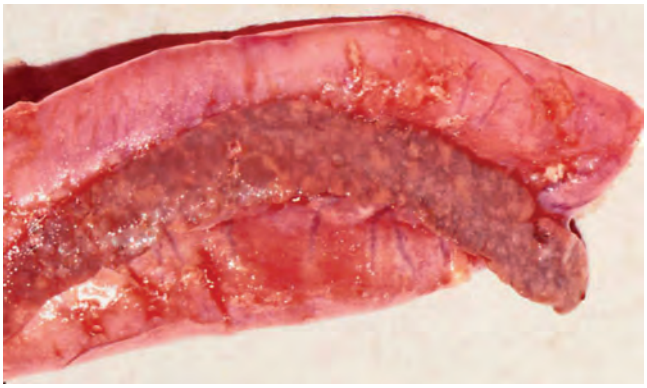

Figure 3.107 Multifocal to confluent pancreatic necrosis typical of what can be seen in zince toxicosis.

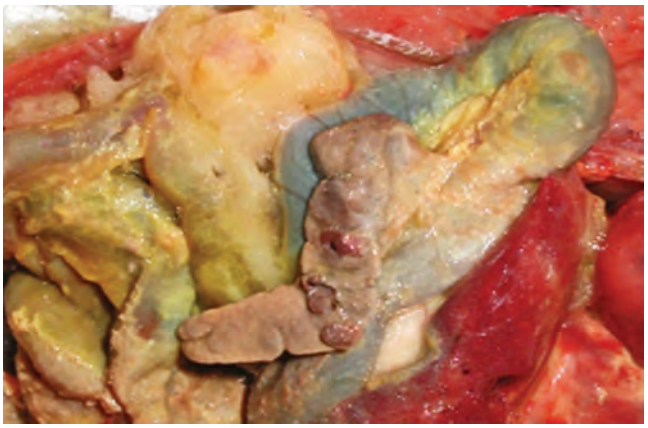

Figure 3.109 Acute, diffuse pancreatic necrosis in a Quaker parakeet. The pancreas is discolored and foci of hemorrhage are seen.

Acute pancreatic necrosis is seen in psittacine birds, particularly Quaker parakeets. Many of these birds die suddenly. Gross lesions include a firm pale pancreas, variable hemorrhage, and adjacent fat necrosis characterized by firm yellow-white foci. A marked serous and serosanguineous effusion has been reported in one cockatoo. Gross changes are due to acute coagulation necrosis of pancreatic acini, hemorrhage within the pancreatic lobules, and multifocal necrosis of mesenteric adipose tissue (Fig. 3.109). The pancreas will be friable and discolored and red foci can be seen. Histologically there is diffuse, severe coagulation necrosis (Fig. 3.110). One of the causes of the lesions maybe a high-fat diet, but the exact cause has not been determined.

Fat accumulation in the pancreatic acinar cells sometimes accompanies severe fatty liver disease, as is sometimes seen in Amazon parrots. This change is usually not grossly visible.

Pancreatic fibrosis of undetermined cause is also seen infrequently. Grossly the pancreas is firm and irregular, and microscopically interstitial fibrosis replaces normal acini (Fig. 3.111).

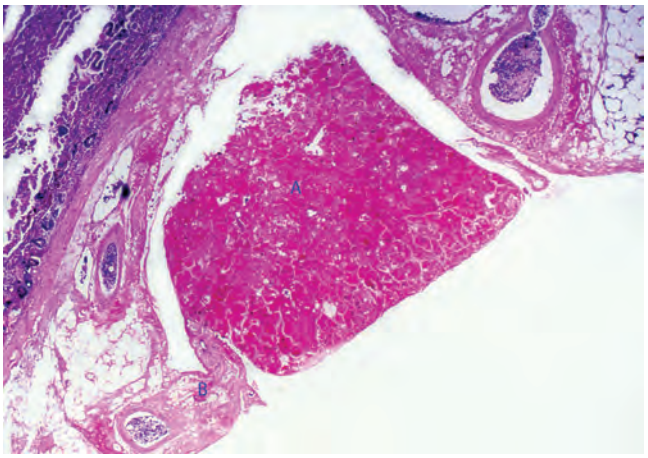

Figure 3.110 Acute pancreatic necrosis. There is total coagulation of pancreas (A) and minimal necrosis of peripancreatic fat (B) and fibrin deposition.

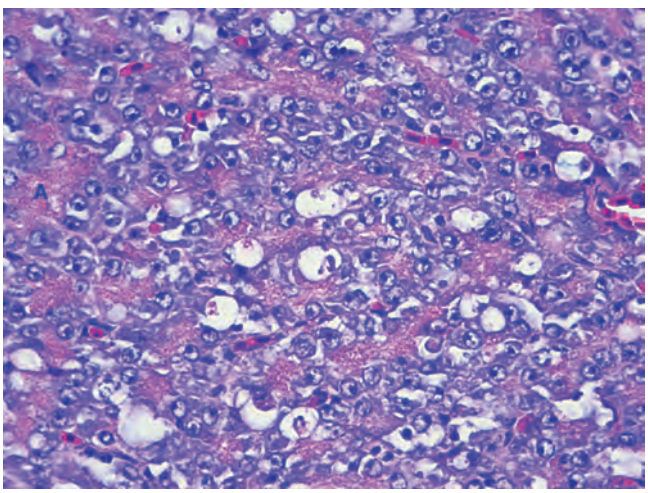

Figure 3.108 Pancreatic acinar degeneration and vacuolation consistent with zinc toxicity. More normal cells are at the lower left.

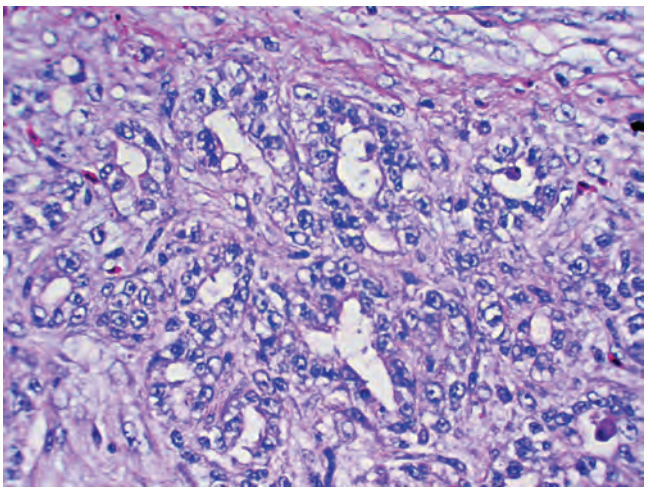

Figure 3.111 Severe pancreatic fibrosis. Acinar remnants are scattered throughout the section.

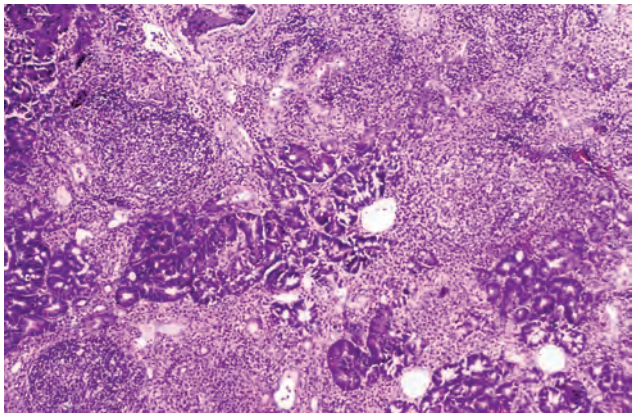

Figure 3.112 Chronic lymphohistiocytic inflammation in the pancreas of a bird with chronic paramyxovirus-3 infection.

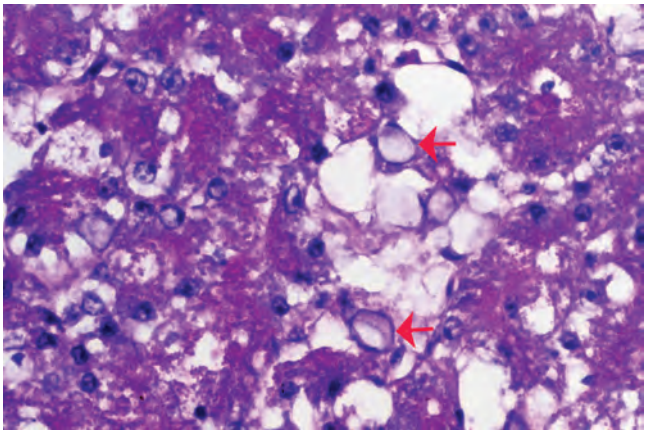

Figure 3.114 Polyomavirus infection. There is karyomegaly and inclusion body formation in pancreatic acinar cells (arrows).

Infectious disease

Viral and bacterial agents reported to cause pancreatitis include herpesvirus, polyomavirus, adenovirus, paramyxovirus (PMV-3), poxvirus, a variety of gram-negative bacteria, and *Chlamydia*. Gross lesions vary from none to hemorrhage and necrosis, and there may be a purulent exudate in cases of bacterial pancreatitis.

Paramyxovirus can cause chronic pancreatitis, particularly in *Neophema* sp. and small passerine birds. Affected pancreases are firm and irregular. A variable lymphoplasmacytic and histiocytic inflammatory response and lymphoid follicle formation characterize the lesion (Fig. 3.112). Fibrosis is seen in some cases.

Herpesvirus, polyomavirus, poxvirus, and adenovirus usually induce pancreatic necrosis and variable inflammation as part of a systemic disease process. Etiologic specificity is determined by finding characteristic intranuclear inclusion bodies (Figs. 3.113, 3.114, and 3.115).

Bacterial infection is histologically characterized by necrosis, fibrin deposition, and a primarily heterophilic response, whereas infection with *Chlamydphila psittaci* results in a nonsuppurative pancreatitis. In systemic mycobacteriosis there may be granuloma formation.

Parasitic pancreatitis can follow the plugging of pancreatic ducts by nematodes or trematodes. Grossly pancreatic ducts are thickened and prominent. Trematodiasis may result in brown-black pigmentation (Fig. 3.116). Histologically the pancreatic ducts are dilated and contain the parasites in the duct. Inflammatory changes are minimal to mild (Fig. 3.117). Pancreatic trematodiasis is seen almost exclusively in Amboina king parrots.

Cryptosporidia have the potential to colonize the epithelium of pancreatic ducts.

Proliferative and neoplastic disease

Pancreatic duct hyperplasia and papilloma formation are seen in some birds with internal papillomatosis. They may accompany bile duct changes or occur independently of them.

Low-grade papillary adenocarcinoma is occasionally seen. These tumors are comprised of moderately undifferentiated cells within acinar-like structures. Groups of these structures form papillary projections (Fig. 3.118).

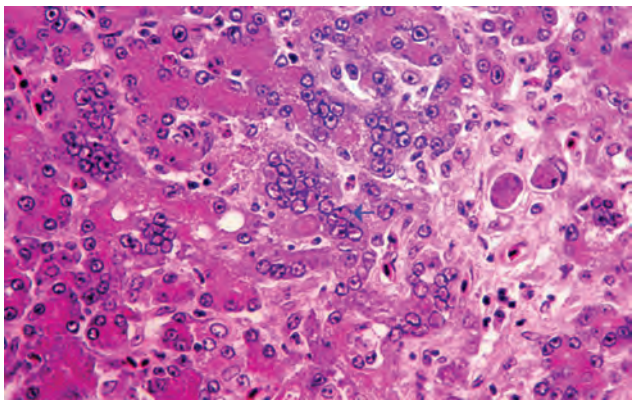

Figure 3.113 Herpesvirus infection of the pancreas. Necrosis, syncytial cell formation, and intranuclear inclusion bodies are seen (arrow).

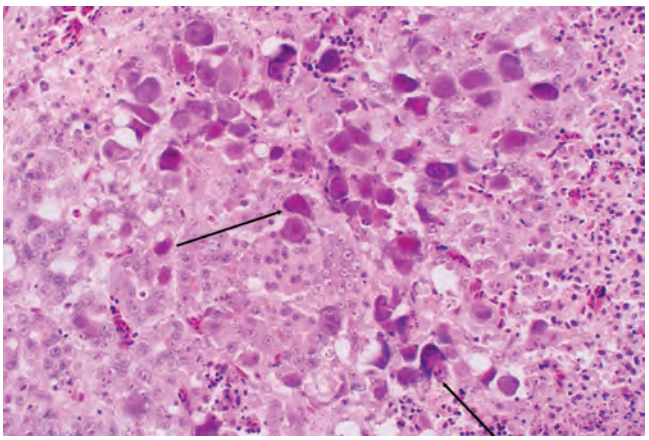

Figure 3.115 Adenovirus infection. Typical large basophilic intranuclear inclusion are seen (arrows).

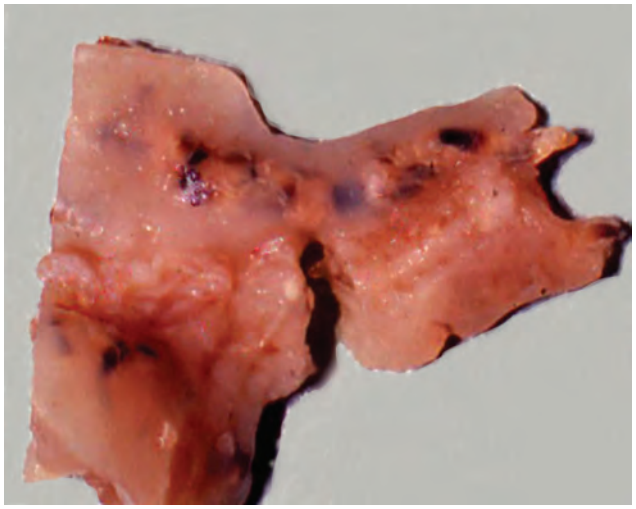

Figure 3.116 Pancreatic flukes (discolored areas) in a king parrot.

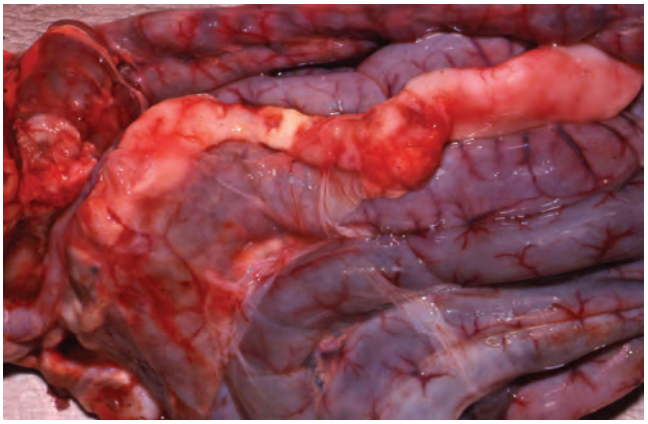

Figure 3.119 Pancreatic carcinoma. The pancreas is irregular with multifocal enlargements. Adhesion to mesenteries and the intestine are seen.

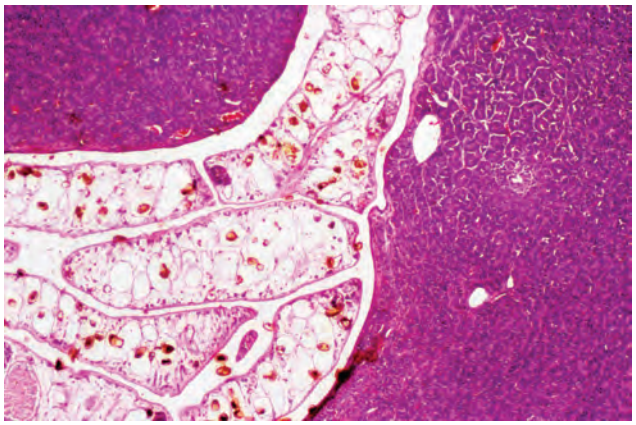

Figure 3.117 Trematode in pancreatic ducts. Variable periductal cellular swelling and edema are seen.

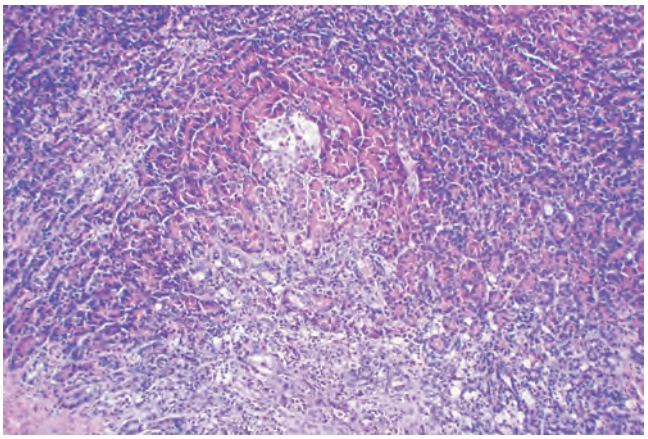

Figure 3.120 Pancreatic carcinoma. Irregular acinar and tubular structures are infiltrating and replacing normal pancreas.

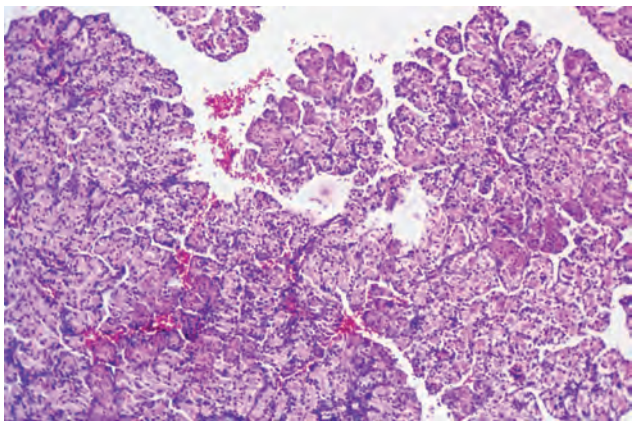

Figure 3.118 Low-grade papillary adenocarcinoma of the pancreas. This type of tumor is unusual in birds.

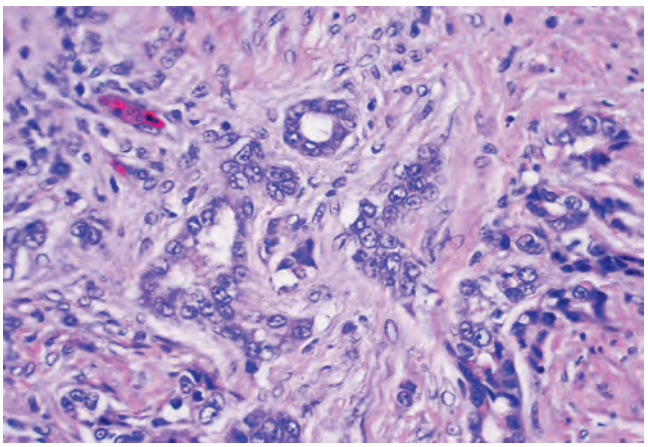

Figure 3.121 Higher magnification detail of Figure 3.121. There is a moderate scirrhous response.

Carcinomas are usually infiltrative, with poorly defined borders. Grossly there may be obvious infiltration of the adjacent small intestine (Fig. 3.119), and, in severe cases, most of the normal pancreatic architecture is lost. There may be severe adhesion formation binding the intestines and other organs into a solid mass. These tumors occur most commonly in cockatiels. Abdominal effusion is another common manifestation of this disease. Carcinomas comprise poorly differentiated epithelial cells that form acini, nests, and trabeculae that efface normal pancreatic tissue and extend into surrounding tissue (Figs. 3.120 and 3.121).

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4 Liver

Normal structure

The avian liver comprises right and left lobes that fuse on the midline in the dorsal middle to cranial third. Cranially and caudally the lobes are completely separated by cranial and caudal incisures. The incisures incompletely penetrate the middle third of the liver as they cross its ventral surface and join. Additional subdivision into dorsal and ventral sections may occur in right or left lobe. The right lobe is usually larger than the left lobe in the majority of species of birds. However, lobes can be of equal size, and rarely the left lobe of the liver is larger than the right in some species. The cranial aspect of both liver lobes surrounds the ventral surface of the heart apex. The ventral surface of the liver is in direct contact with the sternum, and, in the majority of birds, the normal liver does not extend beyond the caudal edge of the sternum. The gallbladder, when present, is located on the visceral surface of the right lobe. It may be pear shaped or long and cylindrical. The gallbladder may extend caudally to the level of the cloaca in some species. Although present in the rock dove, the gallbladder is absent in most species of pigeons and doves, in psittacine birds, and in the ostrich. The proventriculus, ventriculus, and spleen are in contact with, and leave impressions on, the visceral surface of the liver. The right and left hepatic peritoneal cavities are completely enclosed by the posthepatic septum, parietal peritoneum, dorsal and ventral mesenteries, and left hepatic ligaments. Fluid leaking from the liver capsule is trapped within the hepatic peritoneal spaces and does not enter the intestinal peritoneal space.

The liver has two sources of blood: the hepatic arteries and the hepatic portal veins. The right and left portal veins drain the intestines. The right and left hepatic arteries originate from a bifurcation of the celiac artery. Both hepatic arteries and portal veins enter the liver through the hilus. From the hilus, the hepatic arteries and portal veins branch to form a network that extends to the periphery of the liver. As they branch into the liver, branches of the biliary system, which drain the liver, accompany them. The combination of portal vein, hepatic artery, and bile ducts are called the portal triad. The hepatic portal veins drain into the hepatic sinusoids. The hepatic arteries also connect with the sinusoids by arterioles or through a capillary plexus. Hepatocytes are polygonal cells with a large spherical, oval, centrally located nucleus. The cytoplasm of the hepatocytes contains many mitochondria and an extensive system of smooth and rough endoplasmic reticulum. Branching laminae of hepatocytes, one to two cells thick, make up the parenchyma of the liver. The sheets of hepatocytes are separated by sinusoids that are lined by fenestrated endothelial cells and phagocytic Kupffer cells. Between the endothelial cells and the hepatocytes is a space (the space of Disse) that surrounds the hepatocytes with plasma. Bile drains from the hepatocytes into bile canaliculi that are on the opposite side of the hepatocytes from the space of Disse. The bile canaliculi drain into intralobular bile ducts.

Structurally the liver is divided into lobules. Each lobule has a central hepatic vein (central vein) that receives the drainage of the sinusoids. The portal triads are present at the periphery of the lobules. The lobules of some mammals (e.g., pigs) are well defined by connective tissue. The lobules of birds, however, are not defined, and the hepatic parenchyma appears continuous. The central veins drain into the right and left hepatic veins that fuse in the liver to form the caudal vena cava that exits the cranial aspect of the liver on its dorsal surface. The canaliculi drain the lobules into the interlobular ducts of the portal triads. These come together to form the lobar bile ducts, which fuse to form the right and left hepatic ducts and ultimately the hepatoenteric duct, which enters the duodenum. If a gallbladder is present, it is connected to the hepatoenteric duct by the hepatocystic duct. Bile ducts are lined by simple cuboidal or columnar epithelium and surrounded by loose connective tissue. There may be elastic fibers or smooth muscle around larger ducts. The gallbladder has the same layers as the hepatoenteric bile duct.

Microscopically the capsule of liver comprises a thin layer of collagen and elastic fibers. It is continuous with the interstitial connective tissue. Intrahepatic loose connective tissue is most prominent in portal areas.

Normal variations in the gross and microscopic anatomy of the liver are seen in embryos and recently hatched chicks. The liver of precocial species is yellow at hatch and remains that way for 8–14 days before becoming the red-purple of the adult liver.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

Figure 4.1 Congenital biliary cyst in a Pionus parrot. This is an infrequent finding in birds.

The yellow is due to the pigment carried with the lipids that arrive from the yolk sac in the later stages of incubation. Microscopically the hepatocytes will have a foamy appearance due to their large content of glycogen and lipid that is being reabsorbed from the yolk. In altricial species, the liver is usually red-purple from the time of hatching. Extramedullary hematopoiesis occurs in the embryonic liver. Some hematopoietic activity remains for varying times after the hatching.

Hepatic extramedullary erthyropoiesis is a common finding in birds with chronic blood loss. Likewise, hepatic extramedullary granulopoiesis occurs in some birds with chronic inflammatory diseases. The nutritional status of a bird may have an impact on the liver. Birds that have been in a negative calorie balance prior to death will tend to have a smaller liver than that of well-nourished birds. If a bird has recently eaten, hepatocytes increase their glycogen and lipid causing them to enlarge and develop a foamy cytoplasm.

Hepatic disease

Congenital disease

Extrahepatic biliary cysts are occasionally seen in birds (Fig. 4.1). Other anomalous lesions are not reported.

Infectious disease

Viruses

Psittacid herpesvirus-1

Psittacid herpesvirus-1 (PsHV-1) is a heterogeneous group of avian herpesviruses. Serologically three to five serotypes are recognized and there are four genotypes. There is a direct correlation between genotype and serotype. All genotypes can cause an acute fatal disease (Pacheco's disease) in parrots, although there may be differences in the pathogenicity of each genotype for various species. An identical disease caused by a herpesvirus that is reported to have occurred in toucans is assumed to have been caused by a PsHV. There is a single report of PsHV-1 genotype 1 causing a Pacheco's-like disease in a passerine. PsHV-1 is maintained in nature in birds that are persistently infected with the virus. Amazon parrots and certain species of conures and macaws have been shown to shed virus continuously in oral secretions and feces. Ingestion, inhalation, and conjunctival exposure have experimentally been shown to result in infection and disease. Parent-fed offspring of adult birds infected with the PsHV-1 can become infected with PsHV-1 and not develop signs of disease. Horizontal transmission rather than vertical transmission is suspected in these birds.

Pacheco's disease may occur in an individual bird or as an explosive outbreak. Signs of disease are often minimal or entirely absent prior to death. Necropsy specimens are typically well muscled and have adequate body fat. Uncommonly, there will be some degree of atrophy of the pectoral muscle mass. Grossly, the liver may be enlarged and friable. Often, however, the disease progresses so quickly that the liver is not enlarged. In these cases, the liver may appear normal or contain focal areas of discoloration that represent foci of necrosis. Whether the liver is enlarged or not, it often has a variable yellow-gray mottling, with or without hemorrhage (Figs. 4.2 and 4.3). Diffuse color changes in the liver may be mistaken for hepatic lipidosis. Histologically, acute hepatic necrosis is a nearly consistent finding. Necrosis is multifocal and moderate to massive without a specific anatomic distribution. When the necrosis is massive, only the hepatocytes adjacent to the portal triads do not die. The amount of inflammation present is generally minimal and often completely absent. Syncytial cell formation may occur but is uncommon. Intranuclear inclusion bodies are typically abundant but may be rare or absent. When there is massive necrosis, inclusion bodies

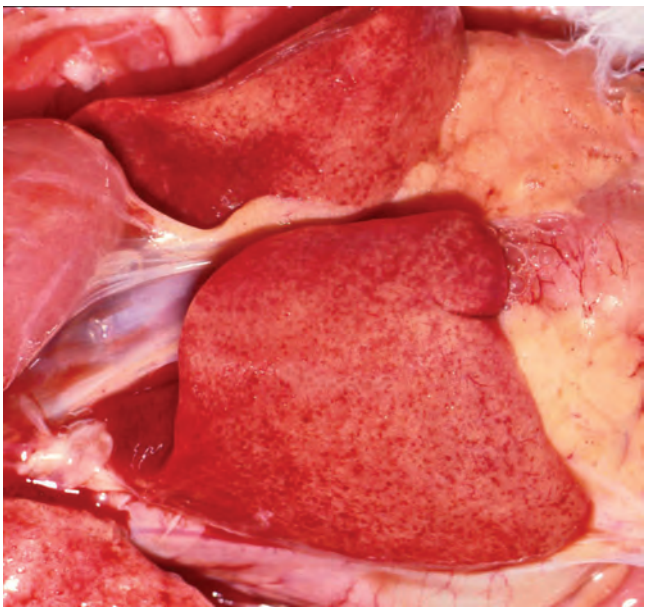

Figure 4.2 Enlarged, mottled liver due to Pacheco's disease. Hemorrhages are seen in the liver and other tissues.

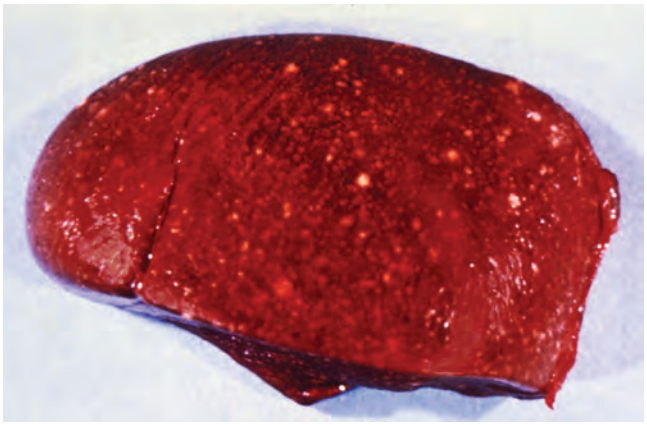

Figure 4.3 Severe necrosis leading to the "scotch grain" appearance of the liver in Pacheco's disease.

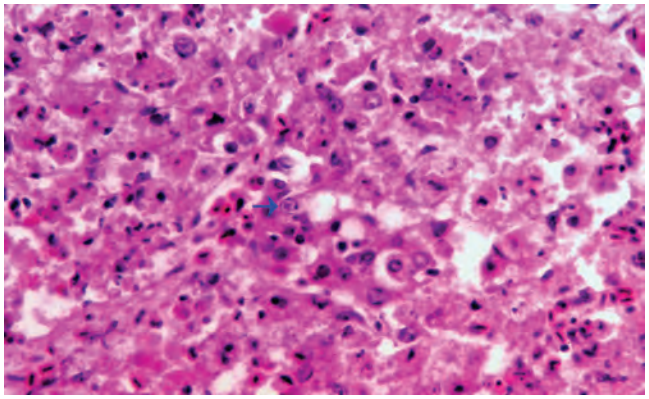

Figure 4.5 Almost complete loss of cellular detail in a herpesvirus-infected liver. Intranuclear inclusion bodies with distinct halos can be seen (arrow).

are often found only in the nuclei of the biliary epithelium. The inclusion bodies may fill the nucleus, or there may be a clear zone between the inclusion and marginated chromatin (Figs. 4.4, 4.5, and 4.6). Inclusion bodies are typically deeply eosinophilic but may be lightly basophilic.

Extrahepatic lesions occur with a fair degree of frequency in PsHV-1 disease. Splenic necrosis with the presence of viral inclusion bodies is common but is less consistent than hepatic necrosis (Chapter 8). Multifocal necrosis and viral inclusion bodies within the pancreas are also relatively common findings. The amount of necrosis is generally mild but may be locally extensive in rare cases. The crop is another commonly affected organ. The crop epithelium is affected by multifocal ballooning degeneration of the basal cell layer, causing erosions, ulcers and, rarely, vesicles. Inclusion bodies are also present in these lesions. Intestinal lesions are relatively uncommon and generally mild, often being confined to the presence of inclusion bodies in the nuclei of crypt epithelial cells (Chapter 3). Rarely a severe necrotizing tracheitis will also be observed (Chapter 2). Extrahepatic lesions may occur in the absence of hepatic necrosis in unusual cases.

PsHV-1 genotypes 1, 2, and 3 are the cause of mucosal papillomas (see Chapter 3). PsHV-1 genotype 3 is the only one of these genotypes that is also the cause of biliary and pancreatic duct carcinomas. These carcinomas can develop within a year of infection with PsHV-1 genotype 1.

Avian polyomavirus (APV) and adenoviruses also cause intranuclear inclusions and hepatic necrosis. Both of these viruses typically cause some degree of nuclear enlargement and generally have lightly basophilic to clear (APV) or deeply basophilic (adenovirus) inclusion bodies. Additional diagnostic tools available for differentiating these viruses include DNA *in situ* hybridization, immunofluorescent staining, polymerase chain reaction (PCR) using herpesvirus-specific primers, electron microscopy of fixed tissues (Fig. 4.7) or the supernatant of homogenized tissues, and virus isolation in primary chicken embryo fibroblasts or embryonated eggs. PsHVs are typical herpesviruses and under the electron microscope are enveloped

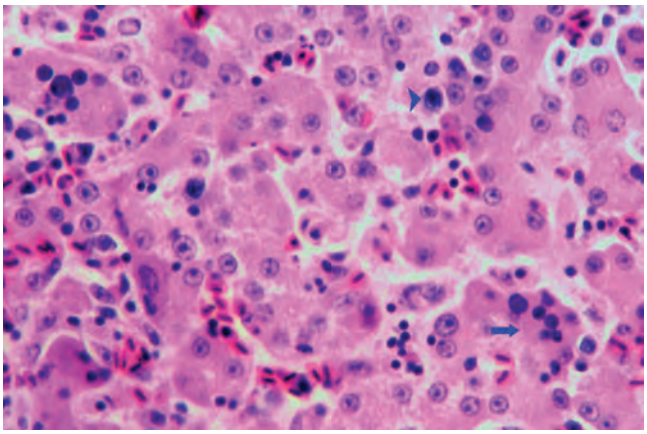

Figure 4.4 Pacheco's disease. There is an area of diffuse necrosis and inclusion body formation, and many dark intranuclear inclusions fill the nucleus (arrowhead). Syncytial cell formation is also present (arrow).

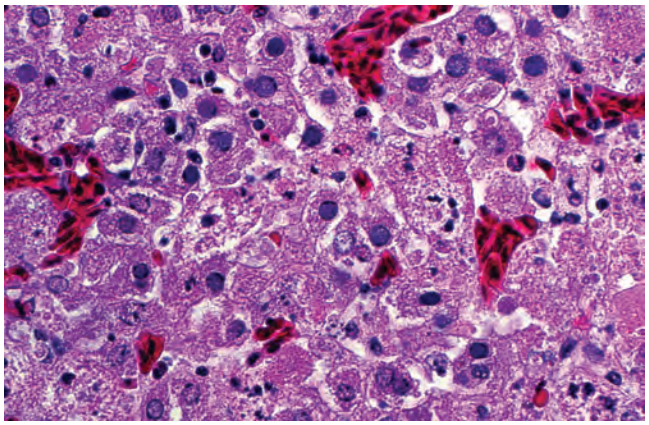

Figure 4.6 Minimal necrosis and well-defined intranuclear inclusion bodies due to herpesvirus infection.

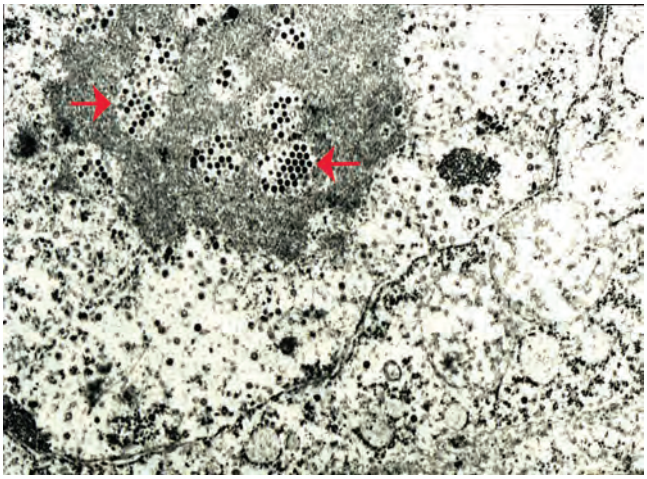

Figure 4.7 Herpesviral particles (arrows) in an intranuclear inclusion body.

and are approximately 180–220 nm in diameter. At the time of death, birds are viremic, and virus can be isolated from lung, liver, kidney, spleen, and brain. All of these organs would also be positive by PCR. PsHVs are found in the liver of some birds that do not have Pacheco's disease. Therefore a positive PCR assay in the absence of characteristic lesions of Pacheco's disease implies that the virus was not the cause of death. Although not precise, with experience, the inclusion bodies of herpesvirus, polyomavirus, and adenovirus can be differentiated on light microscopy, particularly in psittacine birds. In pigeons there are fewer differences between adenovirus and herpesvirus inclusions in the liver.

Columbid herpesvirus 1 (CoHV-1) infection occurs worldwide and is found in virtually every domestic pigeon (rock doves) loft and is widespread in feral rock doves. Once established, it persistently and subclinically infects most if not all birds in a flock. In these flocks, disease is only seen in the pigeons immunosuppressed with a concurrent infection with the pigeon circovirus. However, when CoHV-1 is newly introduced to a collection it can cause a high level of mortality. Hepatic necrosis is a common feature of the disease caused by CoHV-1 and lesions in the spleen, pancreas, and intestine may also be observed. It is now recognized that CoHV-1 is the same virus that causes disease in owls and falcons and that these infections generally result from feeding these birds of prey-infected pigeons. Hepatic, splenic, pancreatic, and intestinal necrosis are all features of CoHV-1 infections in falcons and owls.

Herpesvirus infections also occur in a number of other species of birds that are kept in captivity and in wild birds. These infections include duck virus enteritis that causes massive and localized outbreaks in wild and feral ducks in North America, crane herpesvirus, frigate bird herpesvirus, vulture herpesvirus, and passerid herpesvirus-1 and gallid herpesvirus-1. In many but not all instances, that is, passerid herpesvirus 1, gallid herpesvirus-1, and vulture herpesvirus, hepatic necrosis with inclusion bodies are a common finding in birds with these infections.

Passerid herpesvirus 1

Passerid herpesvirus 1 is the cause of systemic disease in finches. The primary clinical signs and lesions are seen in the respiratory tract (Chapter 2), but the liver also may be affected. Gross changes include yellow-white foci typical of necrosis. Histologically there is necrosis and distortion of intact hepatocytes, many of which have karyomegalic nuclei and large basophilic intranuclear inclusion bodies.

Polyomaviruses

To date, seven polyomaviruses have been discovered that infect birds and it is likely that there are many more. Little is known about the biology and pathogenicity of the butcherbird polyomavirus, the crow polyomavirus, and a recently discovered polyomavirus in budgerigars. The goose polyomavirus causes a hemorrhagic nephritis and less frequently enteritis in commercially raised goslings.

The APV, canary polyomavirus, and the finch polyomavirus cause similar disease in their respective hosts. The best studied is the APV which predominately infects and causes disease in parrots but has been documented to cause a fatal disease in a green aracaris. Although the histologic lesions vary between budgerigars and non-budgerigar parrots, the virus that causes disease in these birds is the same.

Infected birds shed virus in droppings, oral secretions, and feather and skin dander. The most likely route of infection is by inhalation of the virus. It is speculated that vertical transmission occurs in budgerigars. Proof of this, however, is lacking. Once birds are infected, they become viremic, and virus can be found in nearly all organs of both symptomatic and asymptomatic birds. Virus shedding in the droppings follows soon after the onset of viremia.

Infection and disease are not synonymous; in fact, the vast majority of APV infections are asymptomatic. Disease and death are predominantly confined to nestling parrots less than 14 weeks old. Macaws, conures, caiques, eclectus, and ringnecked parrots are most likely to die of APV disease. Small outbreaks of APV disease in adult birds have been reported but are rare. Disease in adult birds is most common in eclectus parrots, caiques, and lovebirds. Psittacine beak and feather disease virus (PBFDV) infection is immunosuppressive and may predispose some adult birds to APV disease.

Gross lesions vary with the species affected. Affected budgerigars are typically 10–20 days old. Grossly, stunting, abnormal or delayed feather development, skin discoloration, abdominal distension, perihepatic effusion and ascites, hydropericardium, hepatomegaly, with focal areas of necrosis, and widely scattered petechial hemorrhages are common lesions. Budgerigars that survive the acute infection will often fail to develop their primary wing and tail feathers, or these feathers will be dystrophic. Non-budgerigar parrots with APV disease are typically well grown, are well muscled, and have substantial body fat. Historically they are being hand fed and not parent fed. Conure nestlings are typically 2–4 weeks of age, macaws 4.8 weeks of age, and eclectus

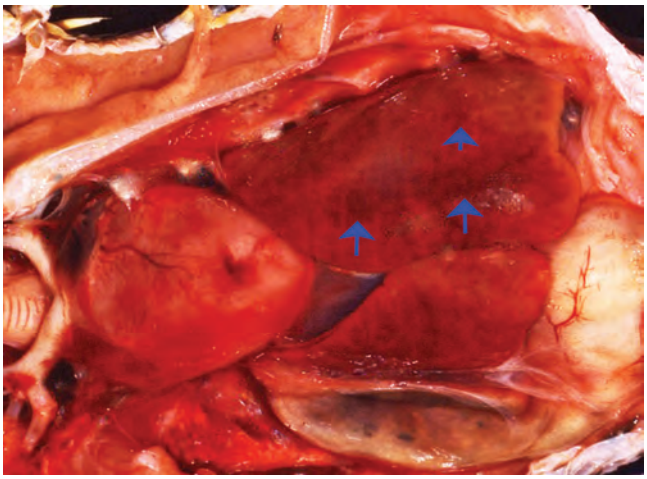

Figure 4.8 Foci of severe hepatic hemorrhage due to polyomavirus infection (arrows).

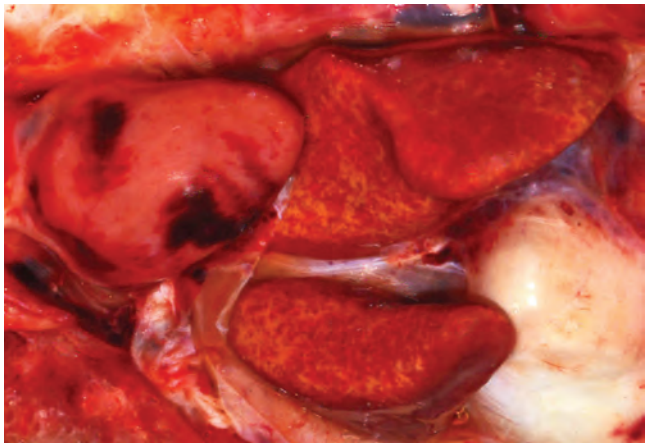

Figure 4.10 Severe polyomavirus-induced hepatic necrosis. The darker areas are foci of intact hepatocytes. There is also severe epicardial hemorrhage.

parrots 4.14 weeks of age. Gross lesions are striking and include a generalized pallor of all tissues, with subcutaneous and subserosal hemorrhages. The spleen and liver are typically enlarged and friable, and the liver may exhibit varying degrees of mottling (Figs. 4.8, 4.9, and 4.10). Less commonly, ascites and pericardial effusion are present. Similar lesions are also seen in adult birds with APV disease. Disease in nestling cockatoos, Amazon parrots, and African gray parrots is relatively uncommon. Liver lesions in these birds are less prominent or may be absent. In finches and canaries, the liver may be enlarged with mottling and hemorrhage is seen in some cases.

Histologically, in budgerigars, the nuclei of virally infected cells are enlarged, have marginated chromatin, and centrally contain a finely granular basophilic to amphophilic inclusion. Inclusions occur in multiple organs and tissue types including, but not limited to, liver, spleen, kidney (mesangial and tubule cells), feather follicles, skin, esophagus, brain, and heart. (See the relevant chapters.) A moderate, multifocal, apparently random, hepatic necrosis is common. Inclusion bodies are often abundant in the spleen and are accompanied by necrosis of the perivascular histiocytes and other phagocytic cells. Massive infection of the germinal epithelium of the feather follicle is also common in APV infections of budgerigars. Inflammatory changes accompanying the aforementioned lesions are generally minimal. A nonsuppurative encephalitis targeting the Purkinje cells in the cerebellum is a variable manifestation of APV disease in the budgerigar and is seen in some outbreaks but not in others.

Histologically, in nonbudgerigar parrots, hepatic necrosis to some degree is present in nearly all cases. Liver necrosis is multifocal to coalescing and, when severe, spares only the periportal hepatocytes. The spaces left by the necrotic hepatocytes fill with blood (Figs. 4.11 and 4.12). Characteristic inclusion bodies as

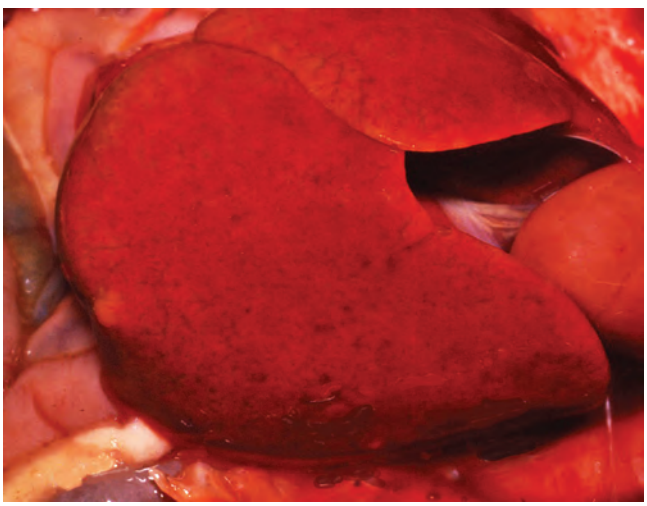

Figure 4.9 Diffuse hepatic discoloration due to polyomavirus-associated necrosis.

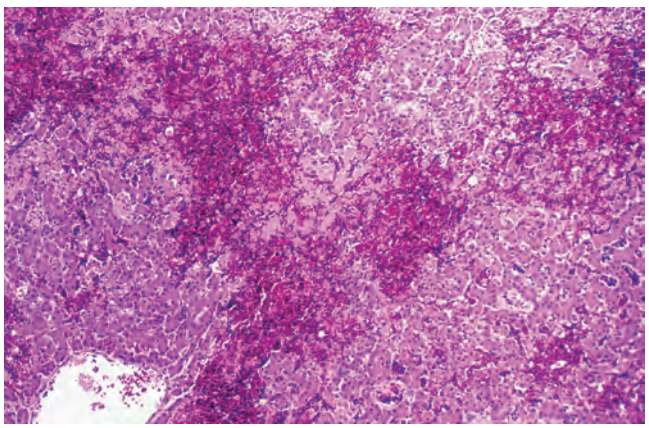

Figure 4.11 Multifocal to confluent hepatic necrosis and hemorrhage due to polyomavirus infection.

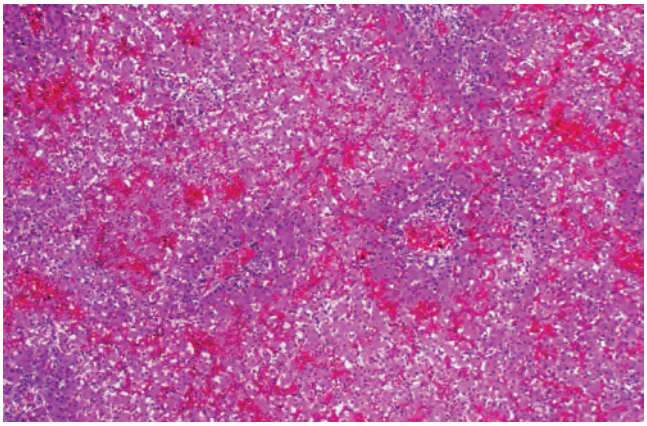

Figure 4.12 Severe midzonal to massive polyomavirus-associated necrosis.

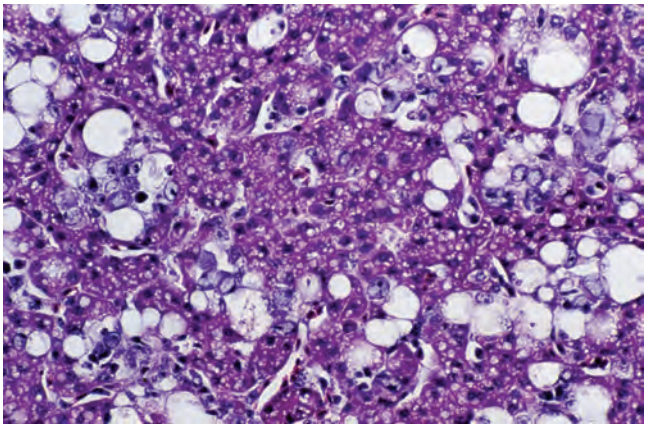

Figure 4.14 Necrosis and inclusion body formation in a finch with polyomavirus infection.

described in the budgerigar (Fig. 4.13) may be seen in Kupffer cells. The amount and severity of necrosis and hemorrhage and the occurrence of inclusion bodies are variable, depending on the species affected. Cockatoos may have no histologic changes. Cockatiels often have multifocal necrosis and few, if any, inclusion bodies. Typical moderate to severe midzonal to massive necrosis is seen in other psittacine birds. Liver lesions in passerines species and the aracaris are similar to those of psittacine birds (Fig. 4.14). Splenic and renal lesions are also common in parrots and passerines with polyomavirus infection and disease. Occasionally APV can be superimposed on birds with chronic-active hepatitis, leading to acute necrosis and inclusion body formation as well as the typical chronic lesions described later in this chapter (Fig. 4.15).

APV disease in lovebirds is somewhat unique. Disease does occur in nestling lovebirds. Hepatic necrosis is a common finding in these birds, but inclusion bodies are commonly found in other organs as well. Fledgling and young adult lovebirds are also susceptible to APV disease. This may also be a manifestation of immunosuppression from a concurrent PBFDV, as this disease is extremely common in this species.

Birds that die of APV disease are viremic. Virus can be found in large concentrations in all tissues and the blood by PCR assays. *In situ* hybridization of paraffin-embedded sections of the spleen or liver (Fig. 4.16) and immunofluorescent staining of impression smears of these organs are assays that can be used to confirm infection. Electron microscopy of fixed sections of tissues or the supernatant of homogenized tissue can also be used to demonstrate the virus. APV is a naked icosahedral virus with a diameter of 42–48 nm. It is considerably smaller than the adenoviruses.

Adenovirus

Adenovirus infections are most commonly recognized as incidental lesions in parrots that died of other causes. This is particularly true in lovebirds and budgerigars where characteristic inclusion bodies are sporadically found in renal tubular cells.

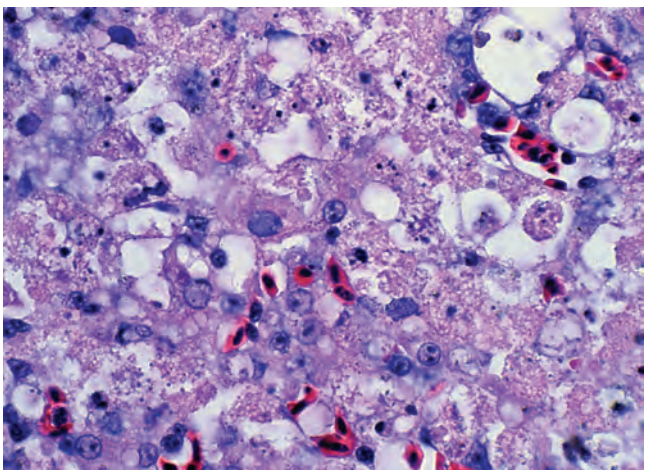

Figure 4.13 Detail of karyomegaly and intranuclear inclusion body formation in polyomavirus infection. The number of inclusions present is typical of the infection in budgerigars.

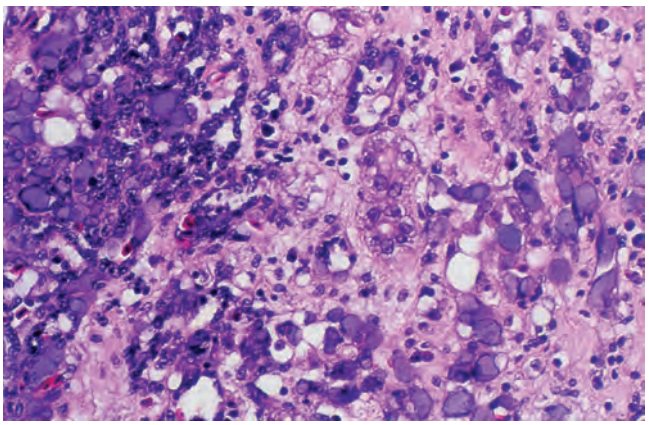

Figure 4.15 Polyomavirus inclusions in a bird with chronic hepatic disease and fibrosis.

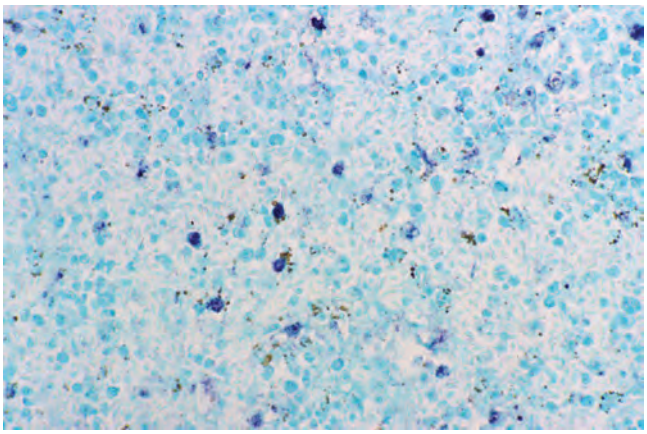

Figure 4.16 Polyomavirus DNA demonstrated by *in situ* hybridization.

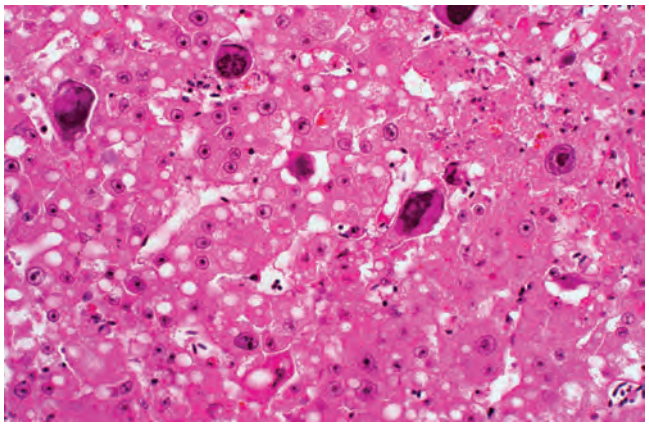

Figure 4.18 Adenovirus infection. Note the necrosis and karyomegaly and typical intranuclear inclusion bodies in the hepatocytes.

Historically, adenovirus disease is reported predominantly in lovebirds. In white-masked lovebirds (*Agapornis personata*) with conjunctivitis, 30% mortality is reported. Inclusion bodies are seen in the conjunctival epithelium and renal tubules. Acute necrotizing pancreatitis, a multisystemic disease, and hepatic necrosis are all attributed to adenovirus infections in lovebirds.

A fatal adenovirus infection causing hepatitis is described in nestlings of Senegal parrots and related genera (Psittacine Adenovirus-1). The disease occurs sporadically within aviaries. In one collection, the disease occurred in 3–4 years in offspring from a single pair of Senegal parrots. Affected parrots typically present acutely ill or are found dead. Grossly the liver is discolored red-black, and scattered yellow-gray areas may be present (Fig. 4.17).

Histologically there is multifocal necrosis with no particular lobular pattern, hemorrhage, nonsuppurative cholangitis, and large, darkly basophilic, intranuclear inclusion bodies within hepatocytes (Fig. 4.18). The inclusion bodies usually are characteristic, but in a few cases there has been minimal nuclear enlargement, and the inclusions have been pale (Fig. 4.19). Infection can be further verified by DNA *in situ* hybridization on paraffin-embedded tissues. Electron microscopy of thin sections or supernatants from homogenized tissues can also be used to identify adenovirus virions. Adenoviruses are naked icosahedral viruses with a diameter of 65–80 nm. They are abundant in the nuclei of infected cells. Similar lesions to those caused by psittacid adenovirus-1 are also reported in a range of other species of parrots, but these viruses have not been characterized.

Psittacine adenovirus-2 has been isolated from a range of psittacine birds. Some were showing nonspecific signs, while others were asymptomatic. Histological lesions for this adenovirus have not been described.

Budgerigar adenovirus-1 causes hepatitis and encephalitis in budgerigars. Adenovirus infections in budgerigars are reported

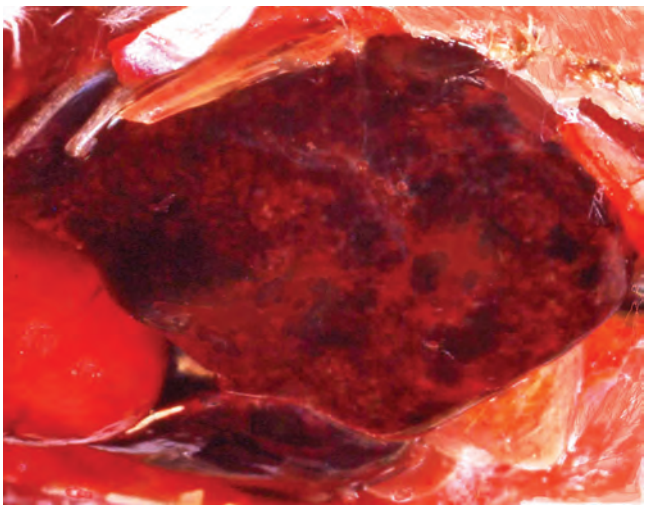

Figure 4.17 Swollen, mottled liver in adenovirus infection.

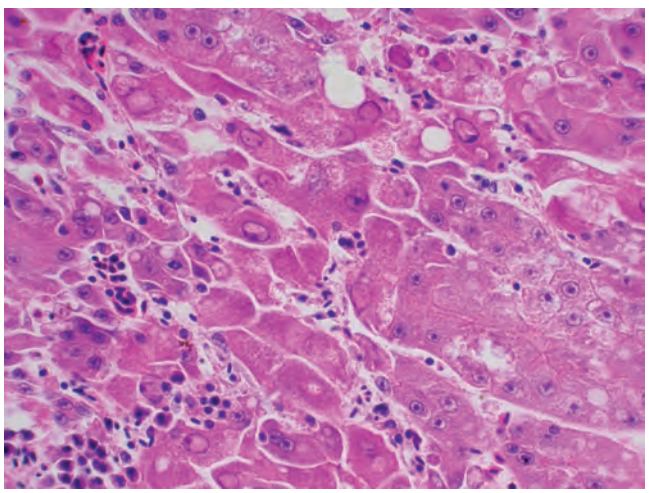

Figure 4.19 Somewhat atypical appearance of adenovirus infection with minimal necrosis and clear, rather than dark, inclusion bodies.

from multiple continents but their relationship to budgerigar adenovirus-1 is not known.

A novel adenovirus has been detected and partially sequenced from Gouldian finches. Inclusion bodies were found in the tubule epithelium of the kidney, and no lesions were seen in the liver. The significance of this virus to the Gouldian finch is not known.

Adenovirus infections cause disease in racing pigeons. A severe adenovirus infection causing enteritis is seen in young birds less than a year of age. Hepatitis occurs in some of these birds but is not a consistent finding. A severe necrotizing hepatitis is caused by a second adenovirus and can cause disease in birds of any age. This virus causes severe necrosis. Inclusion bodies are generally present in significant numbers.

Falcon adenovirus causes a fatal disease in several species of nestling falcons raised in captivity and death in a wild-caught American kestrel. Target organs include the liver, spleen, and intestines with resulting necrosis. Inclusion bodies are common within the lesions.

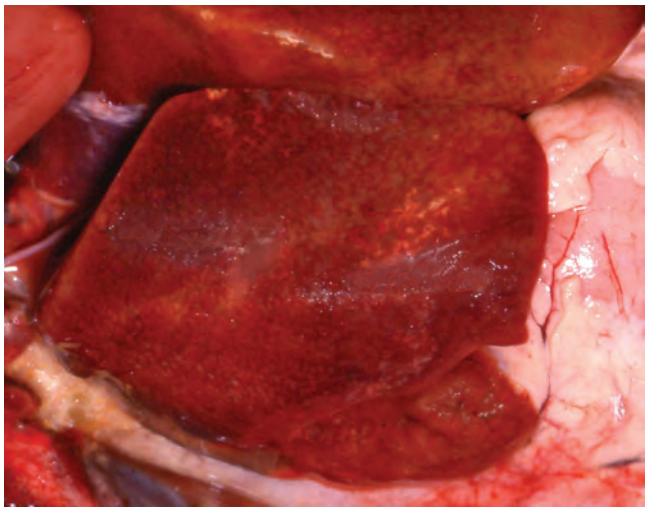

Figure 4.20 Slightly discolored liver in circovirus infection.

Paramyxovirus (PMV)

There are five serotypes of avian PMVs. PMV-1, 2, 3, and 5 are known to cause disease in cage birds. PMV-3 is most common in pet species. The liver is usually a secondarily affected organ, with primary infections seen in the respiratory tract or gastrointestinal tract. The organ systems affected may be dependent on the particular strain of virus. Grossly the liver may be enlarged. Histologically a lymphoplasmacytic infiltrate is present within portal areas. Inclusion bodies are not seen.

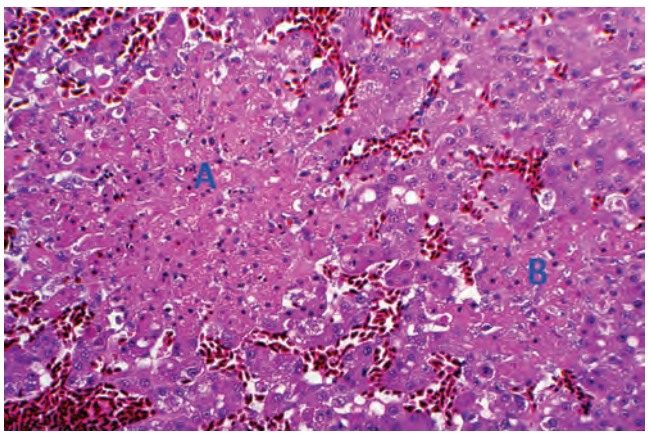

Figure 4.21 Multifocal (A and B) acute hepatic necrosis in circovirus infection.

Psittacine beak and feather disease virus

PBFDV infections can involve the liver, but it is not a common extracutaneous site. Liver lesions are usually present only in young birds with systemic disease but can be seen in some older birds that die with severe feather damage. Usually the liver appears normal, but there may be a few scattered discolored foci (Fig. 4.20).

Histologically there is multifocal necrosis and congestion. Infrequently inclusion bodies are seen in Kupffer cells. A lymphoplasmacytic infiltrate may be present in portal areas (Figs. 4.21 and 4.22). In birds that are immunosuppressed, there may be severe secondary bacterial hepatitis with a minimal inflammatory response. Coagulative necrosis, which may be massive, is regularly seen in nestling and fledgling African gray parrots with PBFDV infection.

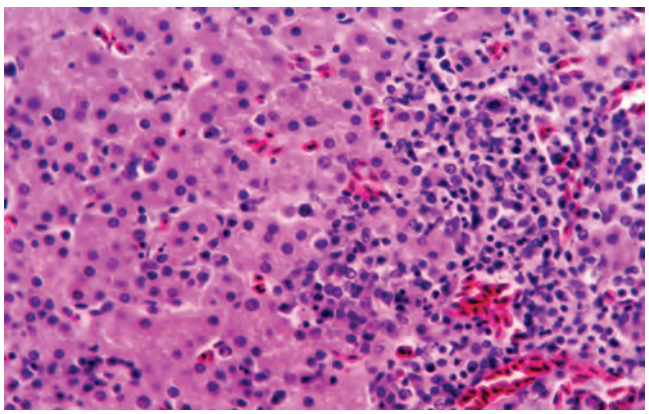

Figure 4.22 Nonsuppurative cholangiohepatitis that is occasionally seen in circovirus infection.

Reovirus

The vast majority of cases of reovirus disease in parrots are reported in the birds that were either in quarantine or had been recently released from quarantine. Disease outbreaks were initially described in imported lots of African gray parrots, but epornitics of this disease have subsequently been documented in other African, Indian, and Australian parrots. A particularly large outbreak occurred in budgerigars in the United Kingdom

and spread to The Netherlands in the first few years of the twenty-first century. This is the only reovirus from parrots to be fully characterized genetically. Although New World parrots died in this outbreak, in general, disease in New World species of parrots is rare. Naturally occurring reovirus disease is often complicated by the presence of multiple concurrent infections, including salmonellosis, aspergillosis, and PMV-3 infections.

Gross lesions are not specific. Hepatomegaly and splenomegaly with focal depressed discolored areas of the hepatic capsular and cut surfaces are the most common lesions described. Enteritis and petechial and ecchymotic hemorrhages are also seen. Multifocal hepatic necrosis with lymphoreticular infiltration is a consistent, but nonspecific, lesion. Necrosis of the spleen, intestinal lamina propria, and the bone marrow is also described. Inclusion bodies are not seen with light microscopy, but intracytoplasmic viral particles can be seen with electron microscopy. Reoviruses are nonenveloped but have a double capsid and are 75–80 nm in diameter. They are readily isolated in chicken embryo fibroblasts and chicken embryo kidney cells. Immunofluorescent antibody staining is another means of confirming infection.

Hepadnavirus

This DNA virus (duck hepatitis B) is one of several viral agents causing hepatitis in ducks. The disease is often subclinical, but there can be persistent infections and vertical transmission. The host range is limited to Pekin ducks and close taxonomic relatives, but it has been experimentally transmitted to geese.

The virus causes hepatic necrosis and periportal inflammatory infiltrates. The virus receptors (gp180) are concentrated in the Golgi apparatus of hepatocytes.

Hepadnaviruses have also been identified in psittacine birds and it is likely that new ones will be found and these viruses will be widespread in captive parrots. To date there is no disease syndrome associated with these viruses.

Hepevirus

One of these RNA viruses causes avian hepatitis E in chickens. Grossly livers are enlarged and pale and may be friable. Hemorrhage and necrosis may be present microscopically and there is a mononuclear inflammatory infiltrate in portal areas.

Other viral disease

A number of viruses can occasionally cause hepatic lesions in birds. These include togavirus, rotavirus, parvovirus, orbivirus, and coronavirus. In cases of hepatic disease that have lesions consistent with a viral infection but no change specific to one of the common causes of pet bird hepatitis and necrosis, these viruses can be considered as differential etiologic possibilities.

Gross and histologic changes are usually not specific, and electron microscopy, viral isolation, or DNA probes are necessary for an exact etiologic diagnosis.

Bacteria

The liver is commonly targeted by systemic bacterial infections in birds. Both gram-positive and gram-negative bacteria cause hepatitis. *Staphylococcus* and *Streptococcus* spp. are the most common gram-positive organisms isolated from the liver. They generally disseminate through the blood from chronic necrotizing skin lesions or may reach the liver by extension from adjacent air sacs. Infections with these bacteria are more common in finches and canaries than in parrots. *Clostridia* are gram-positive rods of intestinal origin that cause hepatitis. Another gram-positive rod is *Listeria monocytogenes*, which causes a systemic disease commonly involving the liver. It is a relatively rare pathogen of cage birds.

Gram-negative bacteria cause most systemic bacterial infections of psittacine birds. Members of the Enterobacteriaceae, including *Escherichia coli*, *Klebsiella* sp., *Proteus* sp., *Enterobacter* sp., *Salmonella* sp., and *Yersinia pseudotuberculosis*, are common isolates. *Pseudomonas* sp. is also a common isolate. Systemic infections with these organisms usually result from invasion from the gut and, less frequently, by extension up to the biliary tree. Infected wounds and respiratory and urinary infections with these organisms may also result in systemic infections involving the liver. *Yersinia pseudotuberculosis* is commonly reported in passerine species, ramphastids, turacos (Cuculiformes), and doves in Europe but is rarely recovered as a pathogen in the United States. *Pasteurella multocida* is another gram-negative bacterium that causes septicemia. This organism is usually introduced into a cage bird by a cat bite. The organism grows so rapidly that it may be seen histologically in huge numbers in all organs and the blood.

Gross lesions caused by *Staphylococci* and *Streptococci* include variable hepatic swelling and multifocal to confluent yellow-white foci within the parenchyma. There may be abscess formation in chronic cases. Varying degrees of hemorrhage may be present in cases of clostridial hepatitis. Histologically, multifocal to confluent necrosis and an inflammatory reaction comprised primarily heterophils and macrophages are seen. Bacteria are sometimes found in the lesion.

Hepatitis caused by gram-negative bacteria results in a grossly swollen and congested liver. The liver may be markedly enlarged and meaty in subacute to chronic infections. Gray-white-yellow foci are seen throughout the parenchyma. Their size and number are variable (Fig. 4.23). Histologic changes are characterized by multifocal necrosis and fibrin deposition, with an inflammatory response that includes primarily heterophils and macrophages (Figs. 4.24 and 4.25). Rod-shaped, gram-negative bacteria can be found free in the lesions. They are most frequently seen at the edges of necrotic foci and in the cytoplasm of Kupffer cells and macrophages (Fig. 4.26). With chronicity, granulomas may form (Fig. 4.27). Colonies of *Yersinia* spp. (Fig. 4.28) have a characteristic appearance. Other gram-negative bacteria cannot be identified by their histologic appearance or the lesions that they cause.

PBFDV infections of young psittacine birds often are accompanied by secondary bacterial infections. Grossly affected livers

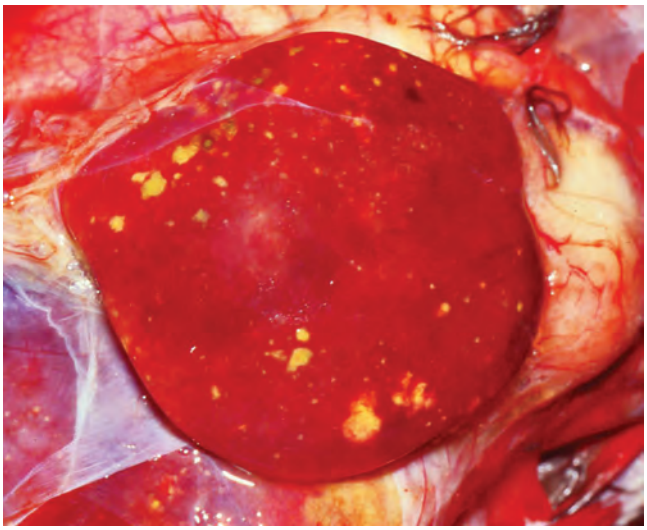

Figure 4.23 Enlarged, pale liver with a gram-negative bacterial infection.

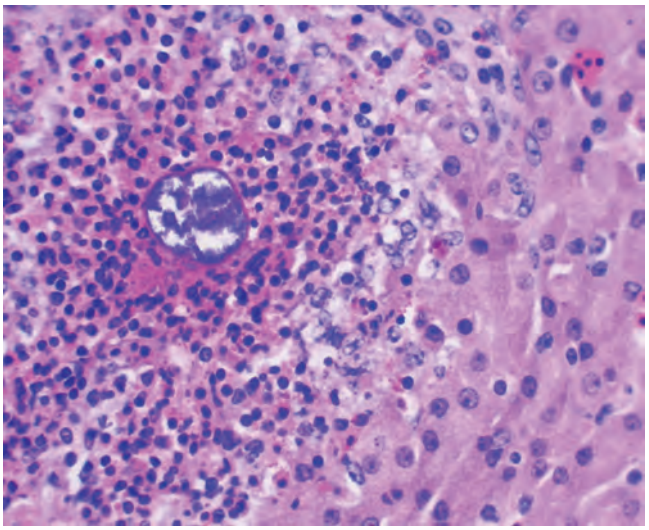

Figure 4.26 Bacterial hepatitis. A bacterial colony is surrounded by a pleocellular inflammatory infiltrate.

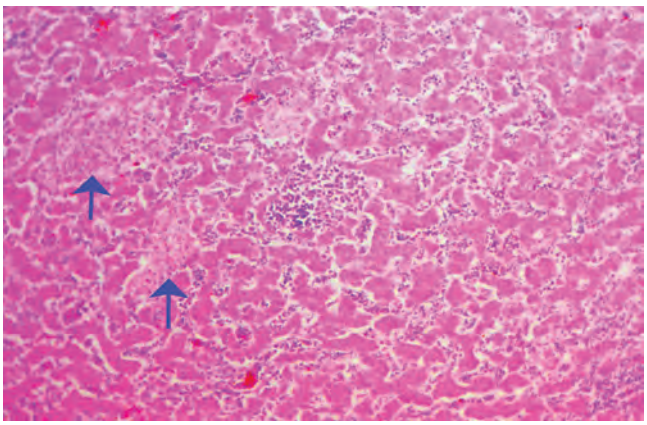

Figure 4.24 Multifocal necrosis and variable inflammation in bacterial hepatitis (arrows).

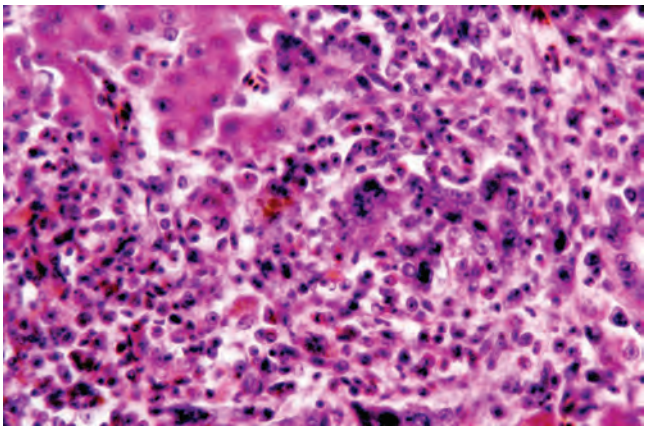

Figure 4.27 Chronic bacterial hepatitis with early granuloma formation.

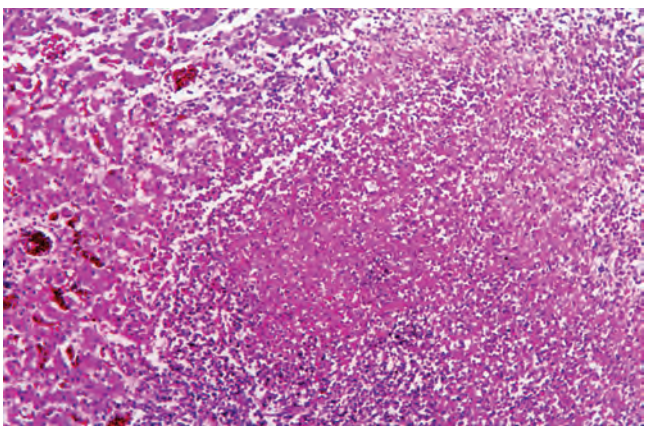

Figure 4.25 Hepatitis due to *Salmonella* sp. Note the pleocellular inflammation, necrosis, and fibrin deposition.

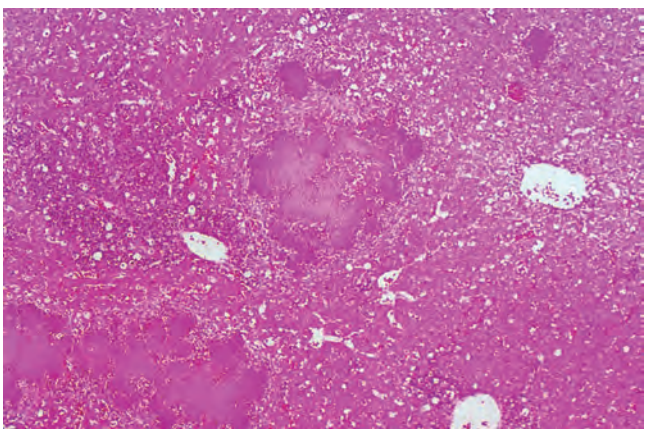

Figure 4.28 Typical appearance of hepatitis due to *Yersinia* sp. Large bacterial colonies are usually found throughout the affected tissue.

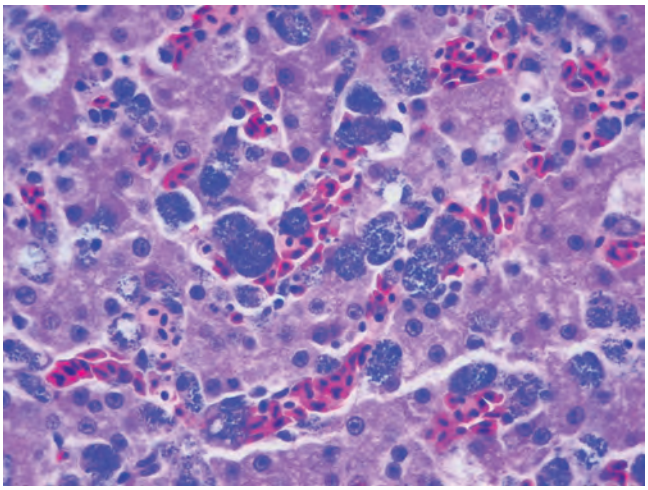

Figure 4.29 Bacteremia and bacterial hepatitis secondary to circovirus infection that led to severe immunosuppression. Numerous macrophages containing bacteria are seen in the sinusoids.

are usually markedly enlarged and mottled. The liver lesion may be the most striking lesion seen at necropsy. If the possibility of circovirus infection is not considered and the bursa of Fabricius not examined histologically, the primary problem may be overlooked. Histologically the hepatic lesion is characterized by a variable degree of necrosis and an inflammatory response that is made up primarily of macrophages, many of which contain bacteria (Fig. 4.29). Free bacteria may also be found in the hepatic sinusoids. The normal heterophil response is lacking, possibly due to the viruses' effect on the immune system (Chapter 8).

Systemic bacterial disease is often seen in nestling parrots that are being hand fed. In these cases, it is very easy to blame the pathogen for the bird's death and not take into consideration the husbandry conditions in which the bird was raised. Incubator temperature, ventilation, and humidity have a strong impact on the health of a chick at hatch. Weak chicks often fail to thrive and are at increased risk for bacterial diseases. Calorie intake, nutrient content of the diet, the chick's hydration, and the temperature of the brooder can all have a significant impact on the chick's growth rate and immune status. Again, problems in any of these areas may result in immune suppression and a subsequent bacterial disease.

The liver is an excellent site for culturing bacteria that can be grown by traditional methods. Often bacteria will be cultured from a liver that has the histologic appearance of a bacterial hepatitis but in which organisms cannot be seen. Heart, blood, and spleen are other excellent sources to culture if a bacterial infection is suspected. Postmortem bacterial invasion of the liver and other organs is common in birds that have undergone decomposition prior to necropsy. These organisms may be seen histologically in the liver but are never intracellular and are not associated with an inflammatory reaction.

Mycobacteria

Mycobacterium avium avium (MA), including multiple genotypes and *Mycobacterium genavense* (MGE) are the most common mycobacteria that infect birds. *Mycobacterium tuberculosis* (MTB) has also been documented in psittacine birds but is uncommon. Probably all species of birds are susceptible to mycobacterial infection. However, infections are relatively uncommon in most species of birds. When outbreaks do occur, they are most frequent in collections of captive waterfowl, zoo birds, gray-cheeked (*Brotogeris pyrrhopterus*) and canary-winged parakeets (*B. versicolorus*), certain species of tropical doves, ring-neck doves, canaries, and Australian finches. Once the environment is contaminated with the organism, infections of other birds in the collection and new birds introduced to the collection are likely. The route of exposure depends on the organism. Birds contract MTB directly from people by inhalation of aerosolized bacteria. By contrast, MA and MGE are contracted by ingestion of the organisms. MA appears to be ubiquitous in the environment. The factors that determine whether a bird will contract MA and MGE are not known but probably include a bird's genetic susceptibility and the number of organisms to which a bird is exposed.

Mycobacteriosis is a chronic disease, so birds that die with this disease are typically thin or emaciated. Mycobacterial disease can be localized or diffused. Localized lesions are uncommon and are generally found on the face, skin, or leg and are generally caused by MTB. MA and MGE typically cause a widely disseminated disease. Following ingestion, they first colonize cells in the intestines. Here changes may be so severe as to interfere with digestion. From the intestines, mycobacteria spread widely. Any organ system can be affected, but the liver, spleen, lung, air sac, skin, and bone marrow are most commonly involved. It should be noted that many birds with systemic disease do not have intestinal lesions.

Affected livers may contain yellow-to-gray-tan, soft nodules or be diffusely enlarged (Figs. 4.30 and 4.31). Amyloidosis of the kidney and liver is a common complication of mycobacterial infections and may contribute to the clinical signs. Microscopically, mycobacterial infections take on two primary forms but may contain elements of both. In the first, classic tubercles contain a central necrotic (caseous) area surrounded by macrophages, multinucleated giant cells, histiocytes, and plasma cells (Fig. 4.32). Bacteria may be scarce in these lesions. More commonly in pet species, early hepatic lesions comprise heterophils and small macrophages within portal areas and scattered in the parenchyma (Fig. 4.33). As these lesions develop, they comprise small foci and eventually extensive sheets of bacteria-laden histiocytes (Fig. 4.34). The specific organism, the species of the host infected, the host's immune response, and the stage of infection all contribute to the nature of the lesion. The amount of necrosis and caseation varies. It may be more severe in waterfowl than in psittacine birds. In hematoxylin–eosin (H&E)-stained sections, the cytoplasms of macrophages infected with mycobacteria are blue-gray and have a finely

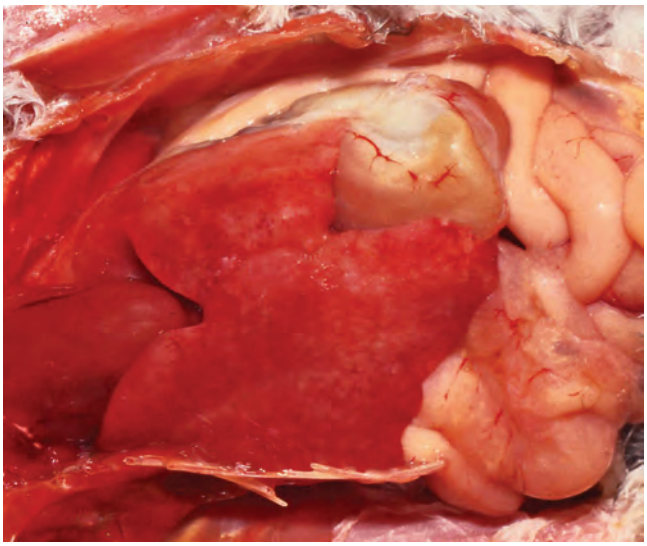

Figure 4.30 Hepatic mycobacteriosis with a slight mottling noted grossly.

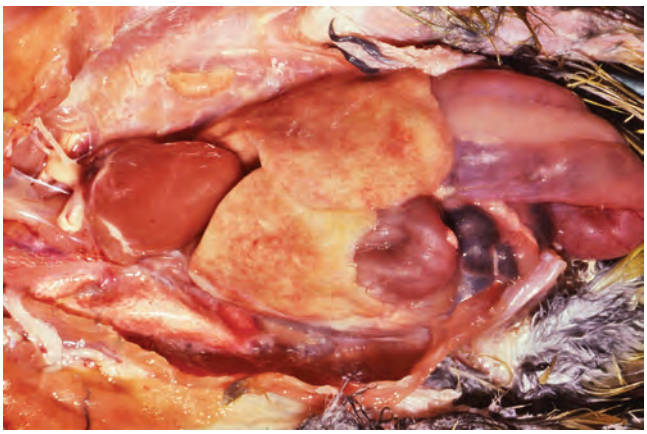

Figure 4.31 Severe hepatic mycobacteriosis with diffuse paleness and irregular nodules in the parenchyma.

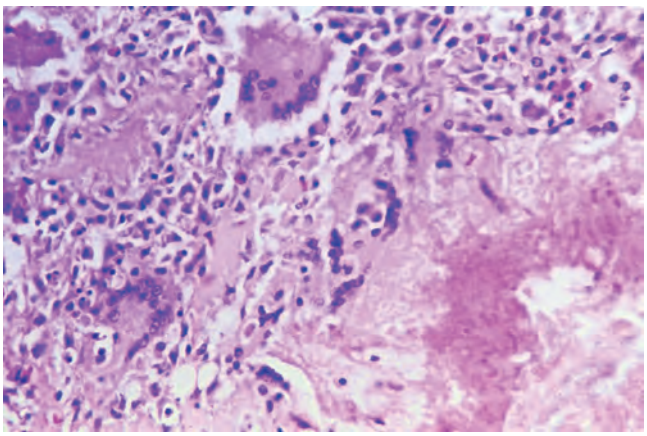

Figure 4.32 Hepatic mycobacteriosis with a focus of caseation and giant cell formation. This type of lesion is not always seen.

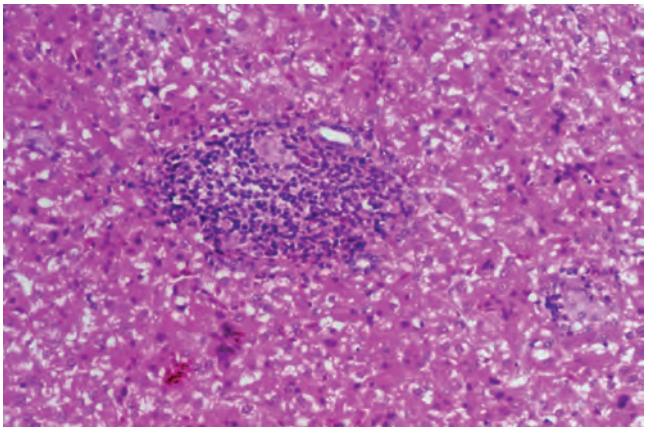

Figure 4.33 Early hepatic mycobacteriosis. Lymphocytes and a few small macrophages are present in the lesion. Organisms may not always be seen at this stage.

granular appearance suggestive of the presence of numerous small organisms (Fig. 4.35). Proof that the organisms are present in the tissue requires acid-fast staining.

Obligate intracellular bacteria

Psittacosis or ornithosis is a disease caused by an obligate intracellular bacterium – *Chlamydia psittaci* – formally *Chlamydophilia psittaci*. The classification of this organism has changed again and it is now back to *Chlamydia* rather than *Chlamydophila*. There are eight serovars within this species. Serovars A and E are found in cage birds. Serovar B is enzootic in pigeons. All avian serovars are potentially zoonotic, and psittacosis is a reportable disease. Pathologists should take precautions to keep from exposing themselves to this organism. Infections can occur by ingestion, inhalation, or conjunctival exposure to the organism. Organisms propagate in epithelial cells of the respiratory tract and then generalize to other organs. The disease in psittacine birds has variable manifestations. Subclinical

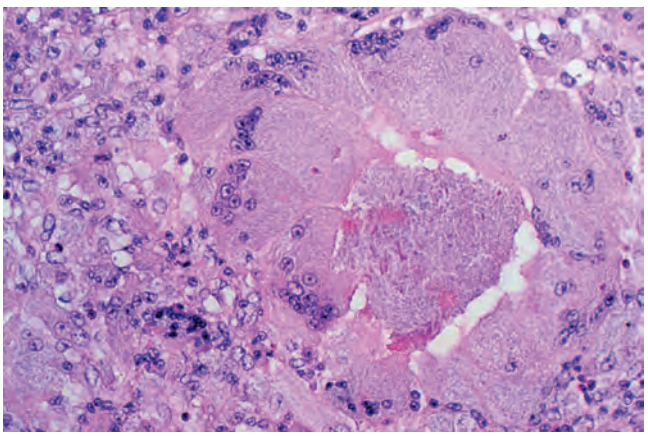

Figure 4.34 Mycobacterial hepatitis with the formation of a granuloma composed of large macrophages containing acid-fast bacteria.

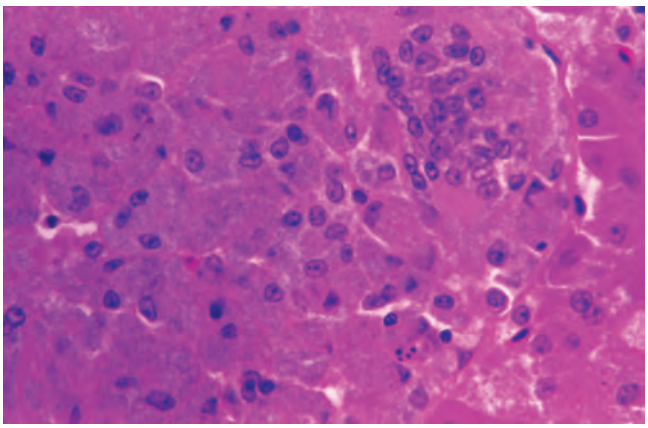

Figure 4.35 Detail of hepatic mycobacteriosis. The granules in the macrophages are acid-fast bacteria that are minimally visible on routine (H&E)-stained sections.

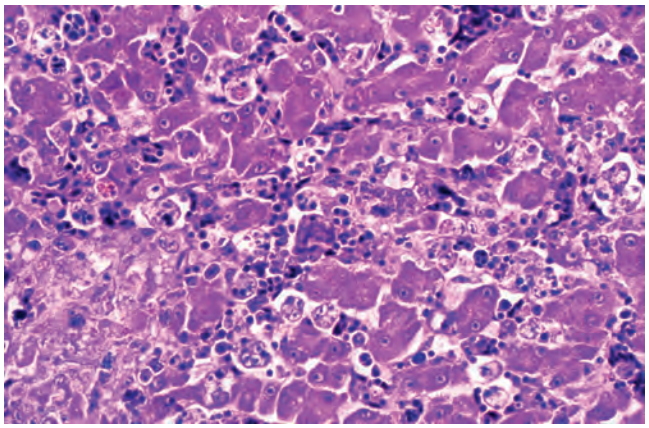

Figure 4.37 Hepatic necrosis and diffuse lymphohistiocytic infiltrate characteristic of *Chlamydia* infection.

infections are common, especially in cockatiels. A mild form of the disease manifesting as a chronic conjunctivitis and sinusitis is also common in cockatiels. New World parrots are often affected with a severe multisystemic disease. Multisystemic disease is also seen in cockatiels and other species of parrots.

Hepatic and splenic enlargement is a common finding in birds with psittacosis. Concurrent air sacculitis is another common manifestation of psittacosis and should alert pathologists that they may be dealing with this disease. Affected livers may have minimal gross changes, but many are enlarged and discolored and may contain numerous gray-yellow foci of necrosis (Fig. 4.36). Histologically there is an inflammatory reaction that is primarily mononuclear and may be diffused within sinusoids. Many of the macrophages contain green-brown pigment consistent with bile pigment and/or hemosiderin (Figs. 4.37 and 4.38). Multifocal to confluent necrosis can also be seen, and some heterophils may be present as a response to necrosis. In some cases, organisms can be found in macrophages and/or hepatocytes (Fig. 4.39). Although sometimes difficult to find on H&E-stained sections, they can be visualized with Giminez's and other special stains (Fig. 4.40). They may be easier to find on impression smears of fresh tissue (Fig. 4.41). In chronic disease, portal fibrosis and bile duct hyperplasia occur.

In many cases of psittacosis, the organisms may be seen in Giminez-stained impression smears of liver, spleen, or air sacs even though not found in fixed tissue. Immunofluorescent staining of impression smears is also a sensitive and rapid method of detecting the organism. PCR with specific primer sets is readily available in many diagnostic laboratories and can be used as confirmatory diagnostic assay. *Chlamydia psittaci* can also be grown in Vero cells, but it may take several days before the organism can be detected.

Bacillus piliformis is a rod-shaped, gram-positive bacterium that cannot be grown in cell-free media. It affects a wide variety of mammals and has been reported in a cockatiel. The organism exists in the environment and may spread via the fecal–oral

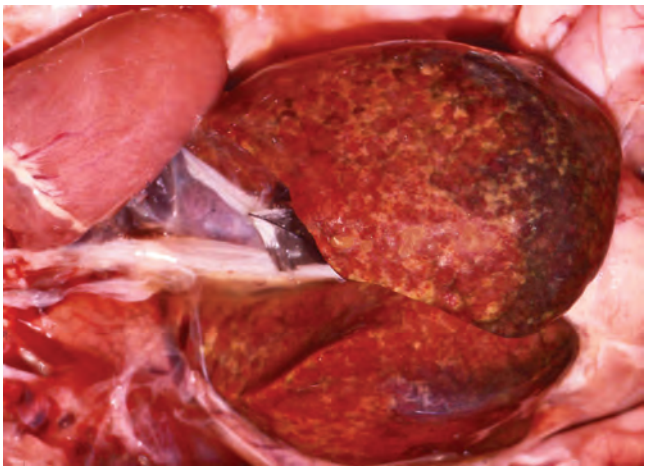

Figure 4.36 Hepatic enlargement and severe necrosis and inflammation due to *Chlamydia* infection.

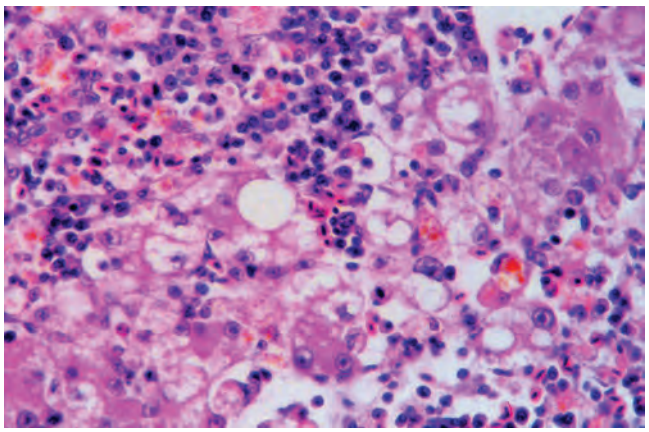

Figure 4.38 Typical inflammatory response in hepatic *Chlamydia* infection.

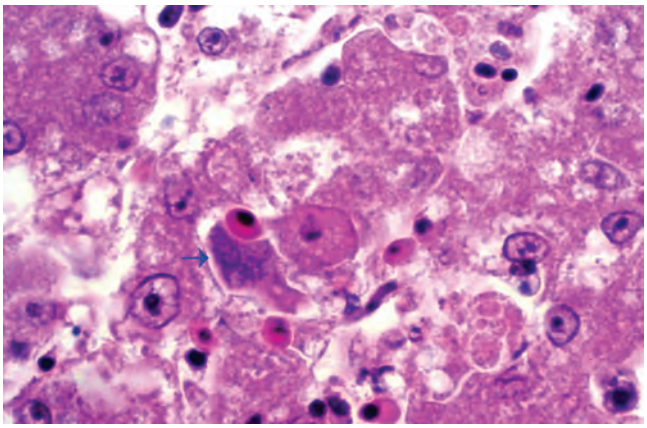

Figure 4.39 Degenerating cell with dark basophilic smudge representing cytoplasmic accumulation of *Chlamydia* organisms (arrow). On routine stains, individual organisms are difficult to see.

route. Stress probably plays a part in the activation of clinical disease. Grossly the liver is enlarged, pale, and mottled, containing numerous foci of necrosis. Histologically there is multifocal necrosis, a variable pleocellular inflammatory reaction, and intracytoplasmic bacilli in hepatocytes. These may be difficult to see without Giemsa or silver stains.

Fungi

The liver is usually involved in mycotic infections as a result of extension from the lung or air sacs, or as a result of hematologic spread. Several species of *Aspergillus* are the most common organisms affecting the liver, but other fungi are occasionally identified. Systemic *Candida* infections, particularly in immunosuppressed birds, may result in liver invasion.

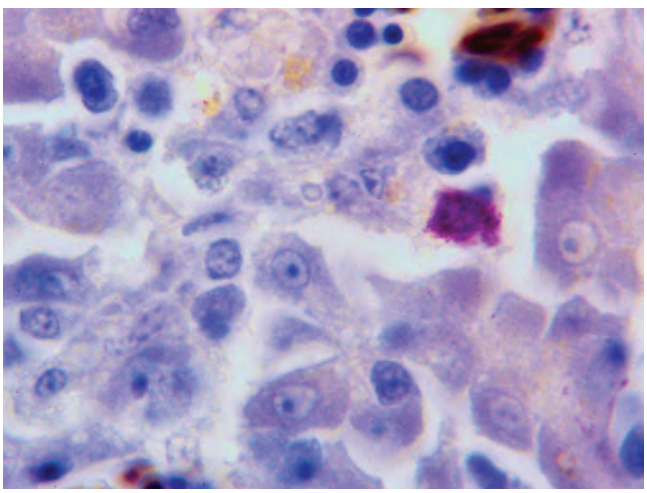

Figure 4.40 Gimenez-stained section demonstrating *Chlamydia* organisms. Many appear as large clumps, but a few individual organisms can be seen.

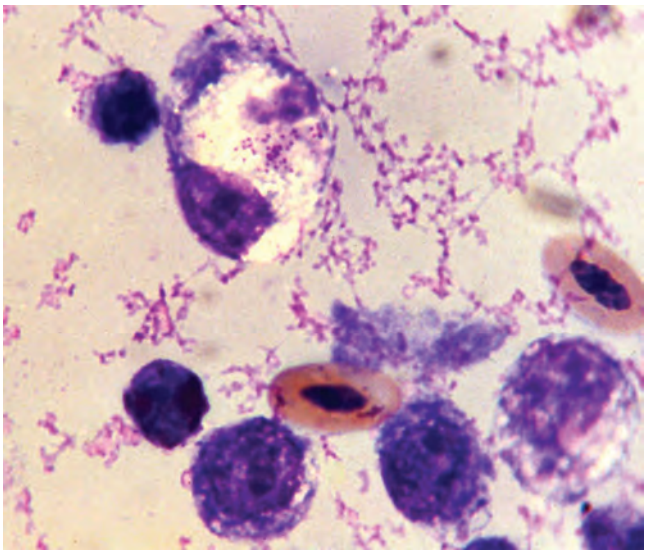

Figure 4.41 Cytology impression from a liver of a bird with Chlamydiosis. Round, red-violet organisms are seen in the cytoplasm of macrophages.

Gross lesions are similar to those caused by bacteria and viruses. Affected livers are enlarged and contain multifocal gray-white areas of necrosis. Histologic lesions are similar to those seen in bacterial infections, being characterized by necrosis and a pleocellular infiltrate including heterophils and macrophages. With chronicity, abscesses will form. Finding fungal organisms in the lesion is necessary for a specific diagnosis.

Parasites

Both protozoan and metazoan parasites cause avian liver disease. Protozoal pathogens come from several taxonomic groups.

Phylum: Apicomplexa

Infections with *Toxoplasma gondii*, *Sarcocystis* sp., and *Atoxoplasma* can all cause significant liver disease. Affected livers are typically enlarged, have rounded edges, and contain multiple diffuse subcapsular white foci (Fig. 4.42). Acute infections may result in a soft friable liver, whereas, in chronic infections, livers may be firm. Lesions caused by all three organisms are very similar. Necrosis is multifocal and random. It may be mild to severe. The accompanying inflammatory infiltrate is composed of macrophages, lymphocytes, and plasma cells in portal areas and sinusoids (Fig. 4.43). Atoxoplasmosis most commonly occurs in finches. The lesions are lymphoplasmacytic and can be dramatic. The lymphoplasmacytic response can be so severe that it can be mistaken for a lymphoid neoplasia. Heterophils may be seen in cases of toxoplasmosis associated with multifocal areas of necrosis. Organisms are usually not seen in *Sarcocystis* infections. When they occur, they are present in vascular endothelial cells. Organisms are also difficult to find when the lesion is caused by atoxoplasmosis. They are typically found in macrophages or Kupffer cells and have a characteristic

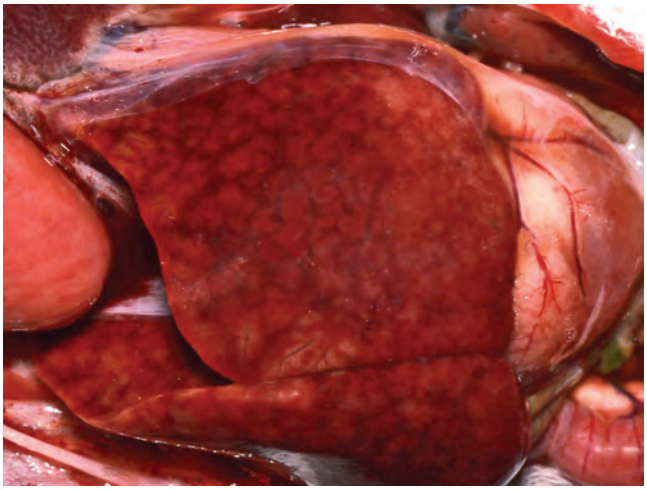

Figure 4.42 Enlarged, discolored liver seen in *Sarcocystis* infection. Both the gross appearance and the inflammatory infiltrate can be similar to *Chlamydophila* infection.

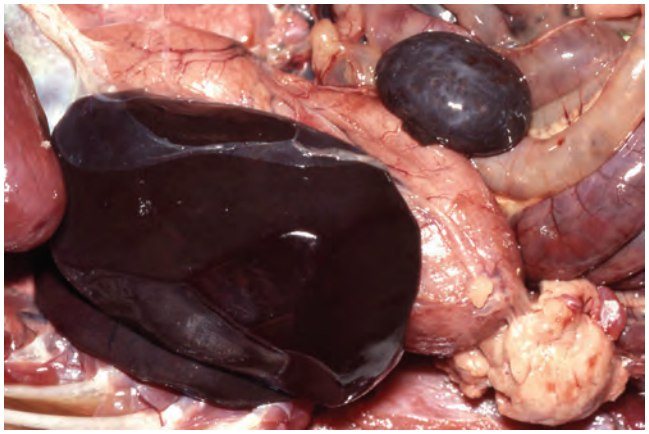

Figure 4.44 The liver of a falcon with malaria. A large amount of pigment is present resulting in the liver being black grossly.

comma-shaped appearance and are 1–3 mm long. *Toxoplasma gondii* organisms are similar in size but are round and usually are more plentiful and are found in macrophages or in extracellular spaces.

Birds affected by hepatic cryptosporidiosis often have no gross hepatic lesions. *Cryptosporidia* attach to the surface of bile duct epithelial cells. There may be some proliferation of bile duct epithelium, and a mild chronic mononuclear inflammatory response is sometimes seen.

Hemoprotozoa

Organisms from the genera *Plasmodium*, *Leukocytozoon*, and *Hemoproteus* are capable of inducing hepatic disease. Classically, hepatic lesions caused by infection with *Plasmodium* sp. have been considered to include liver enlargement and, particularly in falcons and penguins, a diffuse gray-black discoloration (Fig. 4.44). Histologically, numerous macrophages, plasma cells, and lymphocytes infiltrate affected livers. Organisms (exoerythrocytic schizonts) may be found in some of the inflammatory cells (Fig. 4.45). In falcons, malarial pigment is present in macrophages (Fig. 4.46).

Hemoproteus is usually considered nonpathogenic, with no gross lesion seen, but histologically schizonts can be found in endothelial cells of the liver vasculature.

Leukocytozoon schizogony occurs in macrophages and hepatocytes. Infection by *Leukocytozoon* is usually considered to be nonfatal, however there are reports of fatalities associated with rupture of megaloschizonts in the liver. The identification of the organism was made on morphologic criteria only.

With the use of PCR tests, deaths in several species of zoo birds were found to be associated with *Plasmodium* sp. and *Hemoproteus* sp. The gross and histologic lesions were similar to those previously reported as due to *Leukocytozoon*. Since several hemoprotozoa can potentially cause similar lesions, the use of PCR amplification of the organisms' DNA and sequencing of

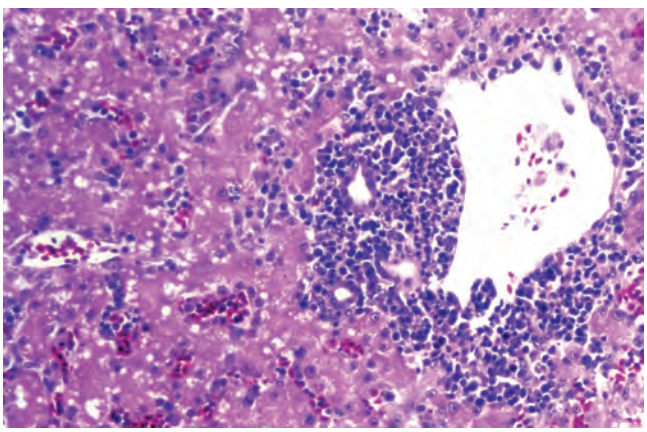

Figure 4.43 Lymphoplasmacytic and histiocytic inflammatory infiltrate seen in sarcosporidial infection.

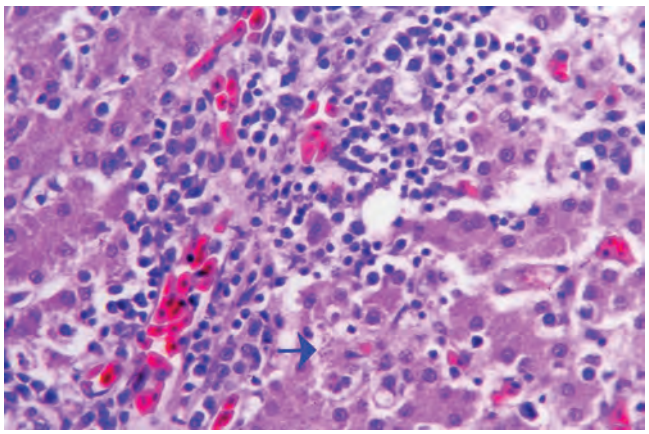

Figure 4.45 Hepatitis associated with malaria in a penguin. Exoerythrocytic schizonts can be seen (arrow).

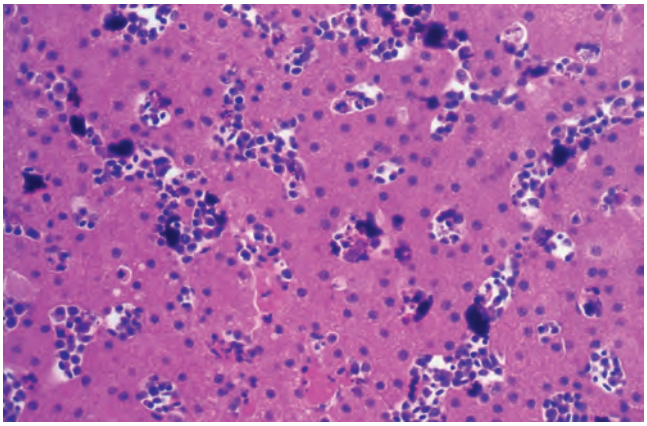

Figure 4.46 Hepatitis in a falcon due to *Plasmodium* sp. The reaction is similar to that in the canary, but malaria pigment is seen in raptors.

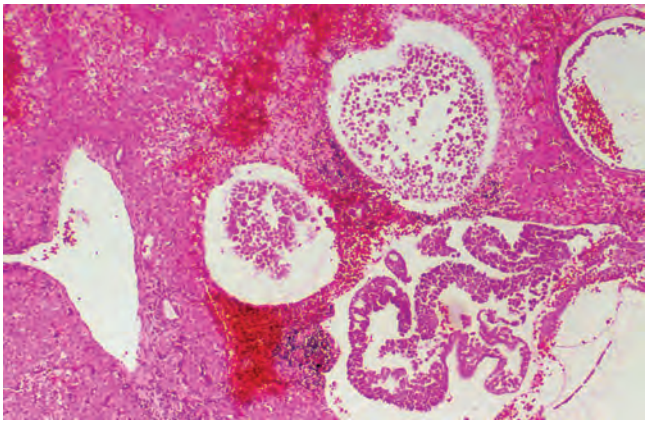

Figure 4.48 Histologic appearance of liver with megaloschizonts of a hemoprotozoa and surrounding hepatic necrosis and hemorrhage.

the amplicons appears to be necessary to achieve an exact etiologic diagnosis.

Grossly affected livers are variably enlarged and pale and contain numerous dark, red-black, raised foci. These foci bleed when incised (Fig. 4.47). Histologically the dark foci are areas of hemorrhage surrounding megaloschizonts (protozoal cysts) and necrotic hepatic tissue. The cysts vary from 110–40 mm to over 600–400 mm. Some schizonts may be ruptured, and released merozoites may be phagocytosed by macrophages. Hepatocytes are usually slightly swollen and vacuolated (Fig. 4.48).

Phylum: Sarcomastigophora

Trichomonas gallinae Trichomoniasis is generally confined to the oral cavity and esophagus. In squabs, however, trichomoniasis can become generalized, and the liver is commonly involved. Affected livers are enlarged with focal to coalescing areas of caseous necrosis. Fibrinous casts of the liver and, less commonly, ascites are seen in more severe cases. Granulomas are also present in the lung, in the intestinal mesentery, and around the heart. A mixed population of inflammatory cells of which a high proportion is heterophils surrounds necrotic areas. Epithelioid cells and giant cells are occasionally present. Organisms are not visible in H&E-stained sections but are readily visible using a modified silver stain. Extensive perivascular heterophil infiltration in the liver and kidney (possibly extramedullary myelopoiesis) is also reported.

Trichomonas stableri has been implicated in the decline of the Pacific Coast band-tailed pigeons in the western United States. It is likely that many new species of *Trichomonas* will be found.

Histomonas meleagridis Histomoniasis is predominantly a disease of turkeys but also causes significant problems in quail, ruffed grouse, and chickens. It is transmitted within the eggs of *Heterakis gallinarum* that are ingested by earthworms. Infection occurs when free-ranging birds eat infected earthworms. The disease is characterized by a typhlitis (Chapter 3) and hepatitis. Grossly, liver lesions consist of multiple, round, yellow-green, depressed foci (Fig. 4.49). Histologically the gross lesions

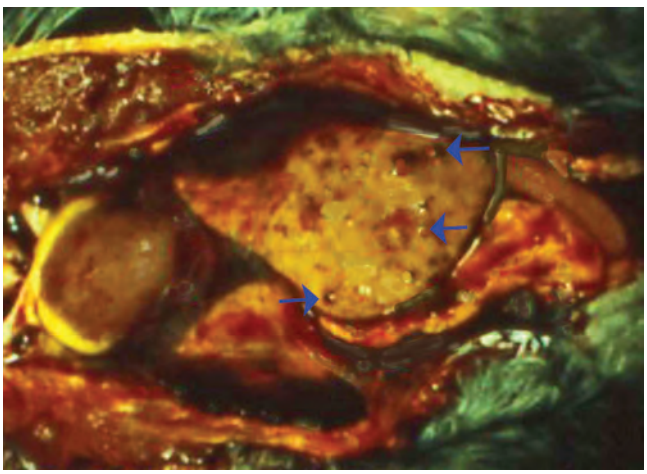

Figure 4.47 Liver from a bird with severe hemoprotozoal infection. The numerous small dark foci are areas of hemorrhage surrounding protozoal cysts (megaloschizonts) (arrows).

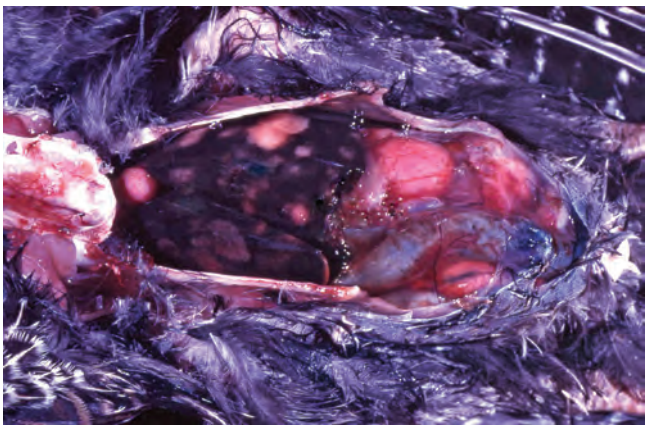

Figure 4.49 Liver lesions in a chicken with severe histomoniasis.

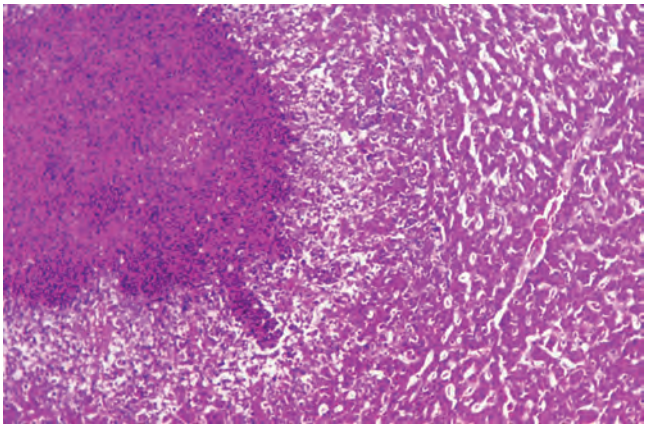

Figure 4.50 Severe hepatic necrosis and inflammation in a bird with histomoniasis.

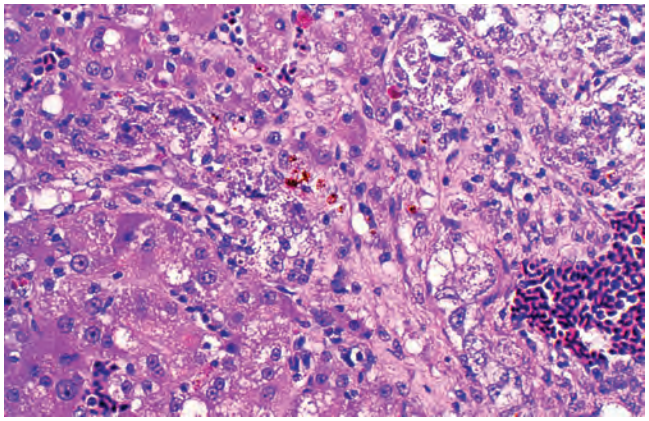

Figure 4.52 Microsporidial hepatitis. Numerous organisms are seen as small, dark foci in the macrophages.

represent multifocal to locally extensive and, at times, coalescing granulomas. The trophozoites are pale, round, and eosinophilic, varying in size from 5 to 20 m. They are generally abundant and are strongly periodic acid–Schiff positive (Figs. 4.50 and 4.51).

Phylum:Microspora

The phylum Microspora contains over 1000 species that infect a huge range of vertebrate and invertebrate hosts. *Encephalitozoon hellem*, *E. intestinalis, E. bieneusi,* and *E. cunniculi* have been shown to infect birds. Only disease associated with *E. hellem* has been described in birds. For the most part, *E. hellem* commonly and asymptomatically infects budgerigars and lovebirds and perhaps other species of birds as well. However, disease does occur in these species and has been also reported in eclectus parrots, lories, a blue-fronted Amazon parrot, ostriches, and hummingbirds. Disease appears most likely to occur in birds that are immunosuppressed. Concurrent infections with the PBFDV are common and may predispose birds to disease. *Encephalitozoon hellem* also causes disease in people who are severely immunocompromised.

Target organs for *E. hellem* are the liver, kidney, spleen, intestine, and, less commonly, the eye. (See the relevant chapters.) Disease, when it occurs, has predominated in flocks of budgerigars and flocks of lovebirds. Varying degrees of morbidity and mortality occur. Live birds may have diarrhea and appear unthrifty. Gross necropsy findings include pasted vents, pale voluminous feces, watery intestinal contents, and undigested seeds in the feces. Liver and spleen enlargement are variable findings, as is liver mottling. Histologically there may be mild to moderate hepatic necrosis and an infiltrate of macrophages and lymphocytes. Round, approximately 1.5-m-diameter, lightly basophilic organisms are found in hepatocytes, bile duct epithelium, and free in the areas of necrosis. Although they stain poorly with H&E (Fig. 4.52), they are readily visible with Brown and Brenn and trichrome stains. When there is substantial hepatic necrosis, infection is often accompanied by a mononuclear cell infiltrate.

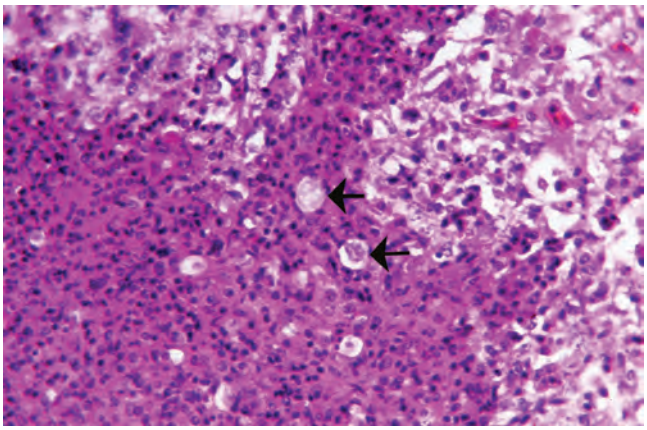

Figure 4.51 Higher magnification of Figure 4.50, illustrating histomonads in the hepatic parenchyma. Most of the organisms are surrounded by a clear zone.

Metazoan parasites: Trematodes

Trematodes have a complicated life cycle that involves one or more intermediate hosts. As a result, infections with these parasites are confined almost exclusively to wild or wild-caught cage birds. Most captive waterfowls are incubator hatched so that, unless these birds are exposed to wild waterfowl, they are not likely to have trematodes either. Flukes, such as *Fasciola hepatica*, damage the liver by migrating through it to the predilection site, the bile ducts. Both cockatoos and emus are reported to be parasitized by flukes that have a predilection for the bile ducts. Once in the bile ducts, trematodes may cause little disease or gross thickening and possible discoloration of the bile ducts (Fig. 4.53). Histologically there may be a minimal mononuclear inflammatory reaction in some cases (Fig. 4.54). Fibrosis and bile duct hyperplasia can be seen in chronic disease (Fig. 4.55).

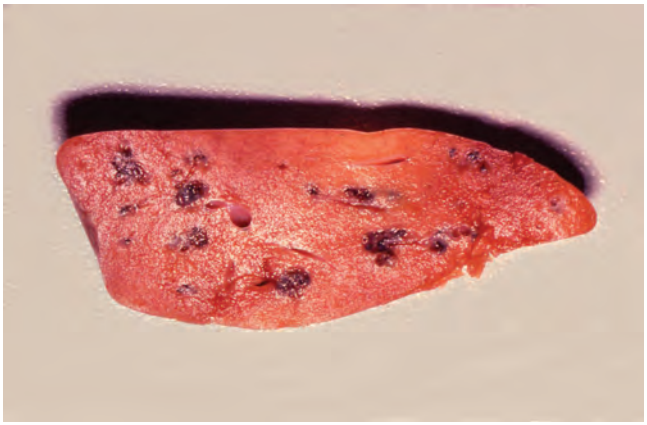

Figure 4.53 Dilated bile ducts containing hepatic flukes.

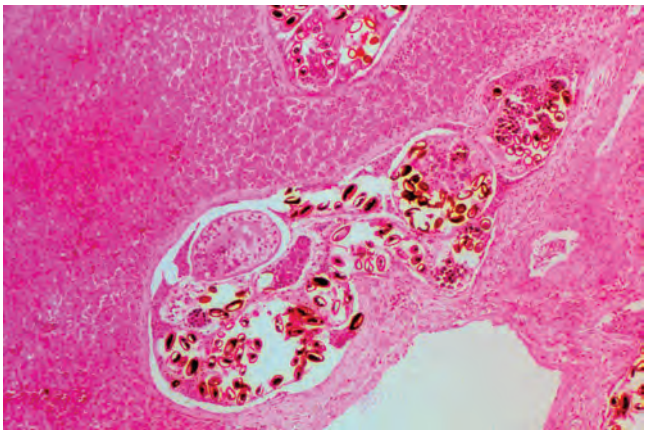

Figure 4.54 Trematode eggs in dilated bile ducts. A minimal inflammatory reaction and mild fibrosis are seen.

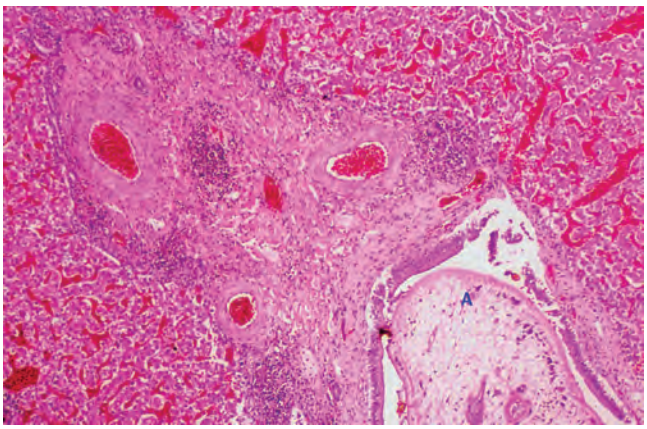

Figure 4.55 A trematode is seen in a dilated bile duct([A). There is periductal fibrosis and inflammation.

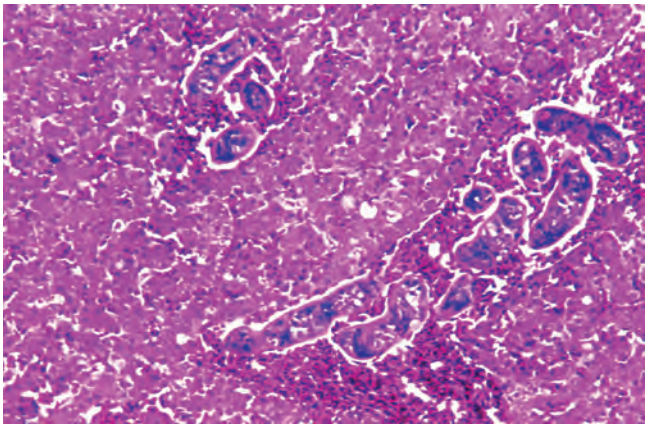

Figure 4.56 Fragments of schistosomes are seen in the hepatic sinusoids.

Emus with *F. hepatica* infection have an eosinophilic reaction, as well as infiltration of macrophages and lymphocytes. There may also be granuloma formation with giant cells and variable degrees of fibrosis. Aberrant colonization of the biliary tree by intestinal flukes may also occur, resulting in similar lesions.

Schistosomes are commonly found in waterfowl but are also reported in passerine species. Birds are infected by cercariae that are found in contaminated bodies of water. The cercariae penetrate the skin and enter the circulatory system, where they develop into adult worms. The adult worms in birds inhabit the portal veins, hepatic sinusoids, the aorta, or the mesenteric arteries, depending on the species of schistosome (Fig. 4.56). Schistosomes release their eggs, which then penetrate small vessels in the intestines and liver. The eggs induce a granulomatous foreign-body reaction.

Noninfectious disease

Nutritional/metabolic disorders

Hepatic atrophy

This diagnosis is uncommonly made in birds, based on the literature and our experience. Congenital atrophy is theoretically possible, but not documented. Acquired atrophy can be secondary to a variety of problems, with a negative calorie balance being the most common. Grossly the affected liver will be small, but shape and color appear essentially normal (Fig. 4.57). Histologically hepatocytes are small and hepatic cords are narrow, with an apparent increase in sinusoidal space. Liver impression smears may contain narrow, irregular cords comprising small hepatocytes with pyknotic nuclei and vacuolated cytoplasm (Fig. 4.58).

Hepatic lipidosis

Hepatic lipidosis is a problem in a wide variety of birds. One cause of hepatic lipidosis in chickens is biotin deficiency, but the exact pathogenesis of hepatic lipidosis in pet species is often not known. Excessive calorie intake, inadequate utilization of fat, hepatic enzyme defects, deficiency of dietary lipotrophs, and

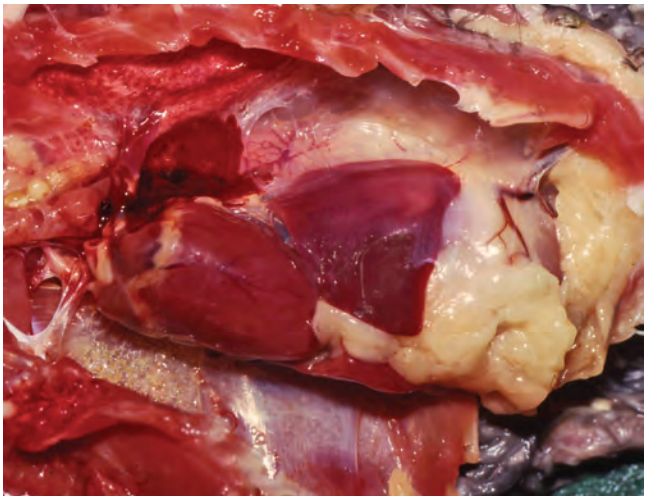

Figure 4.57 Hepatic atrophy. Histology is required to determine the exact underlying process

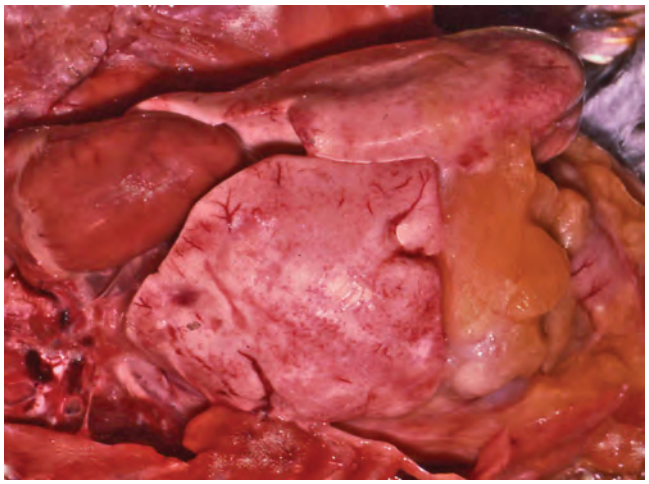

Figure 4.59 Enlarged, pale, friable liver with severe lipidosis.

toxic damage are all possible causes. Hepatic lipidosis, in pet birds, seems to be most common in Amazon parrots, cockatiels, budgerigars, macaws, and rose-breasted cockatoos, as well as in young cockatoos. The cause in older animals is commonly a dietary excess of fatty food. The disease in cockatoo chicks appears to be related to diets that contain excessive fat and/or excessive hand feeding. These chicks usually present with a swollen abdomen and obviously enlarged liver. Adult birds with hepatic lipidosis often die with no premonitory signs. It should be noted that in precocial birds, the liver may appear fatty for the first 2–3 weeks posthatch, as there is a longer presumptive time for yolk sac resorption.

Grossly affected livers are enlarged, pale and/or yellow, and friable (Fig. 4.59). Histologically, in uncomplicated cases, hepatocytes are variably vacuolated and swollen (Fig. 4.60), with no other lesion seen. Mild degrees of lipidosis are commonly seen in birds that have been in a negative calorie balance prior to death. In these cases, hepatocytes may contain one or multiple small lipid vacuoles.

One of the common causes of death due to noninfectious disease in chickens is a condition termed fatty liver hemorrhagic syndrome. There is some disagreement in the literature concerning this condition. It has been considered a problem with caged birds on high-energy diets that lead to an enlarged fatty liver that may rupture and bleed (Fig. 4.61). However in a study of backyard chickens, although most were obese females actively laying, not all birds had hepatic lipidosis. Histologically there was an indication of repeated parenchymal hemorrhage prior to hepatic rupture and death and the name hemorrhagic liver syndrome was proposed. The cause and pathogenesis are still not conclusively known.

Visceral urate deposition (gout)

The liver capsule is a common location for urate deposits in birds with visceral gout. The exact pathogenesis may not always

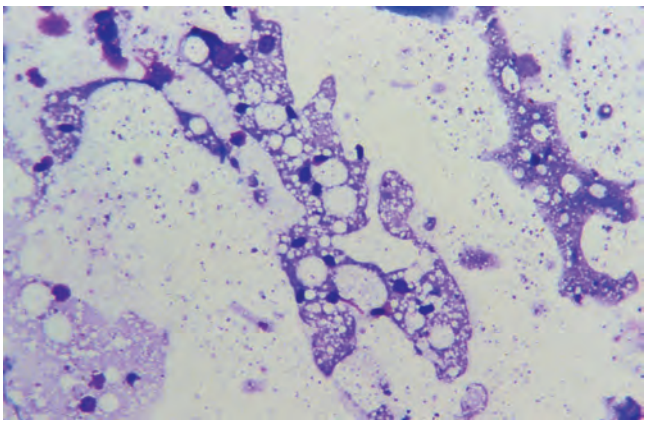

Figure 4.58 Impression smear from a blue-fronted Amazon parrot with chronic liver disease. Hepatocytes are small and vacuolated, and cords are separated.

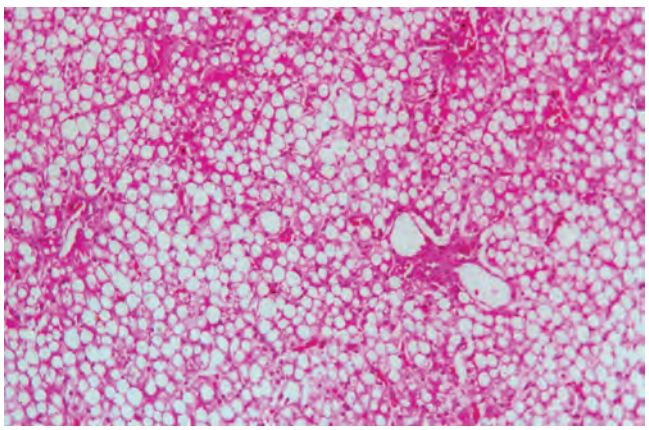

Figure 4.60 Typical histologic appearance of severe fatty liver.

Figure 4.61 Fatty liver—hemorrhagic syndrome in a chicken. The liver is enlarged and yellow and has ruptured leading to hemorrhage.

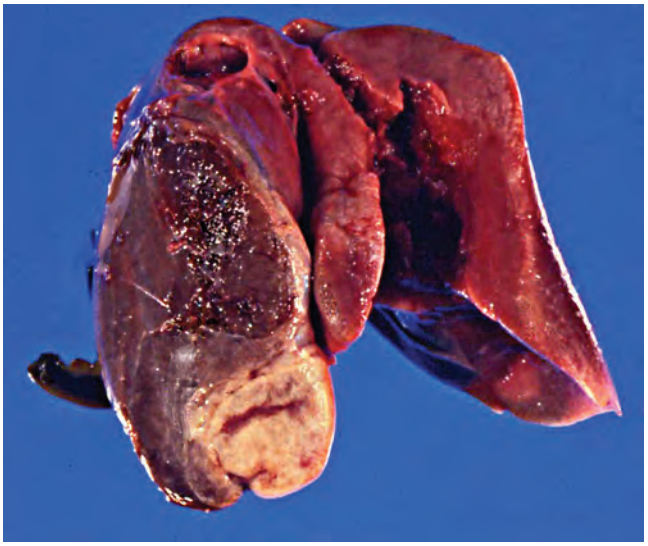

Figure 4.62 Large, pale, irregular liver due to diffuse amyloidosis.

be obvious, but the condition is usually secondary to renal disease or inadequate water intake. Any species of bird can be affected. Grossly the hepatic capsule contains gray-white plaques or streaks, and the urate deposits may completely obscure the underlying liver. Parenchymal lesions can also be seen. Urates are water soluble and will dissolve while the tissue is fixed in formalin. Histologically the radially arranged needlelike crystals are gone, but they leave behind empty spaces of the same shape that are surrounded by a pale amorphous eosinophilic material. Capsular urate deposits are often more amorphous than they are crystalline and therefore appear as irregularly round eosinophilic masses. Necrosis and an inflammatory reaction that are primarily heterophilic may accompany the urate deposits.

Amyloidosis

This is the general term applied to several diseases characterized by the deposition of one of several forms of amyloid. Only amyloidosis caused by the deposition of AA amyloid has been described in birds. AA amyloid is the product of the proteolytic cleavage of serum amyloid A, an acute-phase protein. Serum amyloid A is believed to be persistently elevated in birds with chronic granulomatous disease. Amyloidosis is a common lesion in waterfowl. Additionally the white Pekin duck is genetically predisposed to amyloidosis, and lesions are present in these birds by 2 years of age. Amyloidosis is relatively rare lesion in other birds, including doves, finches, and parrots. The distribution of organ involvement varies from bird to bird.

Grossly, infiltrated organs may be pale, firm, and waxy or friable. Affected organs are enlarged, sometimes massively (Fig. 4.62). On cut section, they stain with iodine. Amyloidosis grossly may resemble hepatic lipidosis. Histologically amyloid is amorphous, pale eosinophilic or amphophilic, and the amount present is variable. Amyloid deposition occurs in the liver in the space of Disse and in the media of blood vessels, and on basement membranes (Fig. 4.63). In severe cases, the amyloid can efface much of the hepatic parenchyma and lead to hepatic failure. Amyloid is differentiated from other acellular eosinophilic material, such as fibrin and immune-complex deposition, by positive staining and birefringence with Congo red stain. Avian amyloid, however, does not consistently stain well with Congo red.

Pigmentary hepatopathies

Iron pigment in the liver is a common histologic finding. When it is confined to phagocytic cells, the iron is in the form of hemosiderin, a metabolite of hemoglobin. Hemosiderosis results from either a higher than normal rate of red cell destruction or decreased utilization of iron for new hemoglobin production. The most common hemolytic disease of birds is heavy metal poisoning. *Plasmodium* infections may result in massive hemolysis and hepatic hemosiderosis. Immune-mediated hemolytic anemia is rare in cage birds, being reported only once in a

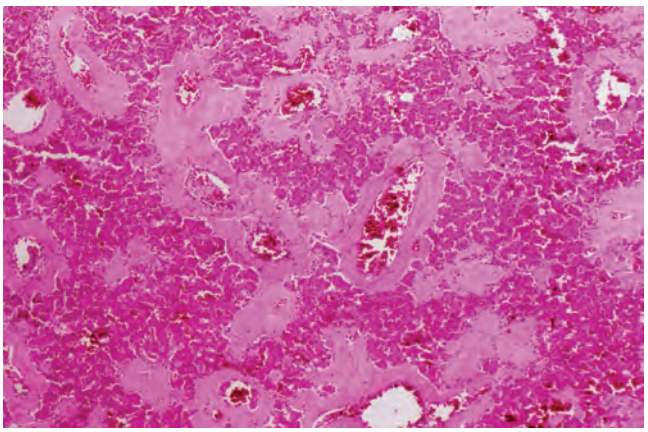

Figure 4.63 Severe hepatic amyloidosis.

blue-crowned conure. One author (DNP), however, has suspected it in a blue and gold macaw, given serum contaminated with hemoglobin from a chicken and in a sun conure with an uncharacterized bleeding disorder. The most common cause of hemosiderosis is reduced red blood cell production. Birds that are in a negative calorie balance or have chronic disease stop producing red blood cells or produce them at a decreased rate. Red blood cell destruction continues, however, at a constant rate, and, as a result, iron accumulates in phagocytic cells in the liver, spleen, and kidney. This is a reversible change and is not associated with liver disease.

Iron accumulation in hepatocytes, iron storage disease (ISD), is an entirely different entity than hemosiderosis. ISD is predominantly a disease of captive mynahs (*Gracula* sp.), birds of paradise (Paradisaeidae), quetzals (*Pharomachrus* sp.), several species of toucans (Ramphastidae), hornbills (particularly frugivorous species), and fairy bluebirds (*Irena puella*). Infrequently it is seen in other species of birds, including parrots. Work done with mynahs suggests that ISD develops in susceptible species because they are highly efficient at absorbing dietary iron and do not downregulate iron absorption sufficiently when fed iron-rich diets. It is presumed that in the wild these birds feed on diets that contain little iron or iron that is in a form that is not readily absorbed from the digestive tract. It is also assumed that the diet fed by these birds in captivity contains either excess iron or iron that is readily digestible, resulting in the accumulation of iron in the liver and other tissues. ISD in lories was traced back to a diet containing a hugely excessive amount of iron, and ISD does not occur in these birds when fed an appropriate diet. ISD has been called hemochromatosis, but this may be inappropriate because hemochromatosis refers to a human disease characterized by a genetic defect in iron metabolism.

Excessive liver iron and ISD are not synonymous. Iron will accumulate in the liver for long periods prior to the onset of disease. Therefore the presence of iron in hepatocytes in the absence of other lesions does not constitute sufficient grounds for a diagnosis of ISD. Birds with ISD may die suddenly and be in good body condition or have chronic muscle wasting. Ascites is a common finding and may be secondary to liver disease or heart failure. The liver in birds with ISD is enlarged and gold-brown. Small, scattered, dark foci may be seen (Fig. 4.64). The histologic appearance varies with the amount of iron deposited. Iron can be seen in hepatocytes and in Kupffer cells and macrophages. There may be an associated inflammatory process that includes lymphocytes and scattered heterophils. In severe cases, there is variable hepatic necrosis and, with chronicity, fibrosis develops. Prussian blue staining will confirm the pigment as iron but is usually not necessary (Figs. 4.65, 4.66, and 4.67).

Bile pigments are commonly found in the liver. The pigments may be present in canaliculi or within Kupffer cells. Bile pigments are seen in the livers of birds that have hepatic diseases that result in bile stasis.

Lipofuscin pigment accumulates in hepatocytes secondary to a variety of diseases. It is considered a "wear and tear" pigment

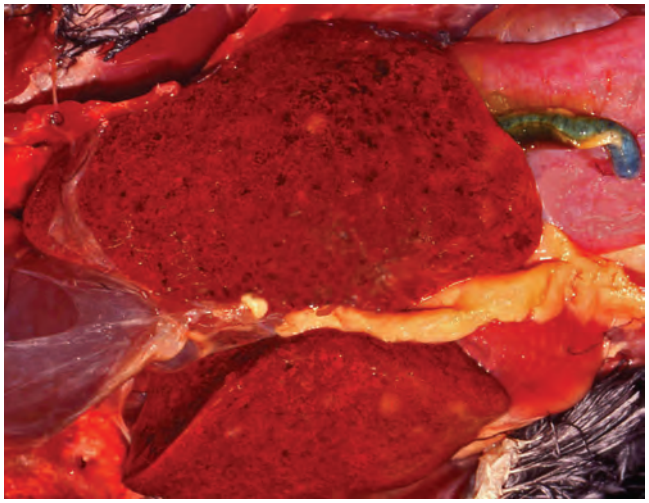

Figure 4.64 Iron-storage disease in a hornbill. The liver is discolored, and the multiple dark foci represent collections of Kupffer cells/macrophages containing pigment.

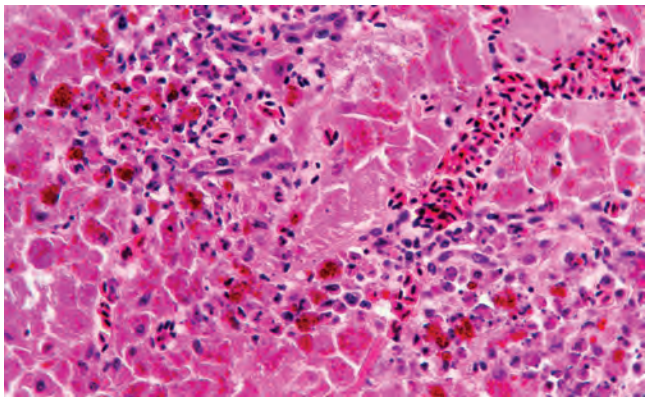

Figure 4.65 Iron-storage disease. The iron can be seen primarily in Kupffer cells and macrophages, although a small amount is in hepatocytes.

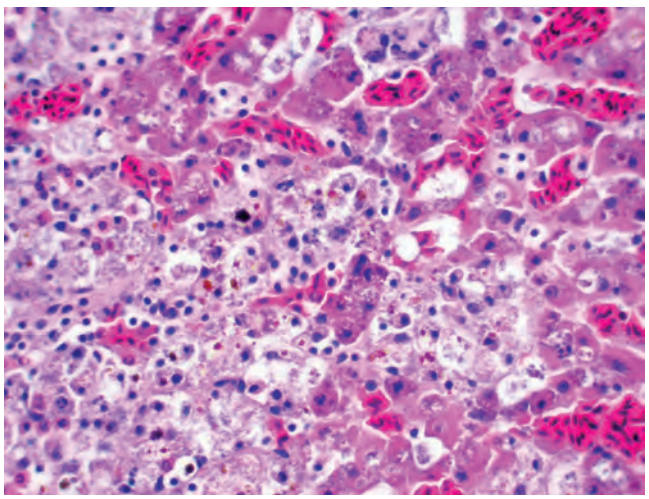

Figure 4.66 Iron-storage disease. In this case, the iron is primarily in the hepatocytes.

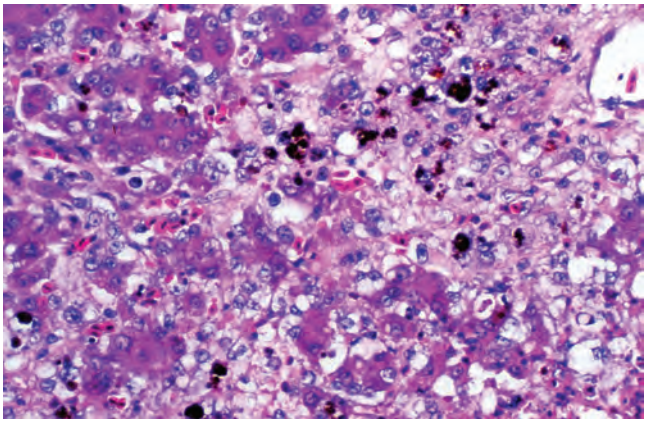

Figure 4.67 Iron-storage disease in a lorikeet. In addition to pigment accumulation in macrophages and hepatocytes, there is variable necrosis.

and is due to excessive biologic oxidation at the cellular level. Vitamin E deficiency is one possible cause. Affected livers may be darkly mottled (Fig. 4.68), and the green-brown pigment is found in hepatocytes histologically.

Lysosomal storage disease

In emus, lysosomal disease is usually considered a nervous system problem (Chapter 10), but lesions may also be found in the liver. Grossly there may be minimal mottling due to histologic foci of finely vacuolated cells that may be macrophages (Fig. 4.69).

Xanthomatosis

Internal xanthomas may be found in the liver, where they comprise numerous cholesterol clefts that efface normal parenchyma (Fig. 4.70).

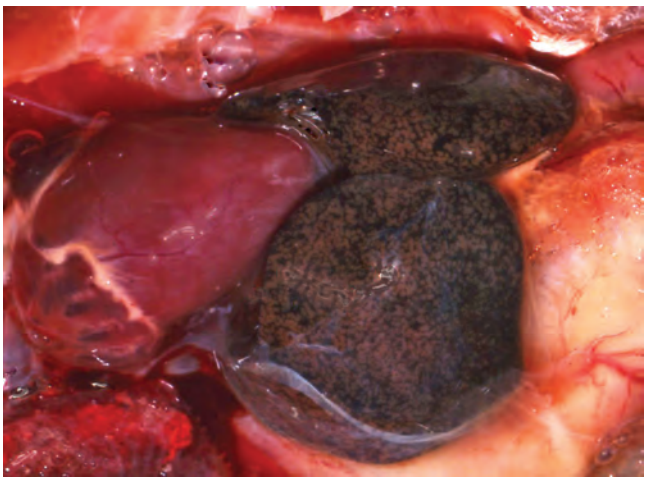

Figure 4.68 Severe hepatic lipofuscinosis. Dark discoloration and mottling are seen. Differential diagnoses would include iron pigment deposition (hemosiderosis) and possible plasmodial infection in some species.

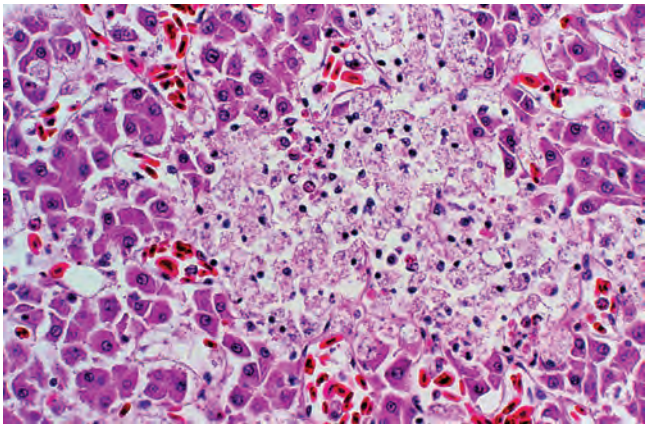

Figure 4.69 Lysosomal storage disease with foci of cells containing finely vacuolated cytoplasm.

Chronic-active hepatitis

Chronic-active hepatitis, or cirrhosis, is relatively common in psittacine birds, particularly Amazon parrots, cockatiels, macaws, and budgerigars. Because of the chronicity of the lesion, the cause of the hepatitis can rarely be determined. Cockatiels are extremely sensitive to aflatoxins, and it has been speculated that chronic-active hepatitis in these birds may result from a previous exposure to aflatoxins. Chronic-active hepatitis, in other species, is seen in cases of chronic infectious diseases, particularly chlamydiosis, and exposure to bile-excreted toxins.

Grossly affected livers are variably shrunken, pale, and fibrotic. The capsule is often thickened, and the edges of the liver are rounded. In extreme cases, there may only be small firm nodules in place of the normal liver (Figs. 4.71, 4.72, and 4.73). Perihepatic effusion is common. The histologic appearance varies with the stage of the disease. Early lesions consist of hepatocyte vacuolation, a pleocellular inflammatory infiltrate primarily in portal areas, bile duct proliferation, and mild fibrosis (Fig. 4.74). The lesion may progress to severe fibrosis and diffuse biliary hyperplasia (Figs. 4.75, 4.76, 4.77, and 4.78). In some cases, severe extramedullary hematopoiesis is seen (Fig. 4.79).

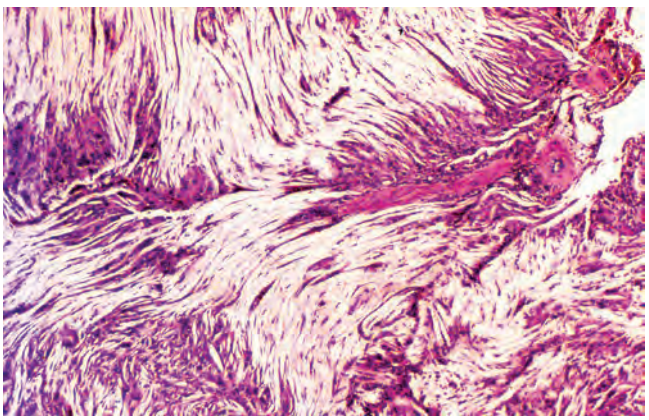

Figure 4.70 Xanthoma within hepatic parenchyma.

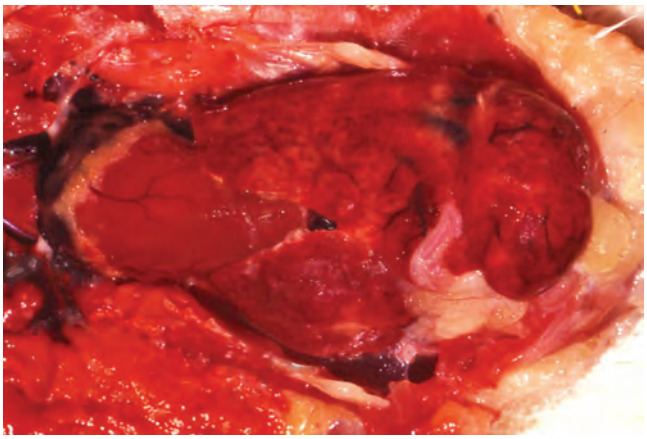

Figure 4.71 Early chronic-active hepatitis. Slight discoloration and irregularity are noted.

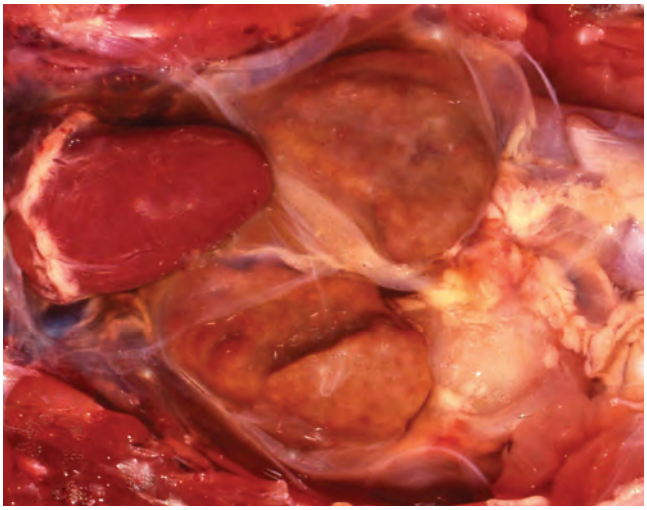

Figure 4.72 Moderate to severe chronic-active hepatitis. The liver is pale, firm, and nodular.

Figure 4.73 End-stage liver as a result of chronic-active hepatitis.

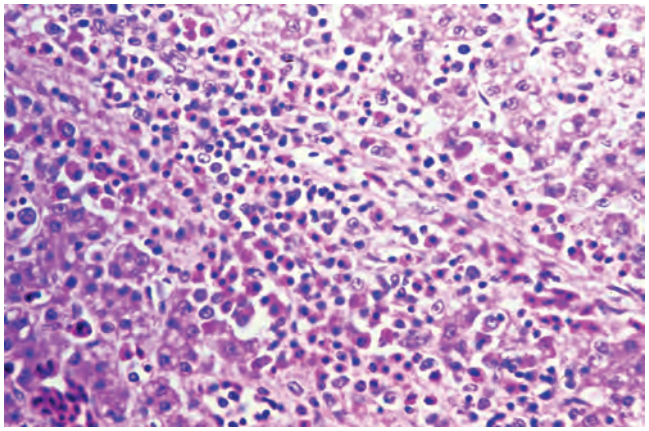

Figure 4.74 Early chronic-active hepatitis with mild fibrosis and diffuse inflammation.

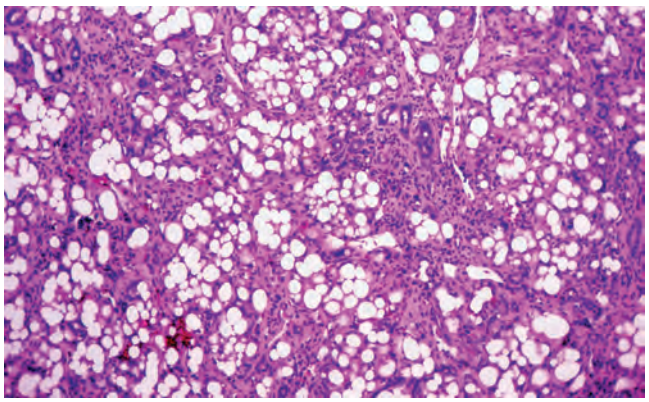

Figure 4.75 Chronic-active hepatitis with moderate fibrosis, bile duct hyperplasia, extramedullary hematopoiesis, and inflammation. The hepatocytes are vacuolated.

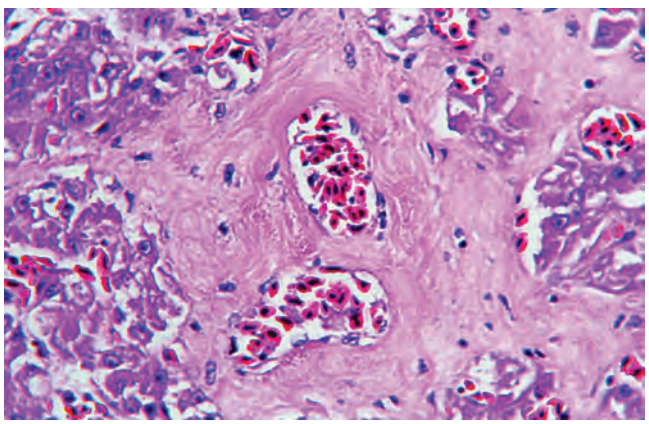

Figure 4.76 Moderate to severe fibrosis with minimal inflammation and hepatocyte atrophy rather than vacuolation and swelling.

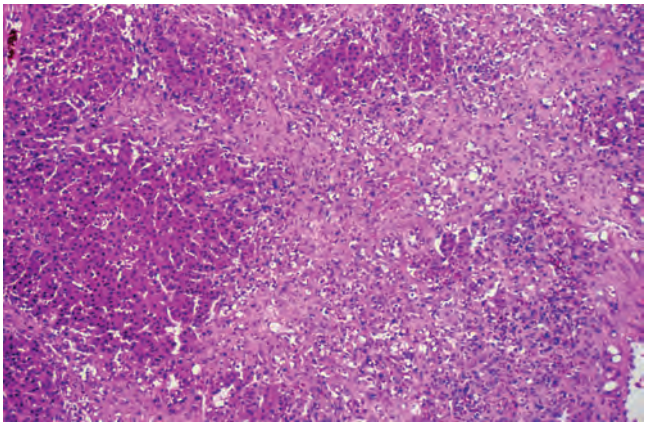

Figure 4.77 Severe chronic-active hepatitis. Marked fibrosis and nodular hyperplasia are seen.

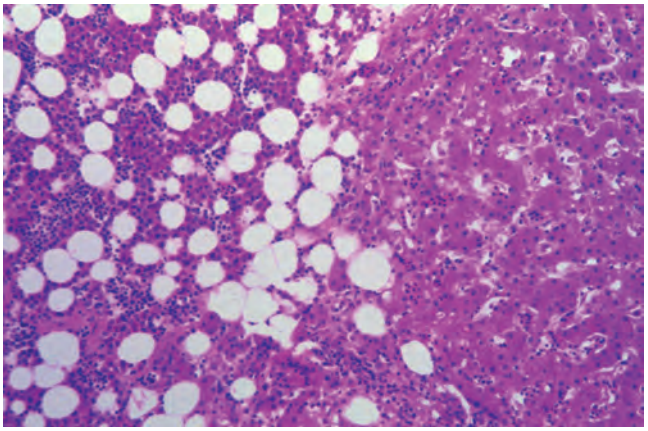

Figure 4.79 Extramedullary hematopoiesis as occasionally seen in chronic-active hepatitis. Nodular hyperplasia is also seen.

Hepatic fibrosis

Fibrosis can be the end result of many processes. Affected livers will be somewhat small, pale, and firm (Fig. 4.80).

Hepatic infarction

There are many potential causes of hepatic infarction, but one that occurs somewhat more frequently is associated with yolk emboli. This may be confined to one lobe. Grossly there is variable necrosis and hemorrhage (Fig. 4.81), and histological specificity depends on finding yolk material in blood vessels.

Heart failure

Right-sided heart failure results in the dilation of the hepatic veins and congestion of the hepatic sinusoids. Initially the liver may be enlarged. Chronic right-heart disease results in severe atrophy of the centrolobular hepatocytes, fibrosis, and capsular thickening. Perihepatic effusion may be prominent. Grossly the liver lobes are small, have rounded margins, and have a gray surface caused by the thickened capsule.

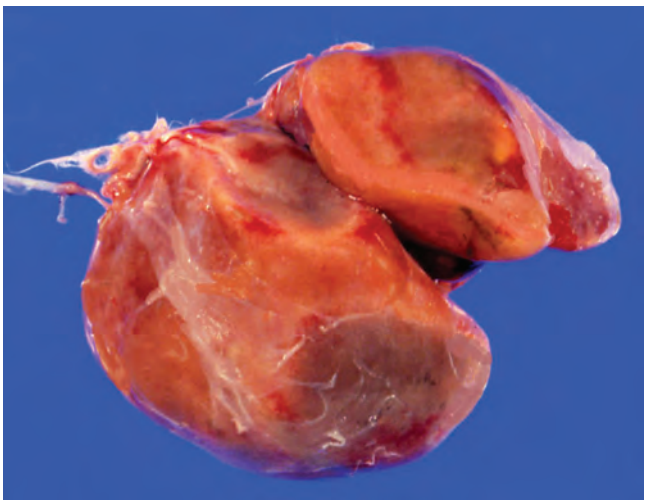

Figure 4.80 Hepatic fibrosis. The liver is small, pale, and firm.

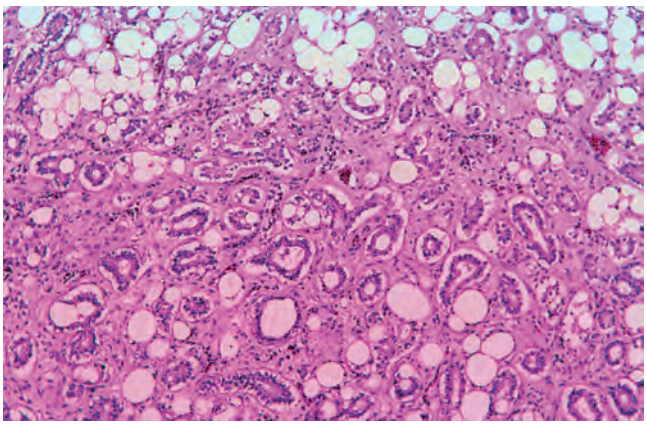

Figure 4.78 Chronic-active hepatitis with fibrosis and severe bile duct hyperplasia.

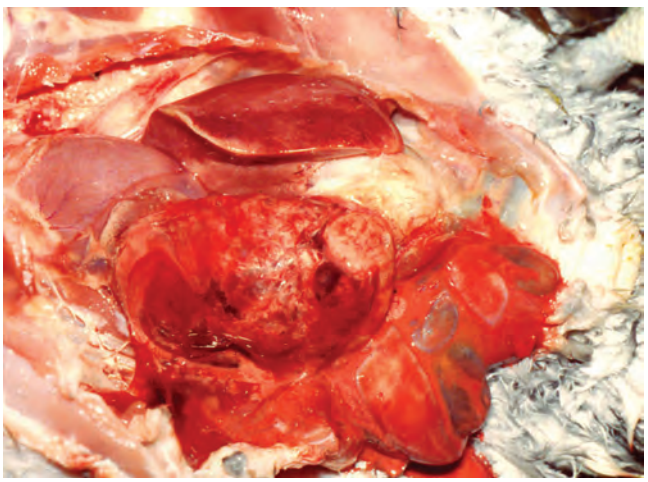

Figure 4.81 Infarcted liver lobe secondary to a yolk embolus.

Toxins

Many toxins can affect the avian liver. Lesions seen are not specific in most cases, and an etiologic diagnosis usually cannot be made on the basis of morphologic changes. In lead toxicosis, there may be some hepatic enlargement. Histologic lesions noted include hemosiderosis and variable hepatocyte swelling. Zinc toxicity may result in hepatic lesions that include hemosiderosis and erythrophagocytosis. Vitamin D_3 or vitamin D_3 analog rodenticides cause secondary liver lesions comprising mineralization of basement membranes of sinusoids and blood vessels. Vitamin D_3 toxicity and possibly excessive dietary calcium may also result in metastatic mineralization. Mycotoxins that are bile excreted, such as aflatoxin, can cause periportal necrosis and inflammation. In chronic cases, there is bile duct hyperplasia and fibrosis as described in chronic-active hepatitis.

Neoplastic disease

Epithelial tumors

Primary tumors may be of hepatocellular or bile duct origin, but bile duct tumors are more common. Bile duct proliferation, and possibly tumor formation (most publications refer to these lesions are bile duct carcinomas), is reported in association with internal papillomatosis. It is caused by PsHV-1 genotype 3 infection of the biliary epithelium. Mucosal papillomas may not be seen in all cases, but cloacal or oral infections may still be present. Herpesvirus-affected birds are predominantly macaws, Amazon parrots, and, less frequently, conures. Gross lesions consist of variably sized masses that vary in consistency from friable to firm and from gray to yellow-white to red-brown (Fig. 4.82). They may be present in one or more lobes of the liver. They are typically multifocal and grow by expansion, crowding out the normal liver. Birds with these masses may die suddenly and be in good flesh, or they may have had a protracted illness with advanced muscle wasting and be devoid of body fat.

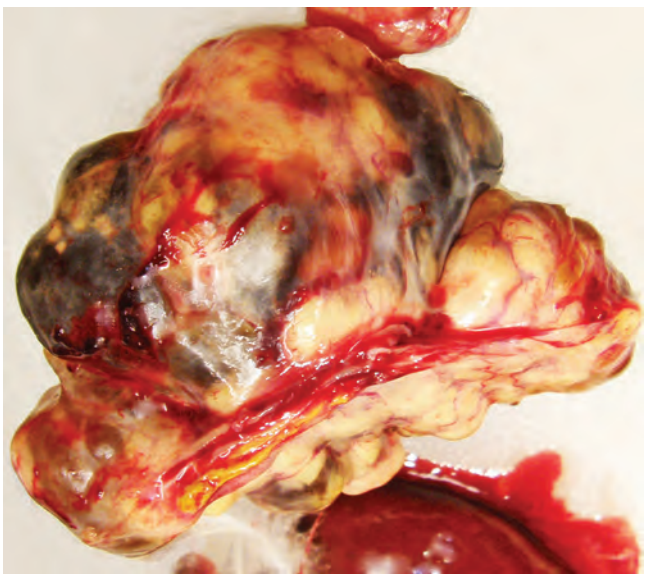

Figure 4.82 Nodular mass typical of bile duct carcinoma.

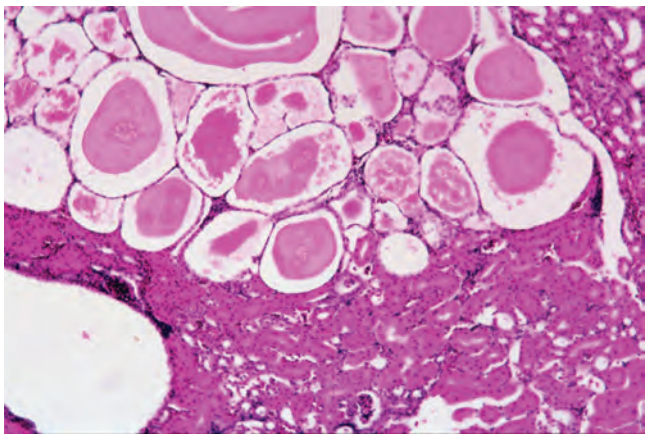

Figure 4.83 Bile duct adenoma composed of irregular ducts lined by fairly well-differentiated epithelium.

Proliferation of fairly well-differentiated ductular structures, accompanied by variable amounts of stroma, characterizes bile duct adenomas (Fig. 4.83). Carcinomas comprise less well-differentiated ducts, nests, cords, and individualized cells in some cases (Fig. 4.84). Hepatic impression smears can suggest the possibility of neoplasia (Fig. 4.85), but histology is necessary for definitive diagnosis and prognosis. Mitotic figures are usually infrequent. Occasionally carcinomas have cystic spaces. Metastasis is infrequently seen.

Hepatocellular carcinomas tend to be red-brown and friable. Masses may be solitary or multiple. Histologically hepatomas contain well-differentiated cells. Portal triads are absent in hepatomas, which is the only characteristic that differentiates them from hyperplastic nodules (Fig. 4.86). Hepatocellular carcinomas comprise moderately undifferentiated to poorly differentiated hepatocytes that form cords and nests. Minimal mitotic activity is noted. There is usually minimal stroma (Fig. 4.87).

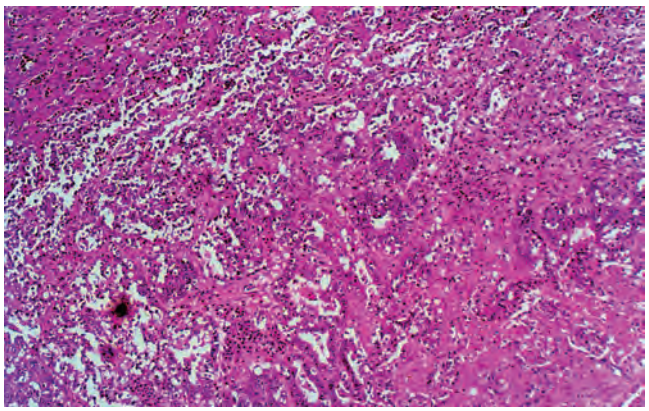

Figure 4.84 Bile duct carcinoma. Infiltrative nests and trabeculae are present, and there is a moderate amount of fibrous stroma.

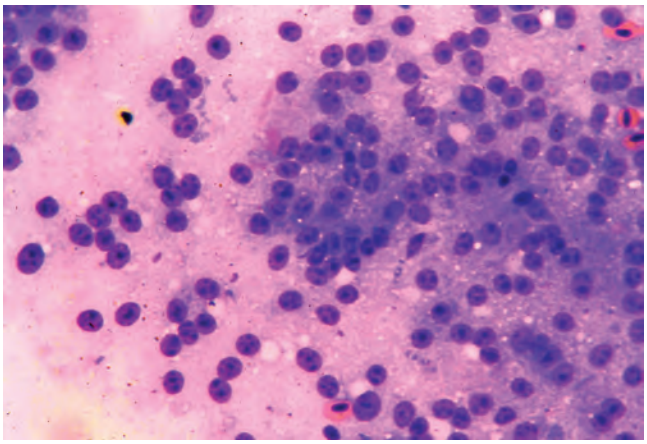

Figure 4.85 Hepatic impression smear from a bird with a bile duct carcinoma. Poorly defined biliary epithelial cells are forming structures that resemble ducts or acini.

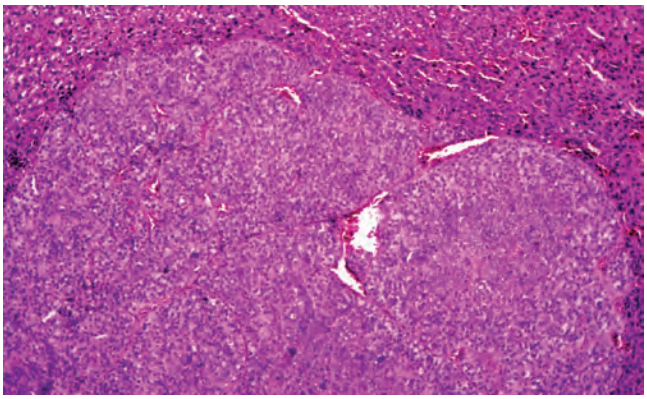

Figure 4.86 Well-demarcated hepatoma growing by expansion.

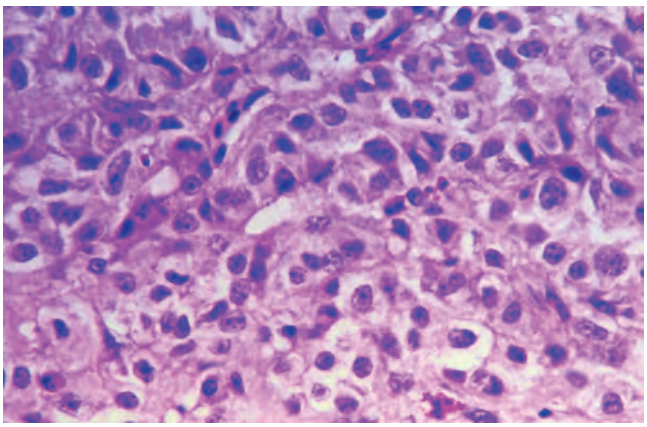

Figure 4.87 Hepatocellular carcinoma. Poorly differentiated hepatocytes form cords separated by minimal amounts of stroma.

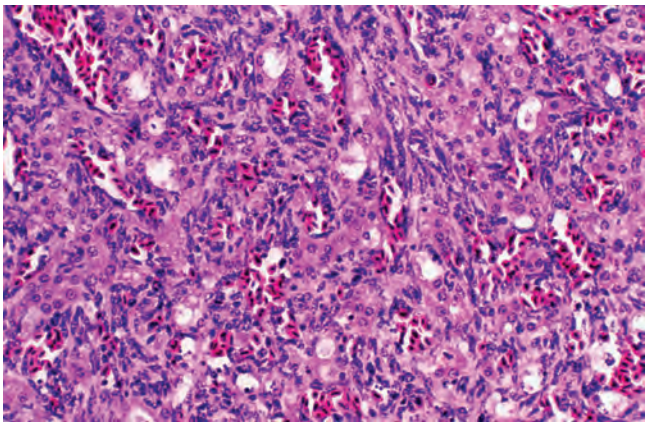

Figure 4.88 Hemangiosarcoma effacing hepatic parenchyma.

Mesenchymal tumors

Primary mesenchymal tumors of the liver include fibrosarcoma, lymphosarcoma, leiomyosarcoma, hemangioma and hemangiosarcoma, and myelolipoma. There are no specific gross features for these tumors. They present as solitary or multiple nodules or masses and are usually firm, with the exception being hemangioma/hemangiosarcomas that may be friable and hemorrhagic.

Histologic features of these tumors are similar to those that occur in any other location, though hemangiosarcomas in the liver tend to be more solid than in other tissues, but with a few vascular channels lined by poorly differentiated endothelial cells (Fig. 4.88). Fibrosarcoma and leiomyosarcoma comprise interlacing bundles of fusiform cells. Fibrosarcomas usually have a much higher mitotic rate (Fig. 4.89). Occasionally, hepatic sarcomas contain large cells with karyomegalic nuclei (Fig. 4.90). Polyomavirus particles have been seen in these cells by electron microscopy, but their significance has not been determined.

Lymphosarcoma grossly may present with multiple gray-yellow foci that mimic some severe infectious diseases (Fig. 4.91). In severe cases, however, entire lobes may be replaced by the tumor (Fig. 4.92). Histologically sheets of immature

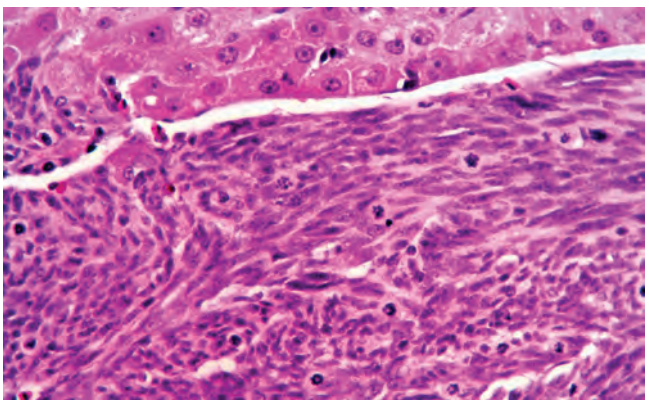

Figure 4.89 Primary hepatic fibrosarcoma composed of interlacing bundles of neoplastic cells.

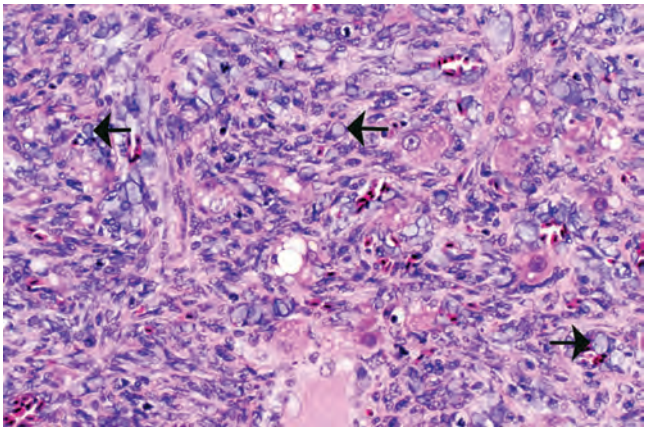

Figure 4.90 Hepatic sarcoma containing scattered cells with karyomegalic nuclei and intranuclear inclusion bodies (arrows). In many cases, these inclusions contain polyomavirus particles.

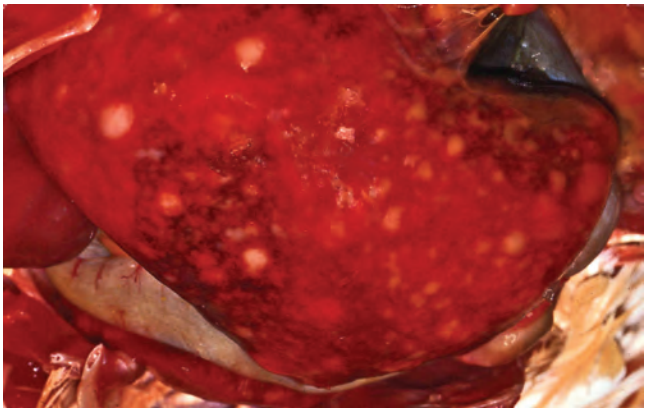

Figure 4.91 Hepatic lymphosarcoma. The gross appearance can be similar to that in severe infectious disease.

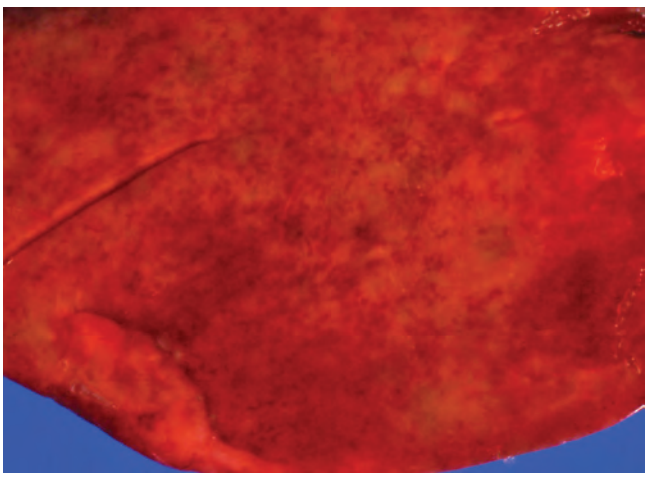

Figure 4.92 Portion of liver lobe almost completely replaced by neoplastic lymphoid cells.

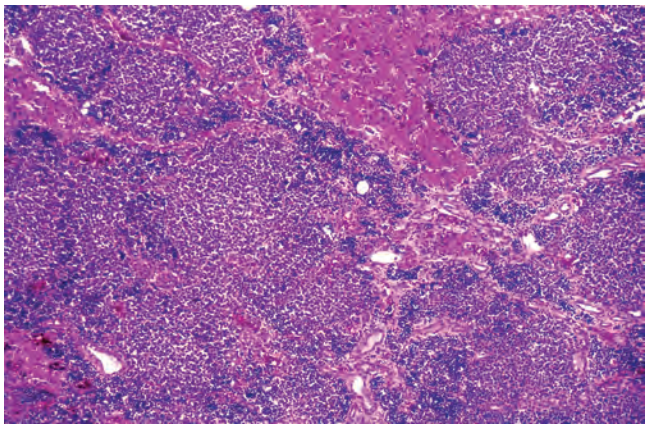

Figure 4.93 Effacement of liver by fairly monomorphic lymphoblasts.

lymphoid cells are seen replacing normal hepatic architecture (Fig. 4.93). Histiocytic sarcomas are also occasionally seen. The cells are pleomorphic with abundant cytoplasm and are diffusely infiltrative (Fig. 4.94). Malignant myeloproliferative disease may also be seen in the liver. Cytology of the lesions may be helpful in establishing a presumptive diagnosis (Fig. 4.95).

Myelolipomas are similar to those in mammals, containing well-differentiated adipose cells and bone marrow elements (Fig. 4.96).

Malignant melanoma

The liver may be the primary site of malignant melanoma. Grossly, multiple, gray-black nodules are seen. Histologically the tumor comprises poorly differentiated melanocytic cells with variable cytoplasmic pigment (Fig. 4.97).

Metastatic tumors

Potentially any carcinoma, sarcoma, or melanoma can metastasize to the liver; however, metastatic liver disease is uncommon. When liver metastasis does occur, it is usually by tumors of renal,

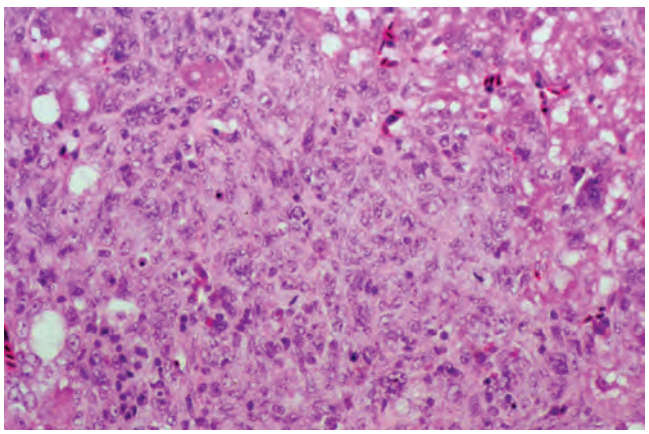

Figure 4.94 Infiltration of liver by neoplastic cells consistent with histiocytes.

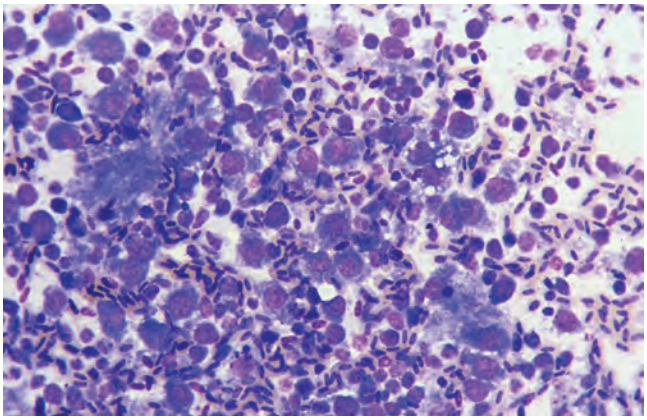

Figure 4.95 Impression smear of a liver from a bird with myeloproliferative disease. Hepatic parenchyma has been replaced by immature myeloid cells.

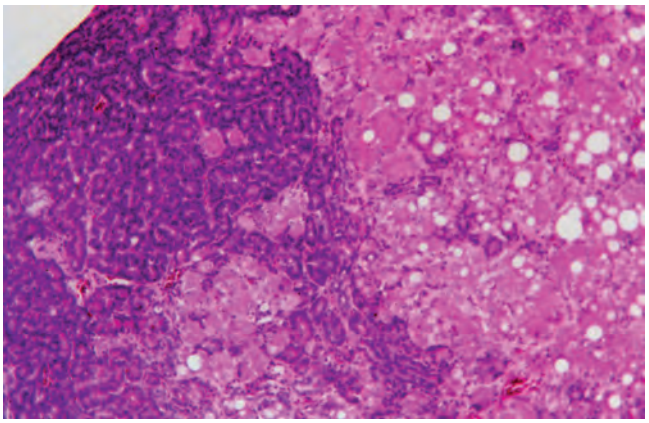

Figure 4.98 Pancreatic carcinoma metastatic to the liver. The light areas are foci of remaining hepatocytes.

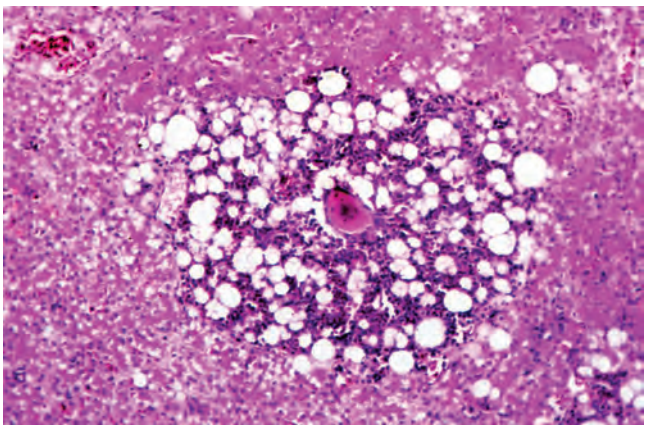

Figure 4.96 Hepatic myelolipoma. These tumors histologically resemble normal bone marrow.

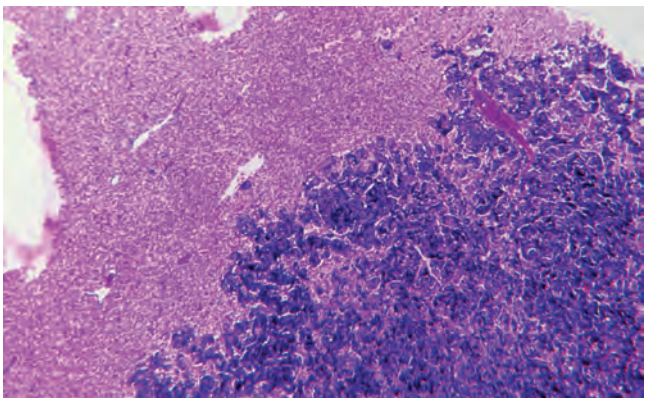

Figure 4.97 Malignant melanoma diffusely infiltrative in hepatic parenchyma.

pancreatic, or proventricular origin (Fig. 4.98). Extension of Sertoli cell tumor from the testicle has also been seen (Fig. 4.99). Grossly these tumors present as variably sized nodules, and histologic examination is necessary for differentiation.

Nonneoplastic epithelial proliferative lesions

Hepatocellular hyperplasia and cyst formation are seen in all birds. There may be nodular hepatocellular hyperplasia presenting as single or multiple red-brown or slightly yellow nodules. Histologically these nodules contain enlarged hepatocytes that may have vacuolated cytoplasm. Portal triads are seen in the nodules, differentiating them from adenomas.

Bile duct hyperplasia is more common than hepatocellular hyperplasia. As mentioned previously, this condition has been associated with internal papillomatosis. Grossly the lesion may vary from multiple yellow-white firm nodules to almost diffuse enlargement of a lobe. Histologically there is proliferation of well-differentiated ducts and moderate to marked amounts of fibrous connective tissue (Fig. 4.100). Bile duct hyperplasia is most common in those psittacine birds that have a high incidence of chronic-active hepatitis but is seen in a wide variety

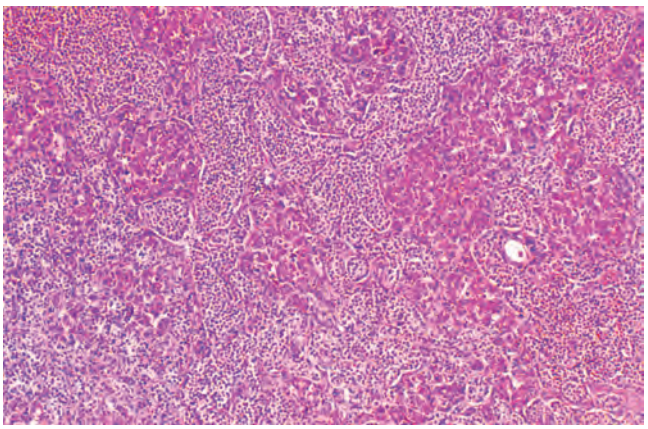

Figure 4.99 Extension of Sertoli cell tumor into the liver.

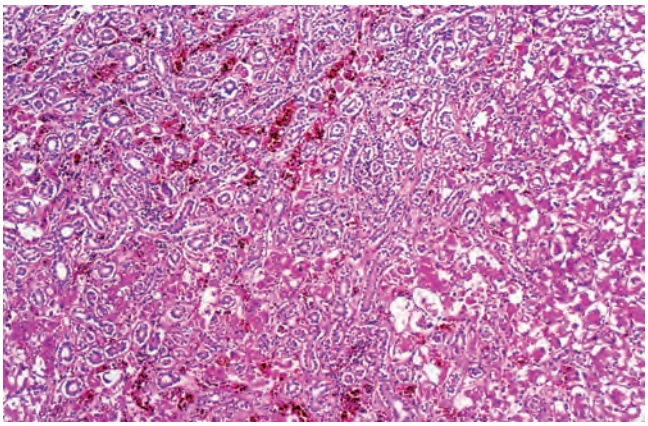

Figure 4.100 Marked fibrosis and bile duct hyperplasia of undetermined cause.

of pet birds. It can be severe enough to compromise hepatic function and be a primary cause of death. A careful histologic examination is necessary to differentiate hyperplasia, particularly when severe, from biliary adenoma.

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5 Urinary System

Normal structure

Kidney

Avian kidneys are bilaterally symmetrical and lie within ventral depressions of the synsacrum that are known as the renal fossae. They are retroperitoneal and firmly fixed in place. Nerves from the lumbar and sacral plexi pass through the kidney, a feature that can lead to secondary neurologic problems with renal neoplasia or other lesions that impinge on these nerves. The kidneys are divided into the cranial, middle, and caudal divisions. The size and shape of these divisions are fairly consistent in psittacine birds but vary considerably in other species. In most passerine species, the middle division is fused with the caudal division. The caudal divisions are fused on the midline in herons, puffins, and penguins. Attenuation between divisions is reported in Old World Columbidae, Coraciidae, Cuculidae, and Strigidae. Hornbills have distinctly separate cranial and caudal divisions, with no intervening middle division. The kidneys represent approximately 1% of body weight in small birds and somewhat less in large birds.

There are three pairs of renal arteries: the cranial, the middle, and the caudal. The cranial artery is a branch of the aorta, and the middle and caudal arteries originate from the ischiadic arteries. The external iliac artery crosses the kidney at the separation of the cranial and middle divisions. The ischiadic artery crosses the kidney at the junction of the middle and caudal divisions. Each artery supplies its respective division of the kidneys. The caudal renal veins receive drainage from the intralobular veins. The caudal renal vein joins the external iliac vein to form a common trunk that runs across the cranial pole of the kidney. The two iliac veins then join to form the caudal vena cava.

The most unique aspect of the avian kidney vasculature is the renal portal system. The joining of the paired external iliac veins and the caudal renal veins forms this vascular ring. Additionally, blood can flow into or out of the renal portal veins through the caudal mesenteric vein, the internal iliac vein, and the internal vertebral venous sinus. Branches from the portal ring supply the interlobular veins.

Microscopically the avian kidney is divided into independently functioning units called lobules. The unit comprising all the lobules draining into a common secondary branch of the ureter is called the lobe. Individual lobes may cross divisions. Lobules are distributed throughout the kidney and may contact the surface of the kidney or be completely embedded within the kidney. Each lobule has a cortex and medullary cone. In cross section, the cortex is defined by a central (intralobular) vein and peripheral interlobular veins. The intralobular veins empty into the capillary sinus that surrounds the cortical tubules. Midway between these veins is a branch of the intralobular renal artery. Afferent arterioles that feed the glomeruli arise from branches of the intralobular renal artery.

Birds have two types of nephrons: the reptilian type and the mammalian type. All of the components of the reptilian-type nephrons remain within the cortex. The reptilian-type proximal convoluted tubules loop out away from the glomerulus toward the interlobular veins and back. Each tubule then comes in contact with its afferent arteriole, forming the juxtaglomerular complex before becoming the distal convoluted tubule. The distal convoluted tubule loops toward the central vein and back, becoming a collecting tubule. The mammalian-type nephron begins with a glomerulus that is located at the junction of the cortex and the medullary cone. Its proximal convoluted tubule extends from the glomerulus and makes a loop in the cortex toward the interlobular vein before descending into the medullary cone to form the nephronal loop. The straight descending section narrows to form a thin segment and then abruptly widens to form the thick ascending segment. The thick limb comes in contact with its afferent artery, forming the juxtaglomerular complex. It then becomes the distal convoluted tubule and follows the same pattern as the reptilian-type nephron. Blood from the efferent arterioles of both the reptilian-type and the mammalian-type glomeruli empties into the capillary sinus, which drains into the intralobar veins. Proximal tubules are lined by cuboidal to columnar epithelium with a well-developed brush border. Cells decrease in size and the cytoplasm becomes basophilic in Henle's loop and distal tubules. Distal tubules also have a narrower lumen and no brush border. Surrounding the lobule are the perilobular collecting ducts, which run parallel to the interlobular veins and drain the collecting tubules. Thus the arrangement of the cortex of a lobule from edge to center is as follows: a surrounding network of interlobular veins and proximal collecting ducts, a peripheral zone

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composed primarily of proximal convoluted tubules, a zone of glomeruli, and a zone between the glomeruli and the central vein composed primarily of distal convoluted tubules.

The medullary cones comprise collecting ducts descending from the cortex and the nephronal loops of the mammalian-type nephrons. In passerine birds, this arrangement is highly structured with a central core of nephronal loops and a peripheral margin of collecting ducts. These elements may intermingle in other species of birds. Avian collecting ducts are dendritic, continuously joining until they become a secondary branch of the ureter.

The appearance of the avian glomerulus is structurally similar to the mammalian glomerulus, but there are several important differences. Mesangial cells, in the avian kidney, are more numerous and are clumped at the vascular pole, instead of the more diffuse distribution seen in the mammalian glomerulus. Additionally there are fewer capillary loops, and the capillary loops are less convoluted in the avian glomerulus.

Ureter

The ureter begins in the cranial division of the kidney and continues caudally in a groove on the ventral renal surface. It receives multiple primary branches, which in turn are made up of secondary branches, each of which drains the collecting ducts of the renal lobes. The ureter is stellate in cross section and is lined by mucus-secreting, pseudostratified columnar epithelium. Its wall contains fibrous connective tissue and smooth muscle. Each ureter terminates in the urodeum of the cloaca.

The developing kidney

Developing tubules and glomeruli can be seen in the kidneys of embryos and in some recently hatched birds (Fig. 5.1). This tissue is present on the periphery of the lobules. The developing tubules and glomeruli appear to be compressed. The tubular epithelial cells are smaller than those found in mature tubules and their cytoplasm is slightly more basophilic. Mitotic figures are common. Extramedullary myelopoiesis is also a normal and common feature of the developing kidney and may range from multifocal to locally extensive.

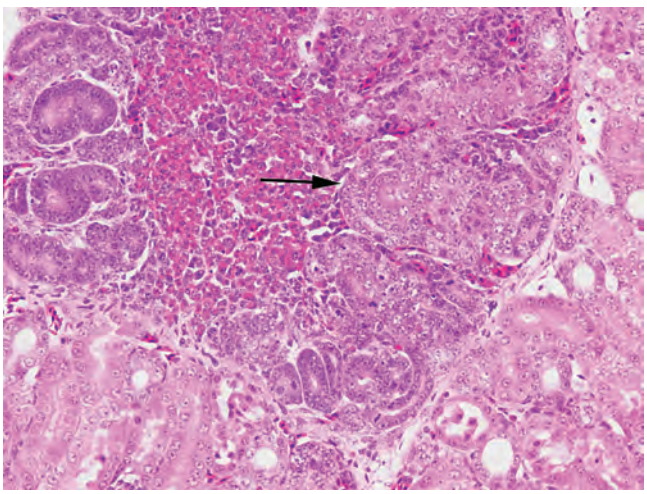

Figure 5.1 Section through the kidney of a recently hatched pigeon. A central area of extramedullary myelopoiesis is surrounded by developing tubules (arrow). Mature tubules are found along the bottom and right sides of the figure.

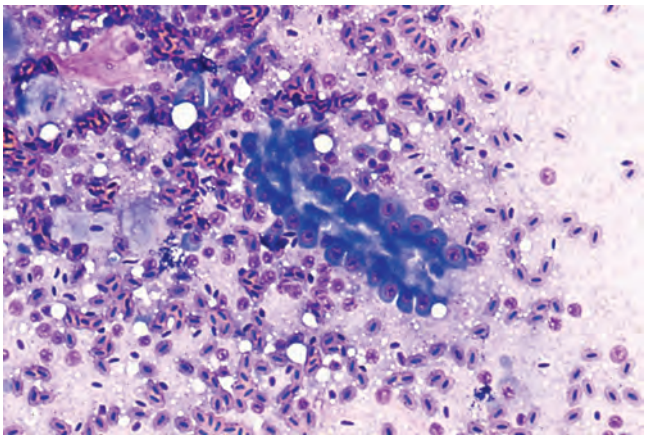

Figure 5.2 Impression smear of a pigeon kidney demonstrating a fragment of a tubule with attached epithelial cells.

Cytology

Cytology can be done on kidney biopsies obtained through the endoscope or by impression smears of samples collected at postmortem. Cytological preparations of the kidney are typically heavily contaminated with blood. Renal tubule cells are the other most abundant cells. They can be singular or multiple that are still present in fragments of tubules. Often the majority will have lost their cytoplasm and be represented by a round nucleus with single prominent nucleoli on a diffuse lightly basophilic background that represents the cells' ruptured cytoplasm (Fig. 5.2). Intact glomeruli can also be present. These appear as a dense ball of cells, whose cellular features are generally not discernable (Fig. 5.3). Inflammatory cells, in excess of those found in

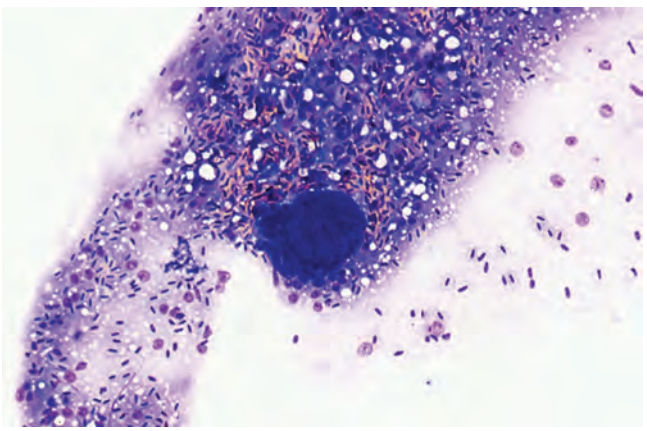

Figure 5.3 Impression smear of a pigeon kidney—a glomerulus.

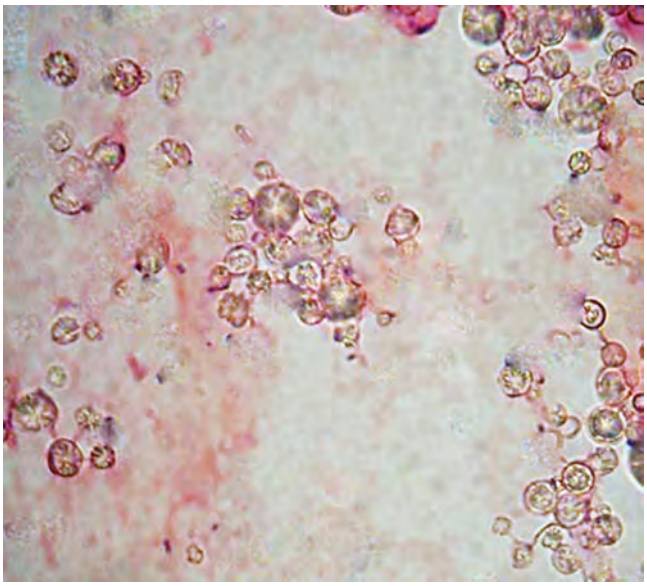

Figure 5.4 Uric acid in a cytological preparation of a bird's dropping.

the peripheral blood, plasma cells, and macrophages would not be normally found in a normal kidney with the exception of heterophils in an impression smear from a still developing kidney with extramedullary myelopoiesis. Urate crystals are water soluble and will be lost in most cytological preparations, but could be seen in an unstained wet prep of kidney tissue (Fig. 5.4).

Systemic effects of renal failure

The predominant nitrogenous waste product produced by birds is uric acid. The majority of uric acid is actively secreted by the proximal tubules. The remaining 10% is filtered by the glomerulus. Severe dehydration, extensive damage to the proximal tubules, lesions that obstruct urine outflow, or congenital malformations of the kidney are necessary for the development of uricemia. Elevations in plasma uric acid levels secondary to kidney failure result in gout, the precipitation of uric acid crystals on mesothelial surfaces and within the kidney. These lesions may be nodular (urate tophi), such as those that are found on synovial surfaces, or they may be diffuse, such as those found in the pericardium, liver capsule, air sacs, and peritoneum. Affected surfaces are chalky white, as are the contents of the urate tophi. Articular gout also occurs, but this lesion is not necessarily the result of hyperuricemia, and renal lesions may not be present.

Renal disease

Nonspecific changes

Congestion, distention of the capillary sinuses with blood, is a very common and nonspecific lesion in the kidney (Fig. 5.5).

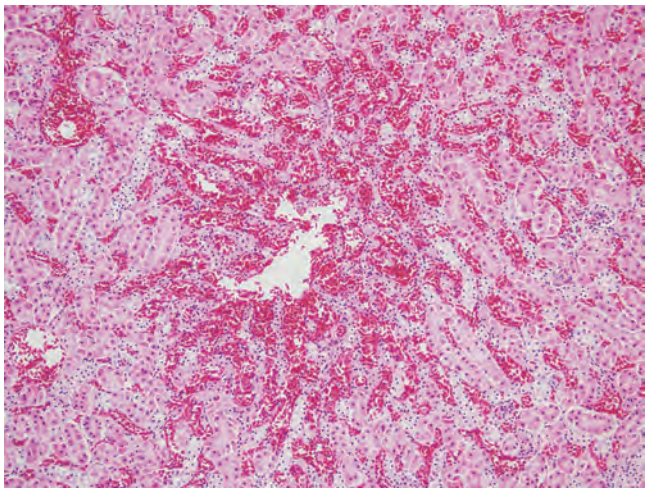

Figure 5.5 Congestion of the kidney with blood distention of the capillary sinuses.

Edema is a less common finding (Fig. 5.6). Presumably edema is caused by right-sided heart failure or low protein, but its cause has not been studied. Extramedullary myelopoiesis (Fig. 5.1) and hematopoiesis within the capillary sinuses can occur in birds that have a disease creating an increased demand for heterophils or birds with anemia, respectively. Because of the birds' diffuse lymphoid system, lymphocytic and at times plasmacytic aggregates and nodules can be found in the capillary sinuses in birds that are responding to diseases resulting in inflammation and infectious disease (Fig. 5.7). The infectious agent may not be impacting the kidney. These types of lesions are most common in the kidneys of pigeons and waterfowl and are uncommon in psittacine birds.

Congenital disease

Renal hypoplasia or aplasia occurs sporadically in birds (Fig. 5.8). It may be unilateral with no clinical signs and is often

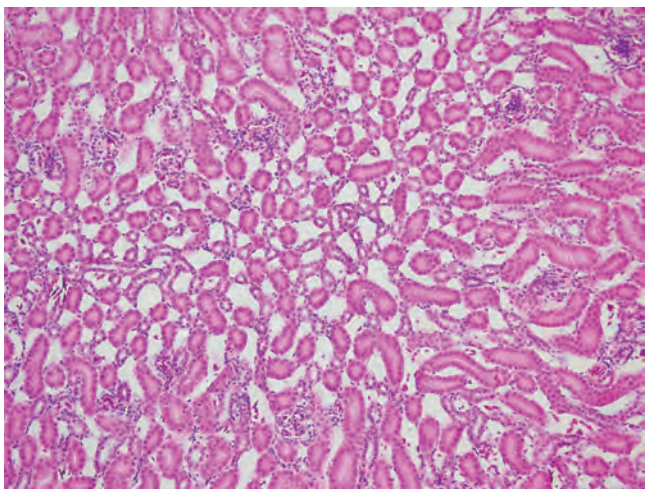

Figure 5.6 Renal edema with distention of the capillary sinuses.

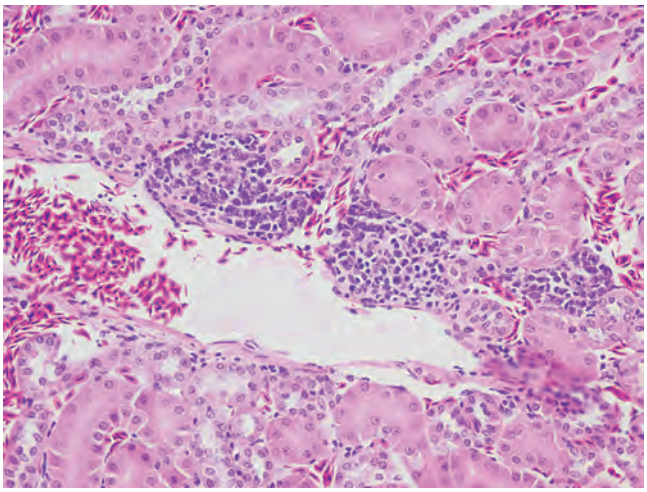

Figure 5.7 Lymphoid follicle within the cortex of a lobule of a pigeon kidney.

diagnosed as an incidental necropsy finding. Divisional aplasia is common in some breeds of chickens. The cranial division is most likely to be absent. The middle and caudal divisions are less commonly affected. Compensatory hypertrophy of the opposite kidney is generally present.

Renal cysts may be solitary or multiple (Fig. 5.9). The condition usually results from failure of fusion of the cortical portions of the tubule with collecting tubules of ureteral origin. If the lesion is severe, the result will be renal failure. Cysts usually have smooth borders grossly, and histologically flattened epithelial cells line the dilated tubules (Fig. 5.10). Congenital urethral cysts may also occur (Fig. 5.11). Glomerular hypervascularity has been reported in canaries. It leads to glomerular deformation but does not result in immediate renal failure.

Hydronephrosis is occasionally seen as a congenital condition. It can also be acquired.

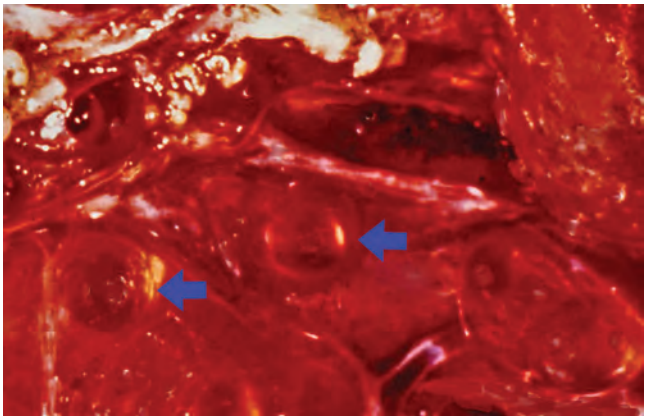

Figure 5.9 Multiple fluid-filled cysts on the ventral surface of the kidney (arrows).

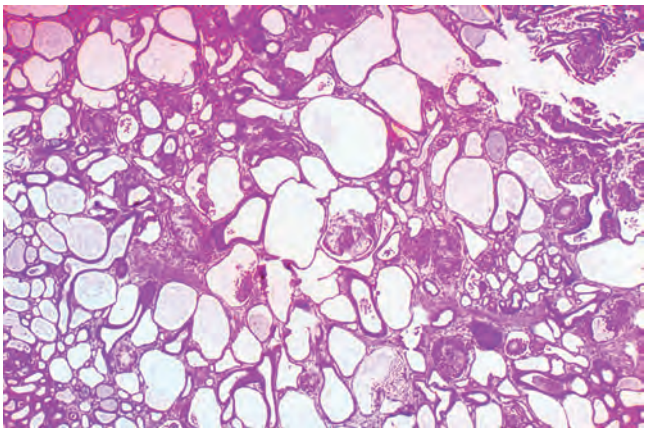

Figure 5.10 Polycystic kidney with multiple cystic tubules.

Infectious disease

Viral disease

Adenoviruses and the avian polyomavirus commonly affect the avian kidney. Birds dying of a psittacid herpesvirus-1 infection (Pacheco's disease) and psittacid herpesvirus-3 will

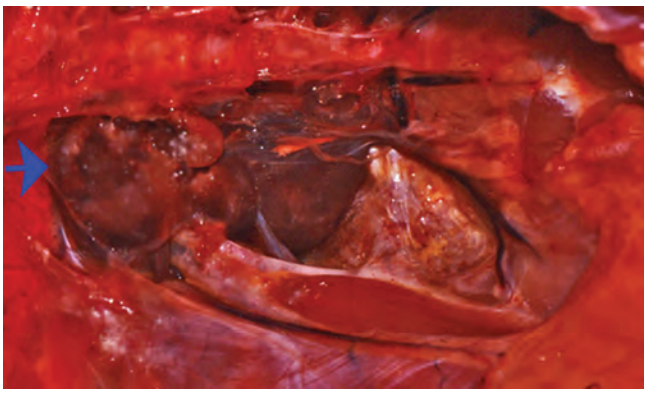

Figure 5.8 Congenital hypoplastic kidney. Only remnants of the cranial portion are present.

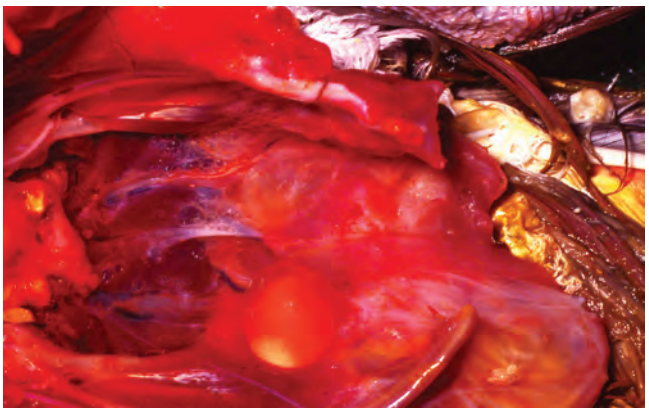

Figure 5.11 Urethral cyst formation. Cysts can be congenital or acquired.

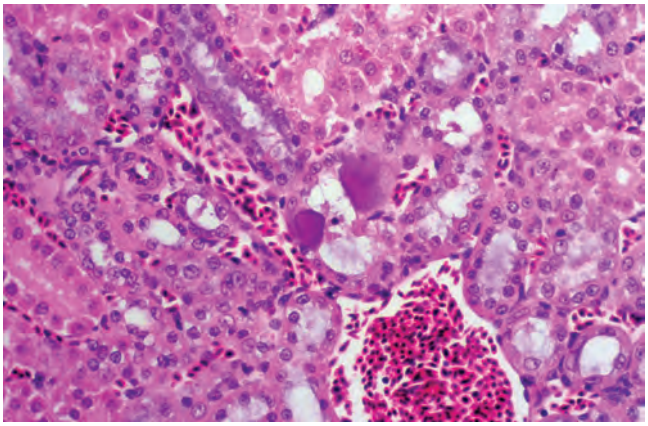

Figure 5.12 Large intranuclear inclusion bodies in renal tubular epithelial cells. These bodies are typical of adenovirus infection.

uncommonly have inclusion bodies in the renal tubular epithelium.

Adenovirus infection of the kidney is seen in a variety of psittacine birds and the Gouldian finch. Renal lesions are most commonly a part of systemic infection, but in some species and some instances the only organ with lesions will be the kidney. Grossly there may be some nonspecific renal enlargement. Microscopic lesions are usually minimal, varying from mild interstitial mononuclear cell infiltration to tubular epithelial cell vacuolation and necrosis. Scattered tubular epithelial cells have karyomegalic nuclei containing large, darkly eosinophilic or basophilic inclusion bodies (Fig. 5.12). In some birds, particularly budgerigars and cockatiels, the only lesion may be large intranuclear inclusion bodies in tubular epithelial cells. Viral particles can be seen by electron microscopy (Fig. 5.13). Adenovirus infections in lovebirds are often found incidentally at necropsy. Most of these birds have only a few widely scattered inclusions.

Polyomavirus infection may cause the kidneys to be slightly swollen and there may be serosal hemorrhages (Fig. 5.14). Histologically, in budgerigars, renal tubular epithelial cells may have karyomegaly, with affected nuclei containing clear or amphophilic, slightly granular inclusion bodies. These can be differentiated from those of adenovirus by their tinctorial properties.

Both primary and secondary lesions may occur in non-budgerigar psittacine birds with avian polyomavirus disease. Intranuclear inclusion bodies and accompanying karyomegaly are commonly seen in mesangial cells (Fig. 5.15). Mesangial cell necrosis is also common. Glomeruli will appear swollen due to capillary endothelial cell swelling. Up to 70% of these birds will develop a secondary glomerulopathy. This lesion is caused by the deposition of dense aggregates of immune complexes. All contain immunoglobulin Y and viral antigen. Less commonly they also contain immunoglobulin M. These aggregates, which are strongly periodic acid-Schiff positive, are found predominantly

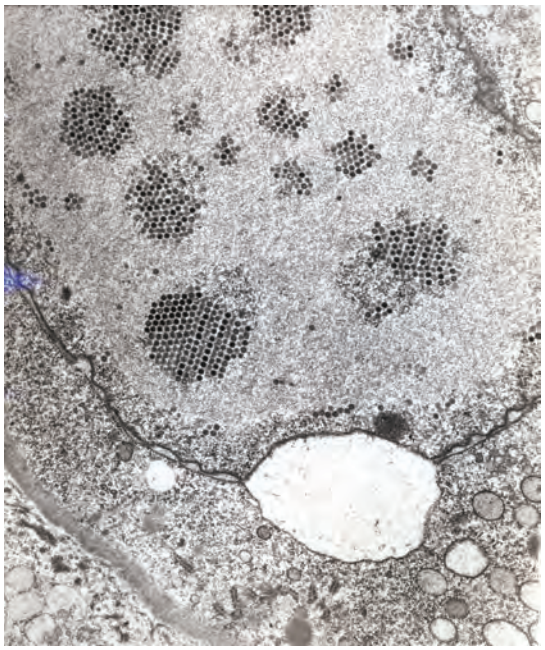

Figure 5.13 Adenoviral particles in renal tubular epithelial cell nucleus.

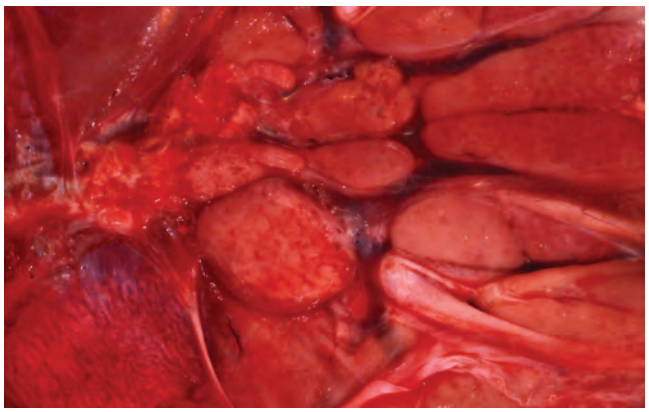

Figure 5.14 Swollen mottled kidneys in a macaw with avian polyomavirus infection.

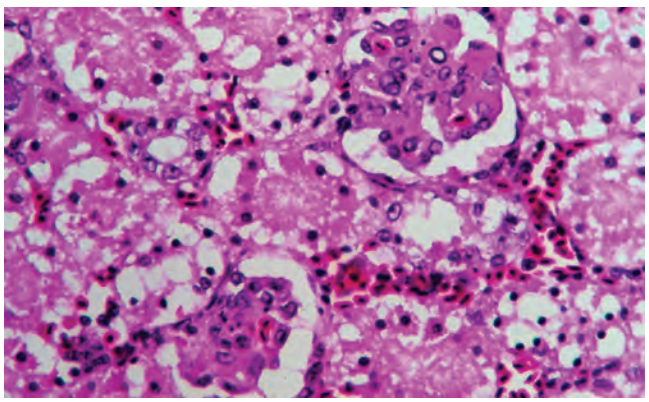

Figure 5.15 Avian polyomavirus infection. Glomerular mesangial cells have karyomegalic nuclei with pale intranuclear inclusion body formation and chromatin margination.

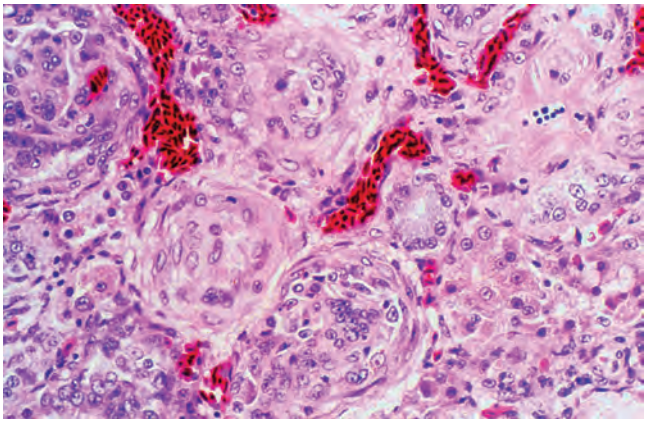

Figure 5.16 Membranous glomerulonephritis in an avian polyomavirus infection. Glomerular capillary basement membranes are thickened.

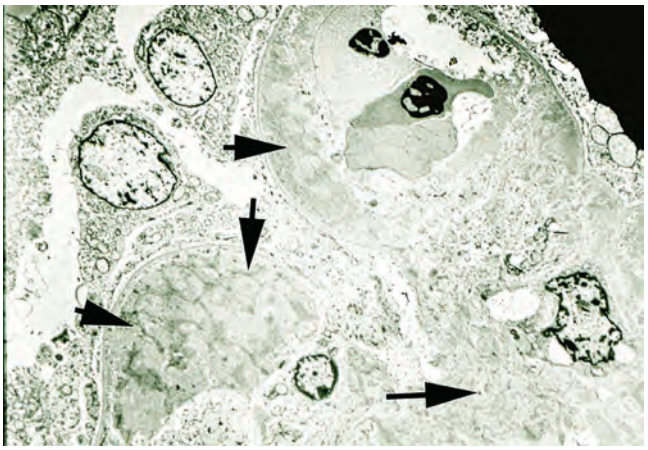

Figure 5.18 Electron microscopic image of a glomerulus of a bird with avian polyomavirus. Immune complexes are seen to completely occlude a capillary (arrows).

within the capillary lumens and the mesangium (Figs. 5.16, 5.17, and 5.18). Subendothelial deposits may also occur to a lesser extent. The immune complexes may be so massive as to occlude the capillary lumens completely. Minimal interstitial nonsuppurative inflammation is occasionally seen. The glomerulopathy is consistent with a type III hypersensitivity reaction.

Finches with polyomavirus infection may have both renal tubular epithelial and mesangial karyomegaly with intranuclear inclusion bodies. Chronic renal disease with glomerular sclerosis is seen in Gouldian finches that survived acute polyomavirus infection.

One of us (DNP) has observed a disease characterized by ascites and anasarca that is seen uncommonly in several species of nonbudgerigar parrots. All birds are positive by polymerase chain reaction for avian polyomavirus infection. Renal lesions include a proliferative glomerulopathy and glomerular sclerosis, lesions expected if a bird were to survive the acute form of avian polyomavirus disease. The anasarca and ascites are attributed to a protein-losing nephropathy and/or decreased hepatic production of albumin following avian polyomavirus-induced hepatic necrosis.

Nonsuppurative inflammation may be present in the renal interstitium in other viral infections, including reovirus and paramyxovirus. Pigeon paramyxovirus 1 variably affects the kidneys and its ability to cause disease is likely to be strain dependent. In some instances there is no renal involvement; in others, there is an interstitial lymphoplasmacytic nephritis. The degree of the nephritis can vary from minimal to severe with associated tubular degeneration, and necrosis with cellular, granular, and hyaline casts present in the tubules (Figs. 5.19 and 5.20). West Nile virus causes a variable lymphoplasmacytic interstitial nephritis as part of generalized disease (Fig. 5.21). Avian Bornavirus infection can also result in a nephritis (Fig. 5.22), but this is relatively rare.

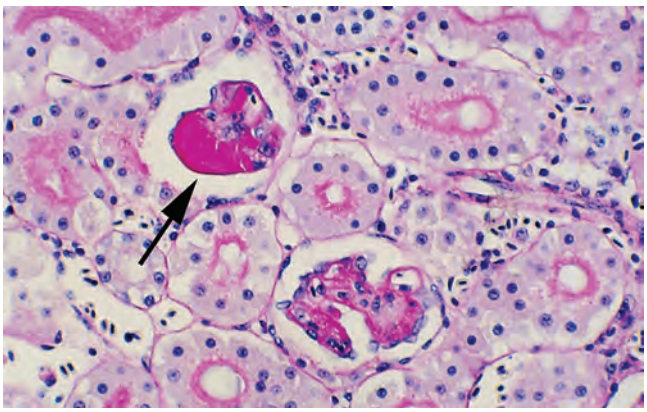

Figure 5.17 Periodic acid-Shiff stain of a diseased and normal glomerulus demonstrating the immune complex deposition (arrow).

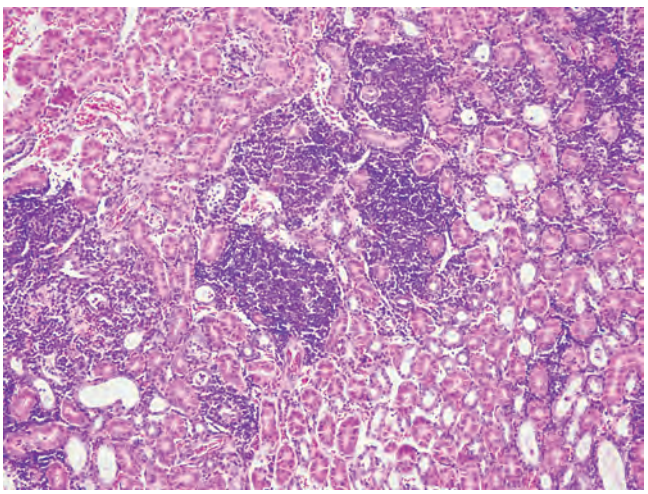

Figure 5.19 Lymphoplasmacytic interstitial nephritis in a pigeon caused by pigeon paramyxovirus.

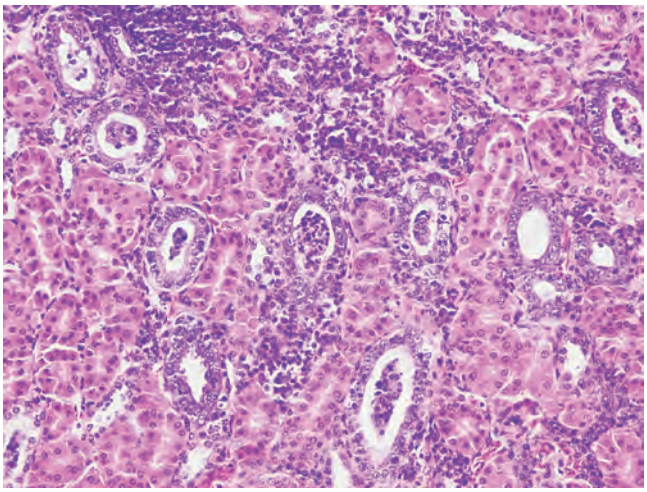

Figure 5.20 Close-up of the kidney of a pigeon with pigeon paramyxovirus showing the cellular casts and interstitial nephritis.

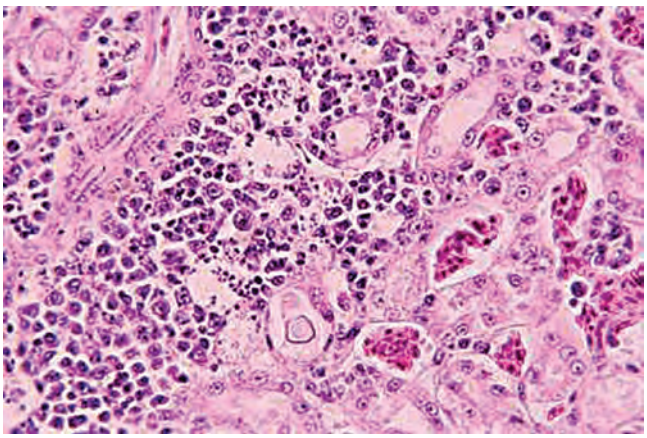

Figure 5.21 Nonsuppurative interstitial nephritis as a part of generalized West Nile virus infection.

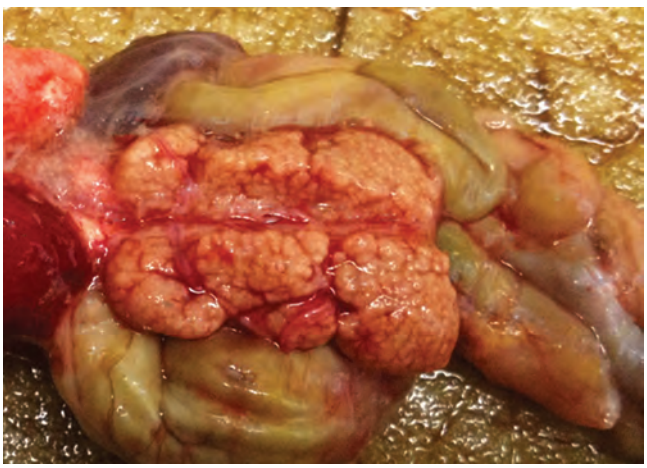

Figure 5.22 Severe interstitial nephritis in a Senegal parrot with Bornavirus infection (proventricular dilatation disease—PDD).

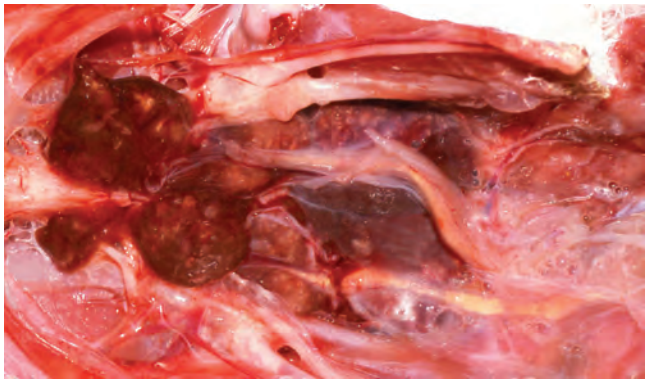

Figure 5.23 Severe nephritis due to bacterial infection. The enlarged kidneys have multiple yellow foci.

Bacterial disease

Bacteria can enter the kidney either by ascending the ureters or by hematogenous spread. In either type of infection, the kidneys may be grossly enlarged, with varying degrees of necrosis. Necrotic areas appear grossly as multifocal white-yellow foci within the renal parenchyma (Fig. 5.23). Initial hematogenous lesions may be present in glomeruli. Organisms may be seen associated with necrosis and a pleocellular inflammatory infiltrate. Fibrin thrombi suggestive of disseminated intravascular coagulation are sometimes noted (Fig. 5.24).

Acute ascending infections that are characterized by abundant bacteria are found in tubules and occasionally in the interstitium. Necrosis of the tubular epithelium is prominent, but inflammation is minimal or nonexistent. Distal collecting tubules and cortical collecting ducts are primarily affected while the medullary areas are spared. Subacute ascending infections have a marked inflammatory response, with heterophils in the lumen of the tubules, degeneration of the tubule epithelium, and

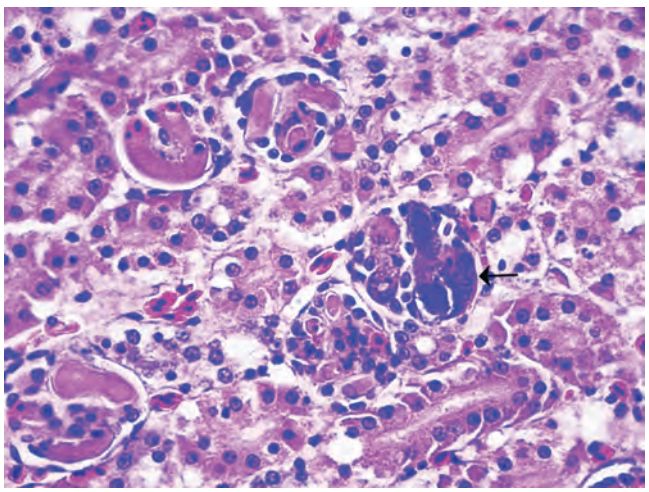

Figure 5.24 Glomerular hypercellularity and small fibrin thrombi associated with bacterial sepsis. Bacterial colonies are present in one glomerulus (arrow).

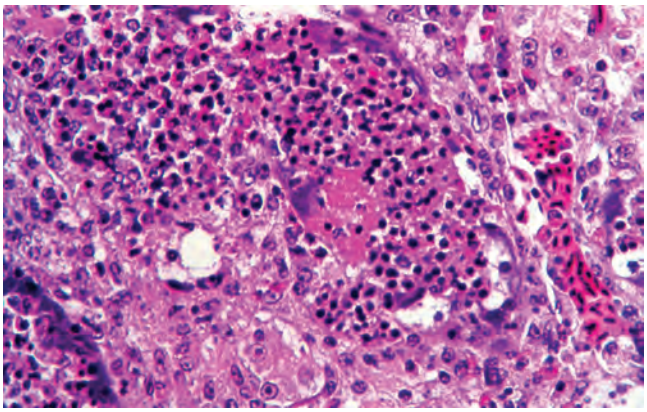

Figure 5.25 Bacterial nephritis with severe necrosis and inflammation involving tubules and interstitium.

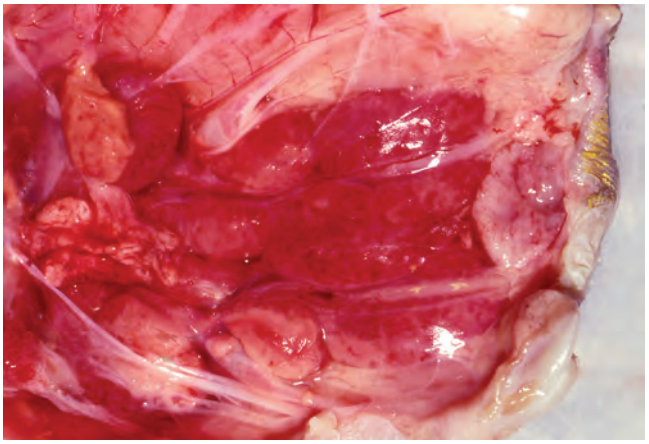

Figure 5.27 Mottled, discolored kidneys in a bird with chlamydiosis.

a moderate to severe heterophilic and early mononuclear interstitial nephritis (Fig. 5.25). Tubulointerstitial lesions are locally extensive and generally spare the glomeruli and the medulla in the affected lobules. With severe locally extensive lesions, it may be difficult to determine whether the infection began in the tubules and involved the interstitium or began in the interstitium and involved the tubules.

Bacteremia and septicemia commonly occur in a number of avian bacterial infections. Birds dying of overwhelming bacterial infections may have bacteria in both the renal veins and the arteries. For unexplained reasons, bacterial localization in the kidney may predominate in the cortical venous sinuses. Alternately, bacteria may be seen only in the glomeruli. Previous or ongoing bacteremias may result in subacute to chronic multifocal to locally extensive interstitial nephritis (Fig. 5.26). These lesions are initially heterophilic but rapidly become granulomatous with necrosis and fibrosis.

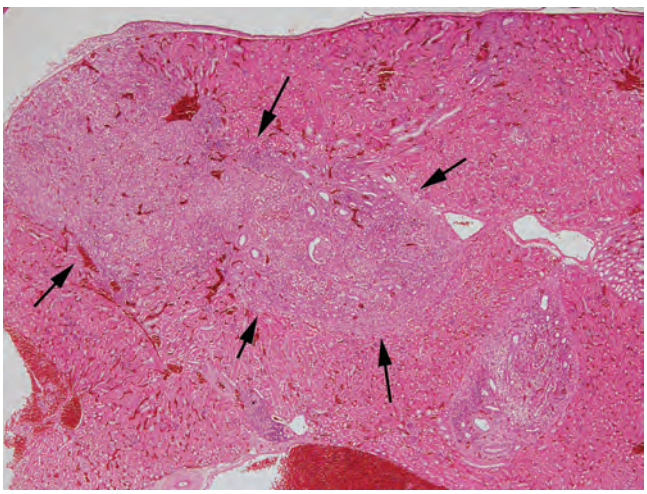

Figure 5.26 Chronic active ascending bacterial infection in the kidney of a pigeon. The infection has resulted effacement of much of one medullary cone and extension into the adjacent cortical tissue (arrows). The medullary cone on the lower right of the figure is also affected but to a lesser degree.

A wide range of gram-positive and gram-negative bacteria is known to cause kidney disease, either as an ascending infection or as part of a systemic disease. *Staphylococci* and *Streptococci* are common pathogens in finches and canaries but are also reported to cause disease in psittacine birds. Other bacteria that can affect the kidney include members of Enterobacteriaceae, *Listeria* sp., *Erysipelothrix rhusiophathiae*, and *Pasteurella* sp.

Mycobacterial and *Chlamydia psittaci* infections are generally systemic. They can cause lesions in the kidney (Fig. 5.27) but often do not. Mycobacterial lesions are similar to those found in other tissues; they include numerous macrophages and giant cells that contain acid-fast bacteria. Necrosis and abscess formation are not always present, particularly early in the disease. Lesions caused by *C. psittaci* are characterized by interstitial inflammation comprised primarily of histiocytes, plasma cells, and lymphocytes. Intracytoplasmic organisms are seen in histiocytes in some cases. Tubular involvement is variable.

Mycotic disease

Fungal infection of the kidney occurs either as an extension of a fungal infection of abdominal air sacs or as a component of systemic infection where a fungus has invaded a vessel, resulting in fungal thrombosis of blood vessels. Fungal infections elicit a severe necrotizing inflammation with a pleocellular reaction involving blood vessels and renal parenchyma. Fungal hyphae in the lesion give it specificity. *Aspergillus* sp. are the most frequently implicated fungus in these lesions, but *Penicillium chrysogenum* and *Cryptococcus neoformans* have also been identified in kidney lesions. The *C. neoformans* outbreak occurred in Brazil in African and Indo-pacific parrots which experienced a systemic disease. In the reported cases, encapsulated yeasts were seen in the kidney, but they did not elicit an inflammatory reaction.

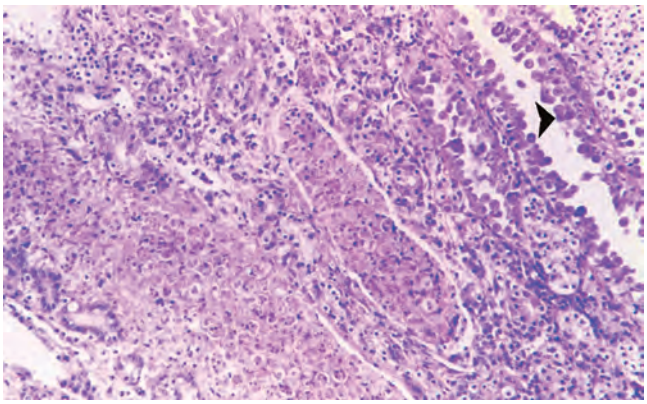

Figure 5.28 Renal coccidiosis (*Eimeria* sp.). Variable tubular necrosis and numerous organisms are seen (arrowhead).

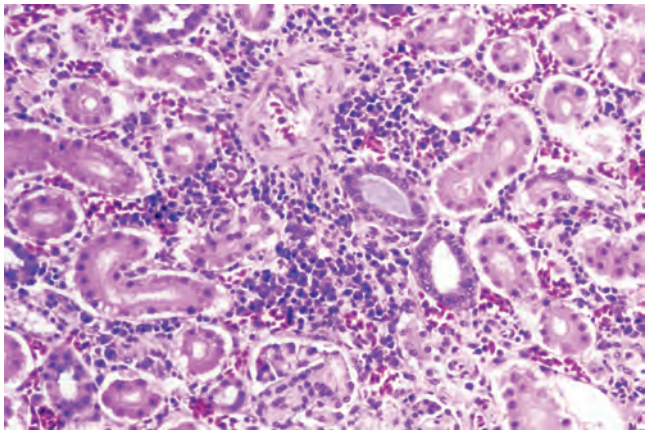

Figure 5.30 Interstitial nephritis in a bird with systemic sarcosporidiosis. Organisms are rarely seen in the kidney in birds with this condition.

Parasitic disease

Isospora and *Eimeria* are found in the kidneys of nearly all species of wild ducks and geese. They are also commonly found in shorebirds and are less commonly seen in birds of prey. Organisms are predominantly found in the epithelium of perilobular collecting ducts and medullary collecting tract. Lesions in adult birds are minimal, with occasional obstruction of and dilation of the tubules and a mild lymphocytic and monocytic interstitial nephritis. *Eimeria truncata* can cause a more severe disease in juvenile waterfowl. Gross changes are often absent. Histologically there is variable tubular necrosis. Organisms are found in tubular epithelial cells or free in the lumen associated with inflammatory cells and necrotic debris (Fig. 5.28).

Cryptosporidial infection of the kidney of birds is reported in a variety of birds. Grossly kidneys appear swollen and pale. There may be slight proliferation of tubular epithelial cells, and organisms are present on the surface of these cells. Necrotic cells are noted in the tubular lumens. An interstitial infiltrate of mononuclear cells and heterophils may be present.

Encephalitozoon hellem is a potential cause of nephritis (see Chapter 4). Lesions are most commonly seen in lovebirds and budgerigars. Gross changes may be absent, or small pale foci may be present in the renal parenchyma. Histologically both cortical and medullary tubules are affected, but organisms predominate in the distal tubules. Necrosis and a mononuclear interstitial inflammatory response characterize the lesion (Fig. 5.29). Small protozoal organisms are present in cells and may be free in the necrotic foci and the lumen of the tubules. Infected cells are distended with the organisms. In chronic cases, there may be tubular hypertrophy. It is also fairly common to find the organisms in the kidney with little, if any, associated inflammation. These organisms are strongly gram positive.

Systemic sarcosporidial infection can lead to interstitial nephritis with an infiltrate that is primarily lymphoplasmacytic (Fig. 5.30). Organisms are usually not seen. Schizonts histologically resembling *Leukocytozoon* can also be found in the kidney (Fig. 5.31). As mentioned in Chapter 4, PCR testing may be necessary to differentiate from other hemoprotozoa. The major

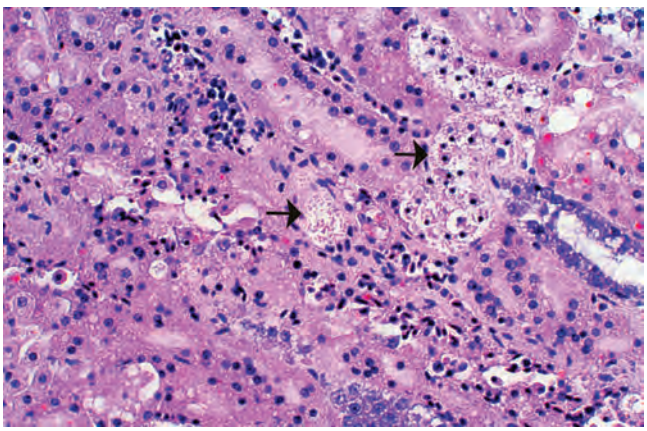

Figure 5.29 Renal microsporidiosis. Minimal interstitial inflammation and aggregates of organisms are seen (arrows).

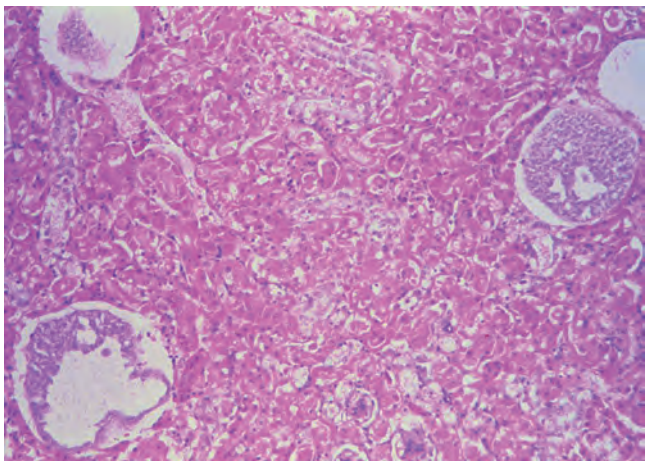

Figure 5.31 Megaloschizonts of *Leukocytozoon* in the renal parenchyma.

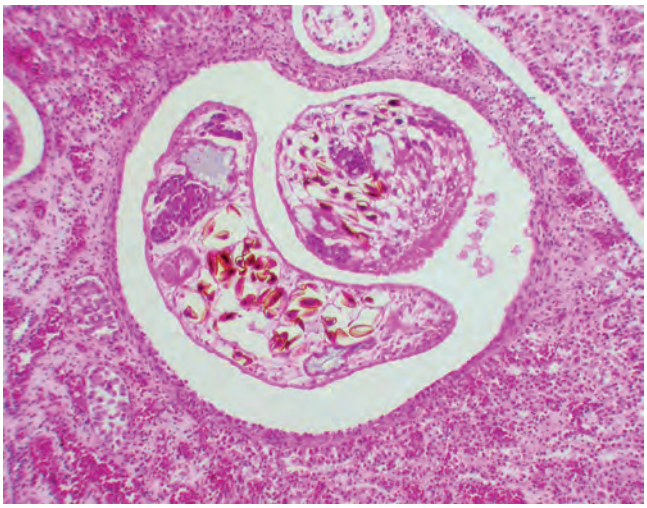

Figure 5.32 Severe dilatation of a collecting tubule containing a trematode.

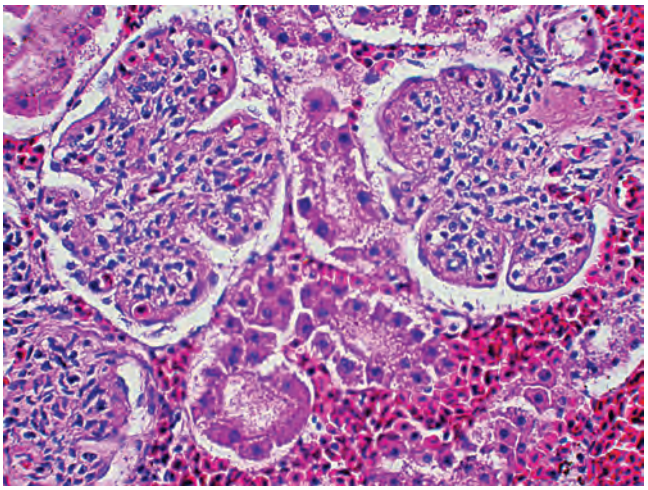

Figure 5.34 Hypercellularity of the glomerular tufts consistent with probable immune-mediated proliferative glomerulonephritis.

targets for the *Toxoplasmosis gondii* are brain, lungs, and heart; however, bradyzoites can also be found in the kidney in some infections in small numbers. They are associated with a mild lymphoplasmacytic interstitial nephritis.

Trematodes may be incidental findings or lead to clinical renal disease in some birds. These infections are most common in waterfowl but also occur in other species including doves and psittacine birds. The flukes are found in collecting tubules in the medullary cone (Fig. 5.32). Affected tubules are dilated, and there is usually minimal or no inflammation. Severe infections result in obstruction of the tubules, variable inflammation, and necrosis and secondary dilatation proximal to the obstruction (Fig. 5.33). Schistosomiasis is common in waterfowl. While the adults are not present in the kidney, these intravascular trematodes lay eggs that are trapped in small vessels, creating a foreign-body reaction and granuloma formation.

Inflammatory disease of undetermined cause

Except as a sequela to polyomavirus infection (previously discussed), immune-complex glomerulonephritis is not well documented in birds. Based on cases examined by the authors, we believe it does occur. In addition to the membranous glomerulonephritis described, we have seen examples of proliferative glomerulonephritis with hypercellularity of the glomerular tufts (Fig. 5.34), and membranoproliferative glomerulonephritis. In chronic cases, there may be proliferation of parietal epithelium and glomerular crescent formation (Fig. 5.35). Eventually there is glomerular shrinkage, fibrous connective tissue proliferation, and sclerosis (Fig. 5.36).

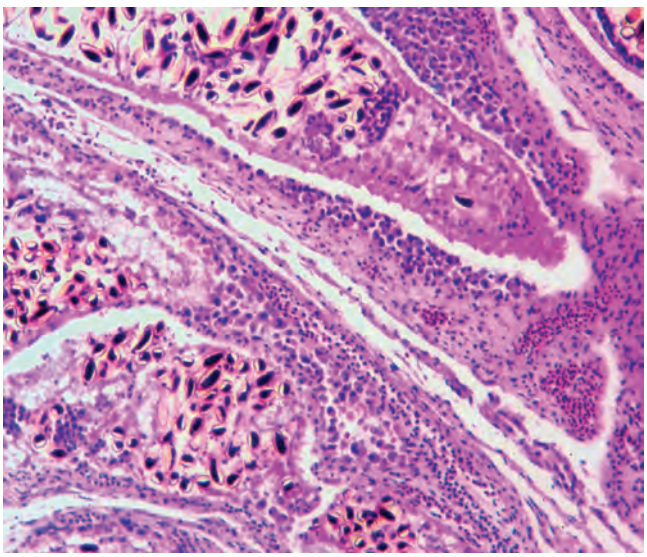

Figure 5.33 Necrosis and inflammation associated with renal trematodiasis.

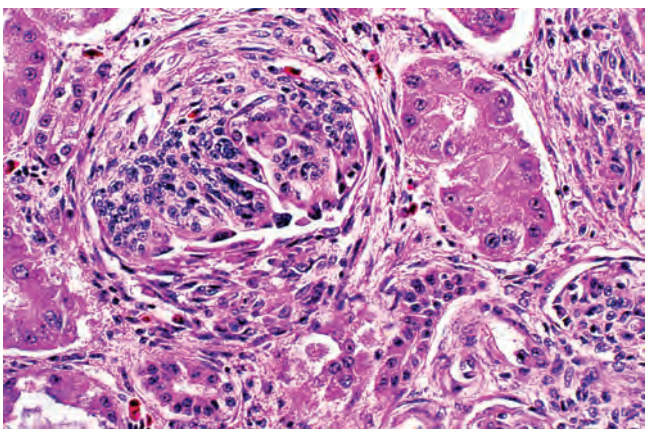

Figure 5.35 Severe chronic membranoproliferative glomerulonephritis with glomerular crescent formation.

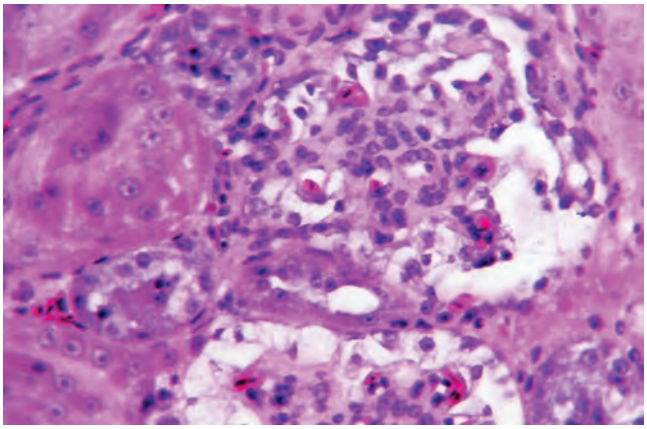

Figure 5.36 Severe chronic glomerulosclerosis.

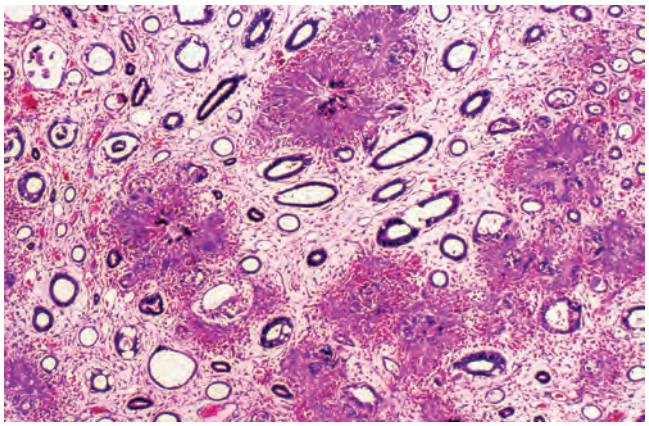

Figure 5.38 Severe renal urate deposition comprising primarily crystalline urates.

Noninfectious disease

Dehydration

Dehydration results in reduced urine flow and sludging of the urate crystals within the tubules. If the dehydration is transient, this lesion is reversible. Persistent dehydration results in renal failure. Gross lesions are characterized by multifocal white to yellow-white foci or streaks that represent urate deposits (Fig. 5.37). The gross appearance is similar to that of mineralization and severe nephritis; therefore histology is necessary for differentiation. Microscopically the urates will be dissolved during the fixation process but will leave behind the characteristic needle-shaped and amorphous spaces surrounded by an eosinophilic protein matrix where the crystals had been. Secondary epithelial necrosis occurs, and the urate crystals induce inflammation that is primarily heterophilic (Fig. 5.38).

Nutritional disease

Metastatic mineralization of the kidney is a common lesion in nestling parrots and, to a lesser extent, in adult birds. It is also seen in pigeons and in chickens. It may vary from mild to severe, resulting in renal failure and systemic gout. This disease disproportionately affects nestling budgerigars, cockatiels, and blue and gold macaws. A nutritional imbalance is suspected. Experimentally diets containing 0.7% calcium or more cause metastatic mineralization of the kidney in nestling and adult budgerigars. Diets containing 0.3% calcium do not cause metastatic mineralization in this species of birds and are adequate for reproduction and growth. Vitamin D_3 concentrations ranging from 500 to 3300 IU/kg of diet did not result in metastatic mineralization in the low-calcium diet. Metastatic mineralization also occurs in poultry when hens that are no longer laying are fed laying pellets that contain high calcium concentrations. Feeding rosters laying will also cause kidney disease.

Mild cases of metastatic mineralization do not cause gross lesions. Advanced cases are grossly indistinguishable from severe nephritis or nephrosis associated with dehydration (Fig. 5.39). Histologically mineralization occurs on the basement membranes of the tubules and within the tubules themselves. The mineral deposits are deeply basophilic and are round

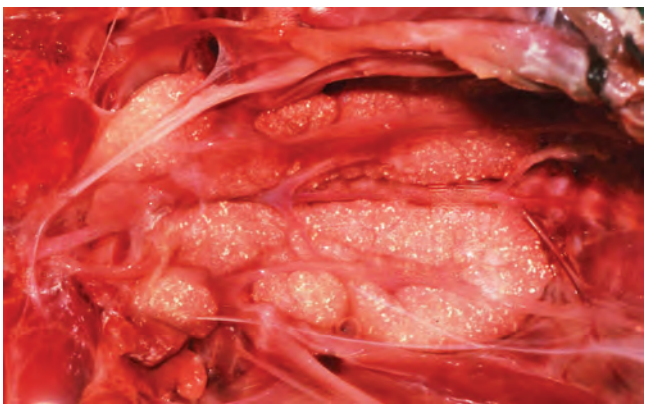

Figure 5.37 Swollen, pale kidneys with severe urate deposition.

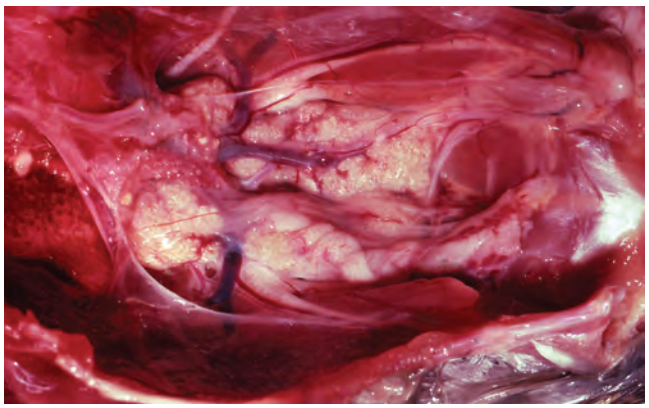

Figure 5.39 Severe renal mineralization. This can be due to a variety of causes. It must be differentiated from urate deposition (compare with Fig. 37).

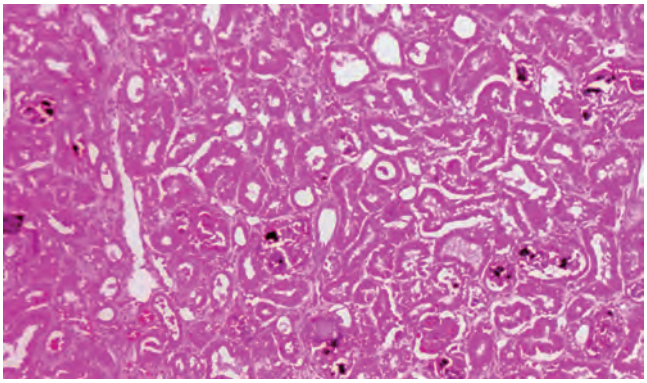

Figure 5.40 Multiple foci of renal mineralization involving tubules.

to crescent shaped. Necrosis of the tubular epithelium occurs when the mineralization is severe (Fig. 5.40). Inflammation may be absent, but, in some extensive lesions, mineralized tissue elicits a foreign-body reaction (Fig. 5.41). In some instances, renal calculi may cause obstruction of the ureter or its branches causing tubular dilation (Fig. 5.42). Renal failure follows, with urate precipitation in the kidneys, the development of a more extensive interstitial nephritis, and fibrosis. Based on one author's observations (DNP) even mild degrees of metastatic mineralization may be correlated with polyuria.

Disorders of protein metabolism may lead to elevation of plasma uric acid concentrations. However, whether this in turn can result in gout has not been proved.

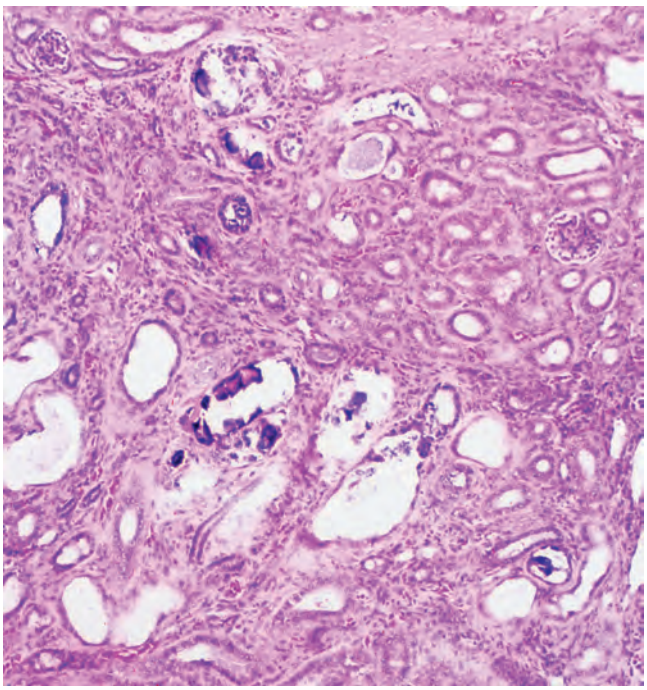

Figure 5.41 Mineralization and chronic inflammation and fibrosis involving renal collecting ducts.

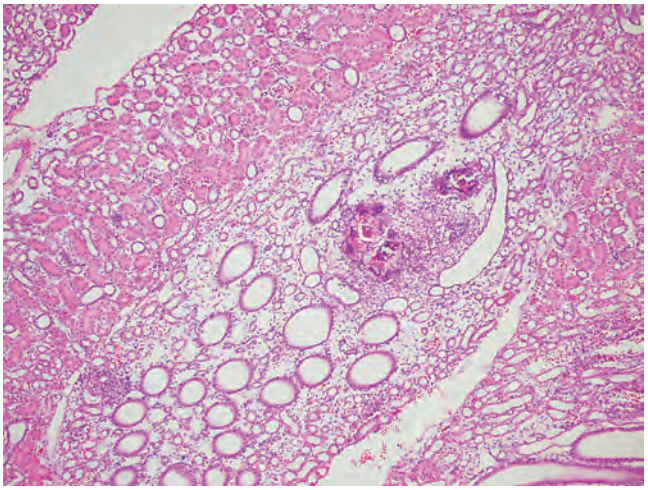

Figure 5.42 Mineralization resulting in obstruction and collecting duct dilation.

Amyloidosis

Renal amyloidosis is most frequently observed in waterfowl and small passerine birds (Chapter 4). Multiple organs, in addition to the kidney, are generally involved. Grossly there may be no discernible change, but, in severe cases, the kidneys are enlarged, pale, and somewhat friable (Fig. 5.43). Histologically amyloid is eosinophilic or amphophilic and may be deposited in glomerular or tubular basement membranes and the walls of renal arteries and arterioles (Fig. 5.44).

Vitamin deficiency

Vitamin A deficiency leads to squamous metaplasia of the epithelium of the ureters and collecting ducts that in advanced cases results in the ureteral epithelium being transformed to a keratinized epithelium (Fig. 5.45). Partial or complete obstruction of the ureters follows. Tubule dilation and intratubular and interstitial urate crystal deposition occur. Secondary bacterial infections are also common.

Figure 5.43 Diffuse amyloidosis of the kidney of a swan resulting renal swelling and pallor.

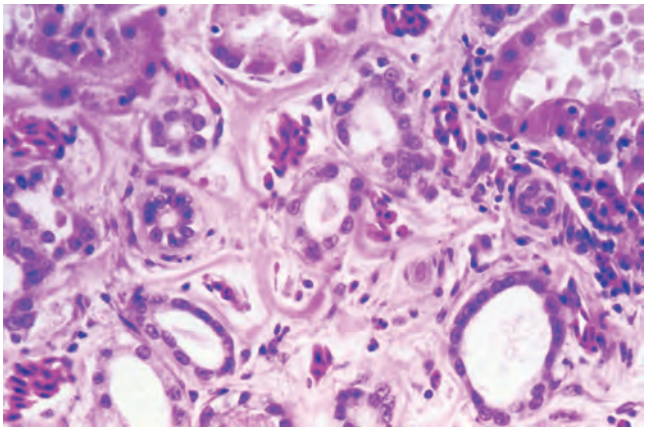

Figure 5.44 Amyloid deposition leading to thickened basement membranes and interstitium.

Lipidosis

Renal lipidosis can be secondary to a high-fat diet or chronic hepatic disease. The latter is relatively common in Amazon parrots and cockatiels that have a high incidence of chronic-active hepatitis. Grossly the kidneys are pale, and microscopically there is fat in tubular epithelial cells. Lipid-containing macrophages are usually present in glomerular capillaries.

Pigmentary nephrosis

Myoglobinuric nephrosis is possible as a sequela to exertional rhabdomyolysis or severe crushing injury to muscle, but this condition is rarely seen in common pet birds. The kidneys may be dark brown. Tubular degeneration and lumenal accumulation of amorphous eosinophilic material resembling myoglobin are seen microscopically in proximal convoluted tubules, and eosinophilic casts are noted in collecting tubules. Hemoglobinuric nephrosis also occurs but rarely (see heavy metal intoxication).

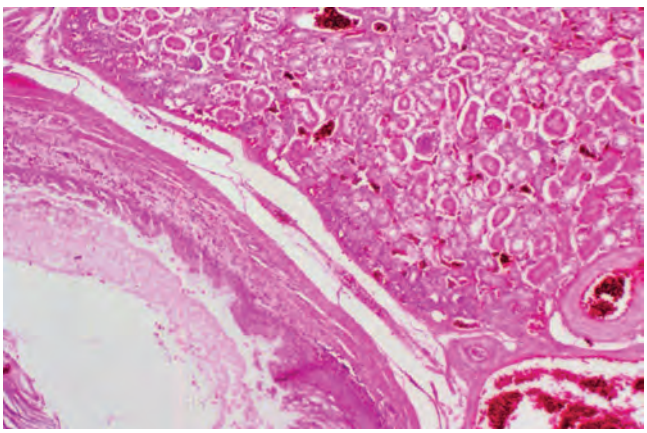

Figure 5.45 Squamous metaplasia and keratinization due to vitamin A deficiency. The affected collecting duct is markedly dilated.

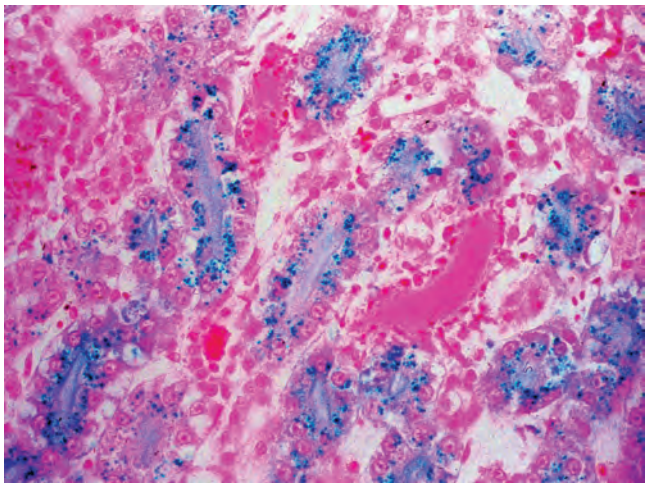

Figure 5.46 Deposition of iron in tubular epithelial cells of a toucan with an iron metabolic disorder. Prussian blue.

Bile pigments are commonly found in the proximal tubules of birds with hepatitis. Polyuria is a common clinical feature of birds with biliverdinuria, but whether biliverdin has a physiologic effect on the kidney is not known.

Iron-storage disease (Chapter 4) primarily affects the liver, but iron pigment is also seen in renal tubular cells in many affected birds. The iron does not cause an inflammatory or degenerative response (Fig. 5.46).

Toxic nephropathies

Most renal toxins cause similar gross and histologic lesions, and therefore a definitive etiologic diagnosis is often not possible based on histopathologic changes alone. Grossly kidneys may be swollen and pale. They contain fine white to pale yellow linear striations that represent tubules dilated with urates. Numerous pinpoint, multifocal, white to pale yellow foci will also be present on the serosal and cut surfaces of the kidney.

Microscopically there is proximal tubule necrosis, proteinuria, tubule dilation, and urate tophi formation within the interstitium. If the insult was transient, the proximal tubules may regenerate. In acute cases, there will be little inflammation. If the bird survives for sometime, the urate crystals may elicit an inflammatory response. Interstitial fibrosis and glomerular sclerosis develop with chronicity.

Rodenticides

Vitamin D_3 and vitamin D_3-analog-based rodenticides are toxic to birds. These rodenticides cause increased intestinal absorption of calcium and a hypercalcemia. There may also be decreased urinary calcium excretion. Calcium is deposited in soft tissues, including the kidney. Affected kidneys are enlarged, firm, and contain numerous yellow-white foci (Fig. 5.47). There is variable renal tubular damage, with mineralization of

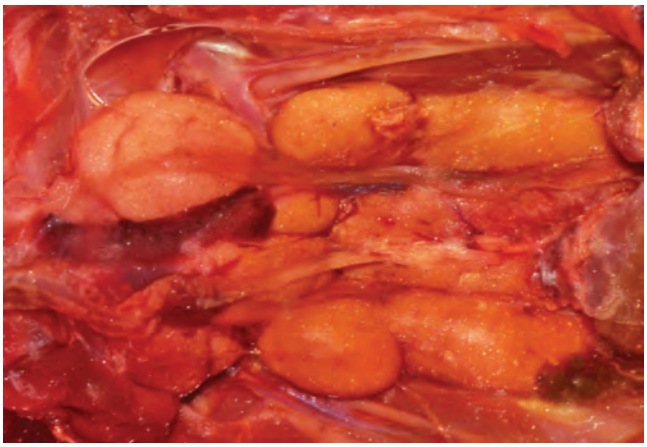

Figure 5.47 Renal swelling and discoloration secondary to vitamin D toxicity.

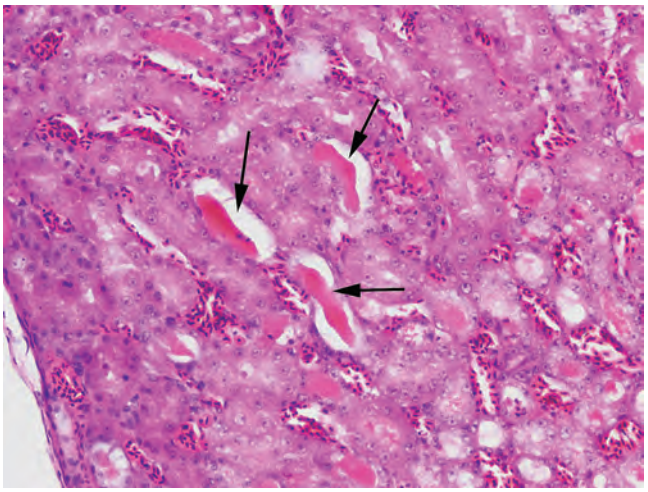

Figure 5.48 Hemoglobin nephrosis in a galah with lead poisoning. Arrows demonstrate the eosinophilic hemoglobin within tubules.

tubular basement membranes. Necrotic epithelial cells and secondary urate deposition are seen.

Aminoglycosides

Gentamicin sulfate and amikacin are two aminoglycoside antibiotics that are rarely used in birds in the past 20 years. Both are nephrotoxic, but gentamicin sulfate is more nephrotoxic than amikacin. Aminoglycoside toxicity results in kidney enlargement and changes resembling other causes of renal failure. Histologically there is tubular epithelial necrosis and secondary urate deposition and inflammation.

Heavy metals

Lead and zinc toxicity both can cause acute tubular necrosis. Gross changes vary from none to swollen pale kidneys. Histologic lesions are similar to those previously described for other toxins. Occasionally, acid-fast intranuclear inclusion bodies are seen in some birds with lead toxicity. Lead and zinc poisoning can also cause hemolysis resulting in hemoglobin leakage from the glomeruli and its presence in the tubules (Fig. 5.48). Cadmium, mercury, and arsenic also are nephrotoxic, but this type of poisoning would only be expected in wild birds. For acute heavy metal poisoning liver and kidney should be submitted for testing. Cadmium and lead concentrations are expected to be high in the kidney.

Zinc phosphide

Zinc phosphide is used as rodenticide. When it is consumed it is converted to phosgene gas resulting in widespread oxidative disease. In barn owls suspected to be poisoned with zinc phosphide there was multifocal necrosis of glomerular tufts (Fig. 5.49).

Mycotoxins

Several mycotoxins, including oosporein, citrinin, and ochratoxin, have been shown to cause disease in poultry or domestic waterfowl. Gross lesions resemble those of other toxins, or there may be no gross lesion at all. Histologically there may be acute necrosis of tubular epithelial cells, followed by hypertrophy and hyperplasia of other cells. Aflatoxins cause degeneration of the proximal convoluted tubules and thickening of glomerular basement membranes.

Nonsteroidal anti-inflammatories

Gyps vultures are exquisitely sensitive to diclofenac poisoning and its impact on the kidney. It also appears to have variable degrees of nephrotoxicity in experimentally exposed birds. Ketoprofen has also caused a nephrosis in spectacled eiders (*Somateria fischeri*) and king eiders (*Somateria spectabilis)* and could be toxic in other avian species. Lesions produced by all of these drugs are similar with necrosis of the tubular epithelium, the presence of protein casts, and the formation of urate tophi. Renal failure results in systemic gout.

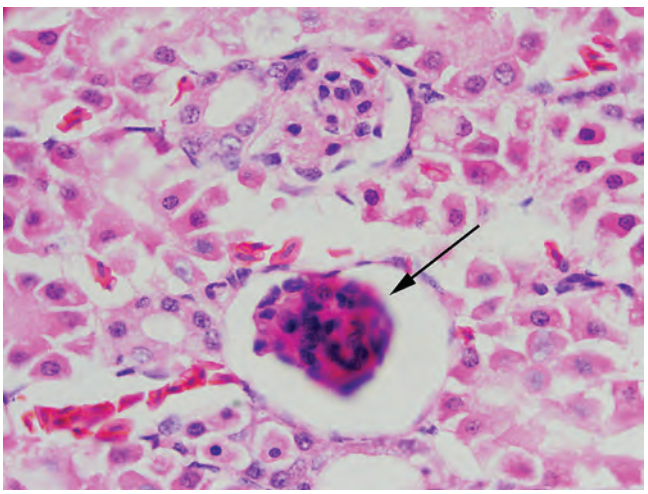

Figure 5.49 Suspected zinc phosphide intoxication in a barn owl. Note the necrosis and collapse of the mesangial tuft (arrow).

Salt
Excessive salt ingestion leads to renal problems that result in urate deposition and gross and histologic changes as previously described. It is documented in birds but rarely diagnosed in pet species.

Plant toxins
Toxicity following force feeding of garlic has been reported. No gross lesion was seen however. Histologically there was hemoglobinuric nephrosis and hepatosplenic erythrophagocytosis consistent with acute hemolysis.

Ethylene glycol
Although not reported in pet species to our knowledge, waterfowls have been poisoned by antifreeze (ethylene glycol). Degeneration of renal tubular epithelium and congestion of kidney and liver were seen.

Physical/other nephropathies
Acute hypoxia/ischemia
These changes are usually related to a localized or generalized vascular problem. The results are tubular necrosis, proteinuria, and urate deposition. Lesions are similar to the various problems discussed under metabolic disorders, and differential diagnoses include many of these conditions.

Hemorrhage
Renal hemorrhage may be secondary to trauma, ischemia, or a variety of primary disease conditions. The hemorrhage may be visible grossly and can affect both the interstitium and the tubules.

Renal fibrosis
The end result of many of the aforementioned conditions can be chronic renal disease (end-stage kidney failure) with severe fibrosis (Fig. 5.50). Unlike many species of mammals with chronic kidney disease, the bird's kidney is typically enlarged and not shrunken.

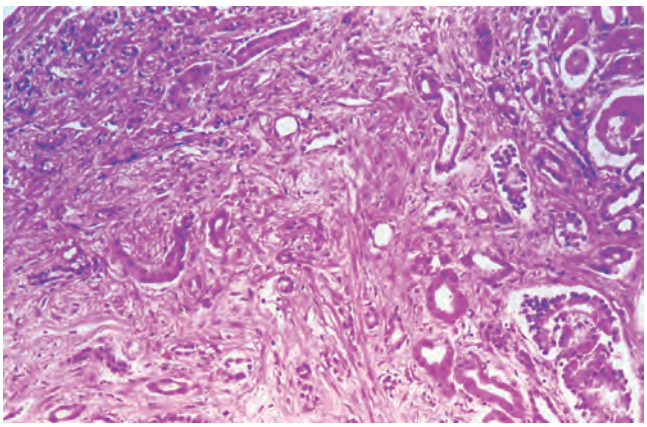

Figure 5.50 End-stage renal disease with marked fibrosis. This can be the result of various insults.

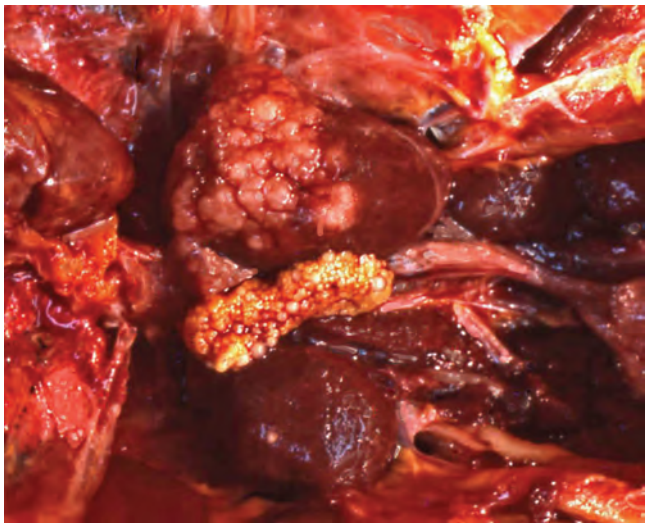

Figure 5.51 Focal renal adenoma. These tumors are less common than renal carcinomas.

Neoplastic disease
Renal tumors are reported in many species of birds but are particularly common in the budgerigar. Renal carcinoma is the most common tumor of the kidney, but adenoma, nephroblastoma, cystadenoma, fibrosarcoma, and lymphosarcoma are also reported to occur in the avian kidney. The most common presenting sign of renal neoplasia is unilateral or bilateral lameness or paralysis. These signs result from compression of the root of the ischiadic nerve as they pass through the kidney or from tumor growth into and adjacent to the synsacrum and ilium.

Renal adenomas are usually localized nodular swellings often in the cranial pole of the kidney (Fig. 5.51). They are light tan to white and fluctuant. Histologically they are comprised of tubular structures lined by fairly well-differentiated epithelial cells. There is usually slight to moderate stroma (Fig. 5.52). Renal carcinomas are large, somewhat friable, and vary from tan to

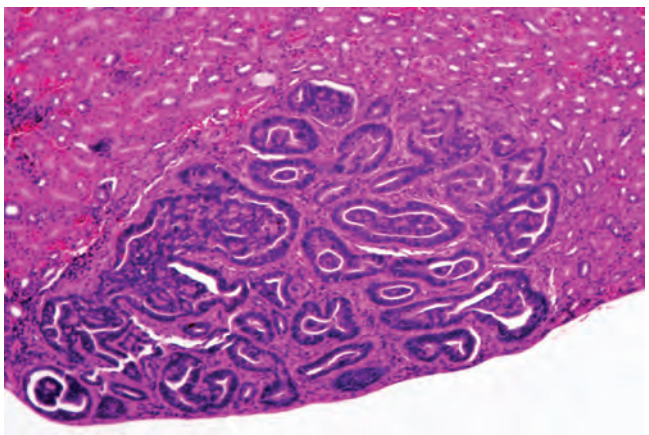

Figure 5.52 Well-differentiated tubular structures in renal adenoma.

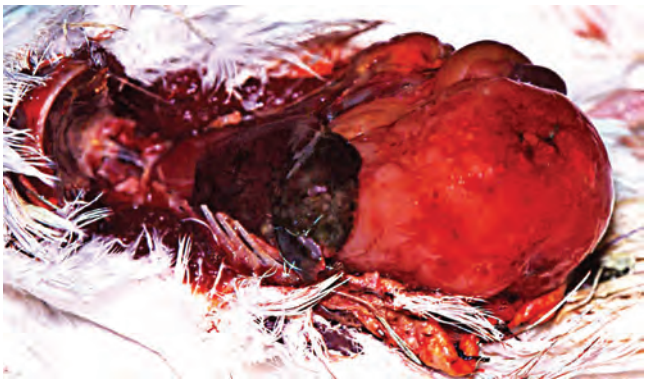

Figure 5.53 Typical renal carcinoma that has become very large and displaced the abdominal viscera.

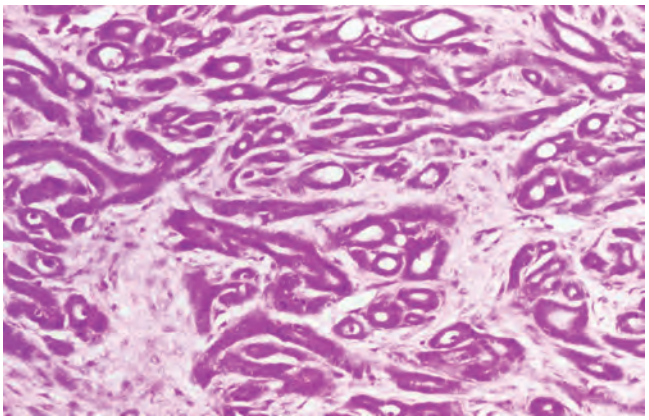

Figure 5.55 Anaplastic renal carcinoma with marked scirrhous stroma.

red-brown (Fig. 5.53). Microscopically they are comprised of anaplastic epithelial cells forming tubules, nests, and sheets, usually with minimal stroma (Figs. 5.54 and 5.55). Extension into surrounding tissue is seen, and metastasis to the lung and liver is occasionally seen (Chapters 3 and 4). Impression smears of these tumors reveal poorly differentiated pleomorphic cells, some with multiple nuclei (Fig. 5.56).

Embryonal nephromas (nephroblastomas) are most commonly reported in chickens but are also found in psittacine and small passerine birds. They are usually unilateral, but may be bilateral, and are grossly similar to carcinomas. Histologically there are tubules and glomerular-like structures as well as sheets of undifferentiated epithelial cells (Fig. 5.57). The latter may predominate in some cases. Some tumors have abundant amounts of stroma.

Lymphosarcoma may be isolated to the kidney but usually is a part of generalized neoplastic disease. Grossly the kidneys are pale and may appear mottled. They are moderately firm. The cell infiltration is either nodular or diffuse, with renal tissue effaced by immature lymphoid cells. Plasma cell tumors and myeloproliferative disease are also seen in the kidney, being grossly similar

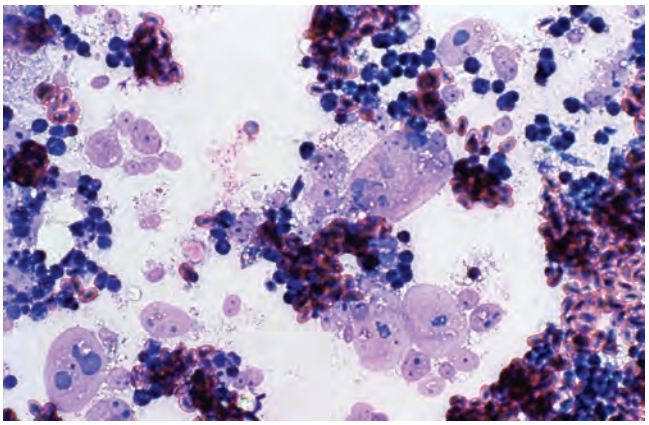

Figure 5.56 Impression smear from a renal carcinoma. Poorly differentiated pleomorphic cells, some with multiple nuclei.

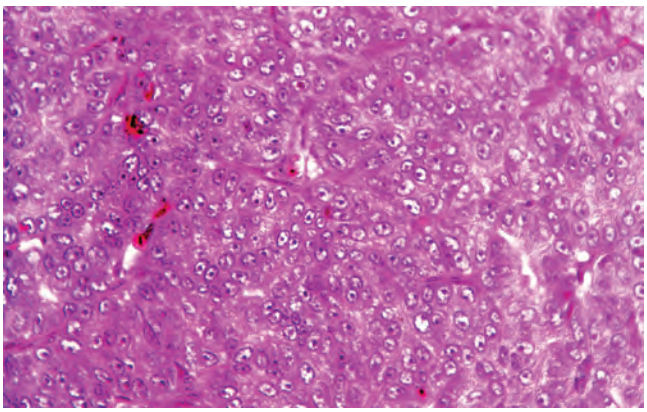

Figure 5.54 One of the histologic presentations of renal carcinoma with poorly defined tubular structures and minimal stroma.

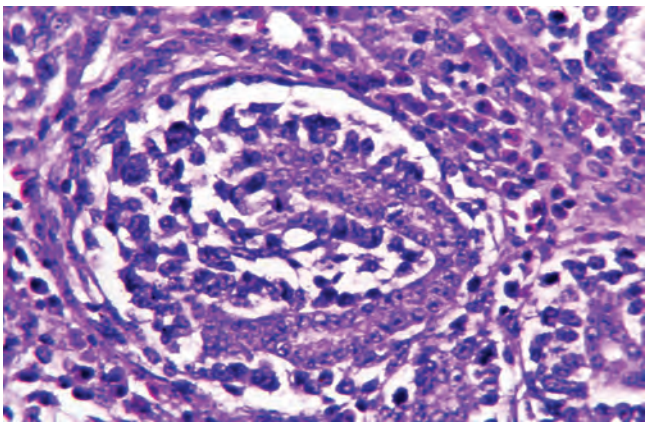

Figure 5.57 Glomerular-like structures in nephroblastoma. Abundant stroma is present.

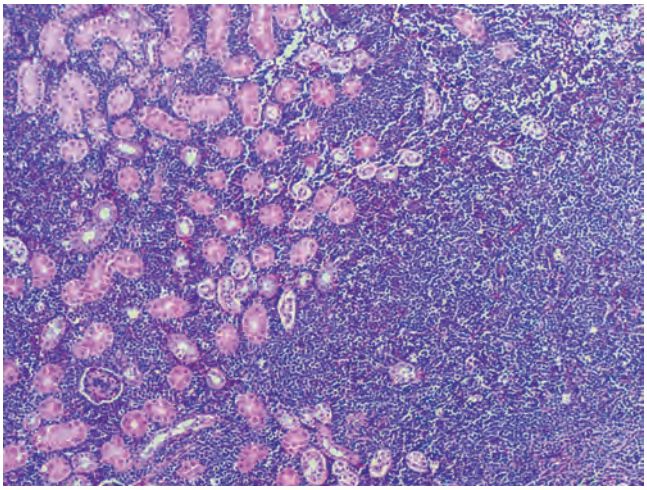

Figure 5.58 Effacement of renal parenchyma by neoplastic myeloid cells. Lymphosarcoma has a similar appearance at low magnification.

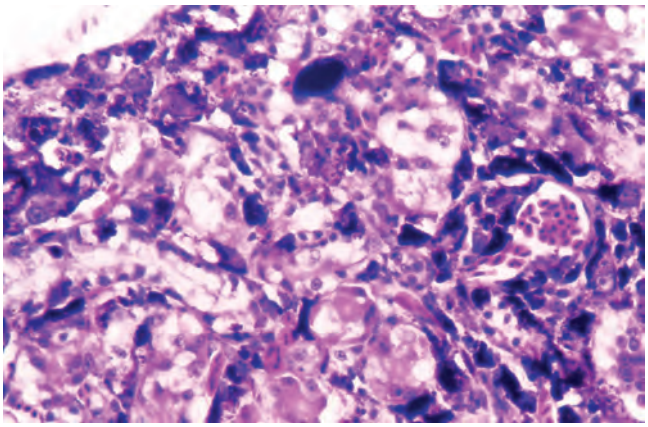

Figure 5.59 Metastatic malignant melanoma. Neoplastic cells are infiltrating the interstitium.

to lymphosarcoma. Histologically there is parenchymal effacement, and diagnosis is based on the morphology of the infiltrating cells (Fig. 5.58). Renal involvement is relatively common in chickens with Marek's disease.

Metastatic tumors are not usually seen in the kidney. However, there are several tumors that have been reported to be metastasized to the kidney, and these include air sac cystadenocarcinoma, hemangiosarcoma, seminoma, mast cell tumor, and malignant melanoma. The air sac cystadenocarcinoma was described in an African gray parrot. In the kidney, it produced multifocal fluid-filled cysts that were lined by a single layer of flattened to cuboidal epithelial cells. The hemangiosarcoma occurred in a Java Sparrow (*Padda oryzivora*) and had a characteristic appearance. The seminomas were reported to occur in an aged population of white carneau pigeons. A description of the metastatic lesion was not provided. The mast cell tumor occurred in a black-masked lovebird and the primary tumor was cutaneous and metastasis occurred widely. Round cells occurred in sheets replacing normal kidney structures. The cells had a slightly basophilic granular cytoplasm. Metachromatic granules were identified with special stains confirming their origin as mast cells. Malignant melanomas may be the most common tumor to metastasize to the kidney. Grossly there may be brown-black foci and masses. Microscopically, neoplastic cells are noted infiltrating the renal interstitium (Fig. 5.59).

Additional reading

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6 Reproductive System

Male reproductive system

Normal structure

The reproductive system of the male bird is composed of the testes, the efferent ducts, in passerines the seminal glomus, and, in several unrelated birds, a phallus. The paired testes are located on the cranioventral aspect of the cranial pole of each kidney just to the right and left of the midline. The cranial pole of the testes also partially covers the ventral surface of the adrenal gland. When a bird is in breeding season, the enlarged testes will completely cover the ventral surface of the adrenal gland.

Immature testes are smooth and somewhat flattened. However, they always have a smooth surface and rounded cranial and caudal poles. Usually, in immature birds, the left testicle is larger than the right. As male birds become sexually mature and come into breeding season, the testes enlarge from 10 to 500 times. The fully mature testes is yellow and rounded but is longer than its width and has prominent capsular blood vessels. White cockatoos, the golden conure, the blue and gold macaw, some species of passerine birds, and the keel-billed toucan have melanoblasts in the testicular interstitium, causing the testicles to be grossly black. During the nonbreeding season, the testicles will become small again but will never be as small as they were when the bird was a juvenile. Histologically the testis is similar to that in mammals. During the nonbreeding season, a single layer of cells lines each seminiferous tubule. Transition to breeding season is marked by the proliferation of spermatogonia and the development of spermatocytes, secondary spermatocytes, spermatids, and sperm. Following breeding season, spermatocytes and Sertoli cells die, and their debris occludes the lumens of the seminiferous tubules.

The efferent ducts include the rete testis, the epididymis, and the ductus deferens. The epididymis is under hormonal control and enlarges during the breeding season. Unlike in mammals, it is not divided into a head, body, and tail. The ductus deferens connects the epididymis to the urodeum and runs across the ventral surface of the kidney. In the nonbreeding season, it is narrow and straight. It becomes torturous and distended with semen during the breeding season. At the distal end of the ductus deferens in passerine birds is the seminal glomus. This structure enlarges many times in breeding birds and is believed to store sperm during its final stages of maturation.

A copulating organ is seen only in waterfowl, screamers, cracids, ratites, kiwi, and tinamous. In the ostrich, kiwi, and tinamous, there is no cavity. There are right and left erectile fibrolymphatic bodies within the organ. Dorsal sleeves are present in which the vas deferens ejects semen. A ventral elastic body with an inner layer of erectile tissue is seen. In the emu, cassowary, rhea, and in anseriformes, there is a cavity. It is a blind-ending tube in anseriformes. The superficial portion of the cavity is lined internally by keratinized stratified squamous epithelium. There is an opening at the tip into the deep blind end of the tube.

Diseases of the testicle

Congenital disease

Congenital abnormalities of the testes are uncommon to rare. They include abnormally shaped testicles, fusion of the cranial poles of the testes, spermatocele formation, hypoplasia, and agenesis.

Noninflammatory disease

Noninflammatory testicular lesions include degeneration, atrophy, and initially, acquired spermatocele formation. Due to the seasonal variation in the size of the avian testis and presence or absence of spermatogenesis, changes in size of the testes or an abscess of spermatogenesis must be carefully interpreted. Atrophy can be the end result of a degenerative process and has been associated with generalized malnutrition and can be caused by vitamin E deficiency.

Degenerative changes will usually affect mature spermatozoa first, with eventual involvement of immature germinal cells and the formation of spermatidic giant cells (Fig. 6.1). Eventually there may be nothing but irregular empty tubules. Hemorrhage is occasionally seen (Fig. 6.2). In some cases mineralization of the tubules is noted (Fig. 6.3).

A variety of toxins affects avian testicles. The changes are primarily degenerative without inflammation. In general, there will be reduced spermatogenesis regardless of the toxic agent. Cystic degeneration of seminiferous tubules has been reported

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

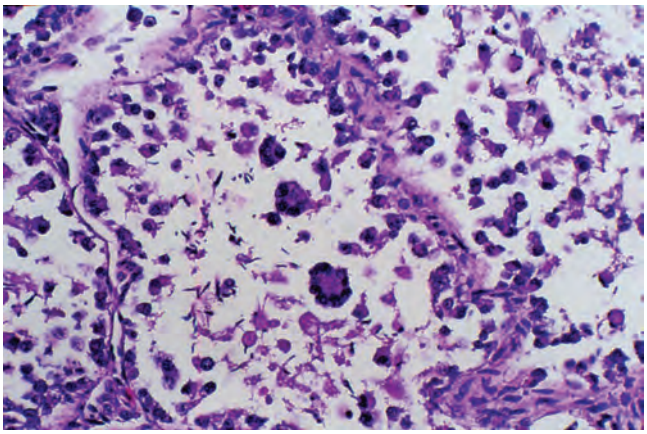

Figure 6.1 Testicular degeneration with the formation of spermatidic giant cells. This is a nonspecific lesion whose cause is often not determined in individual cases.

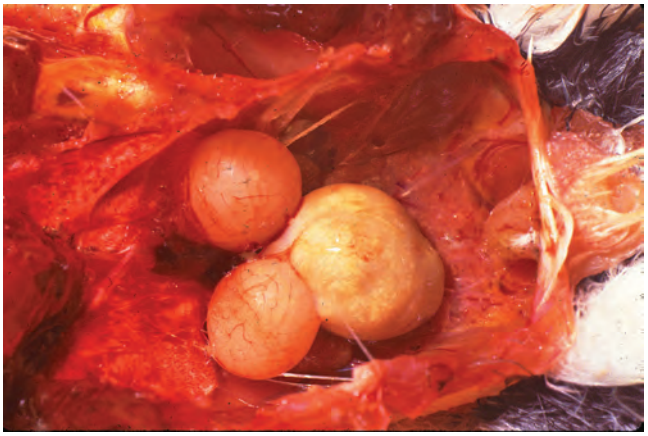

Figure 6.4 Large, irregular mass affected the ductus deferens and a portion of testicle.

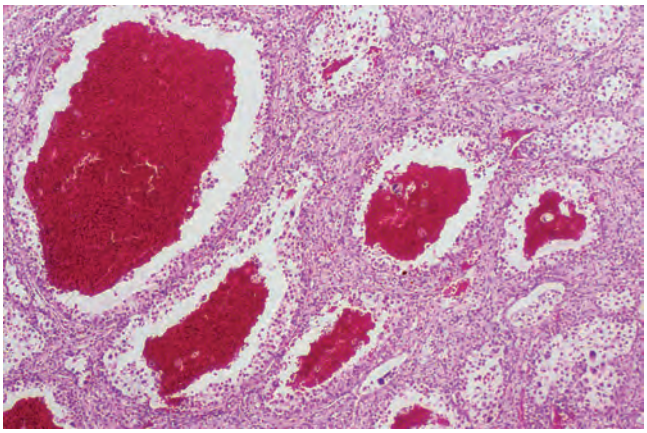

Figure 6.2 Severe testicular degeneration with dilatation of tubules and hemorrhage.

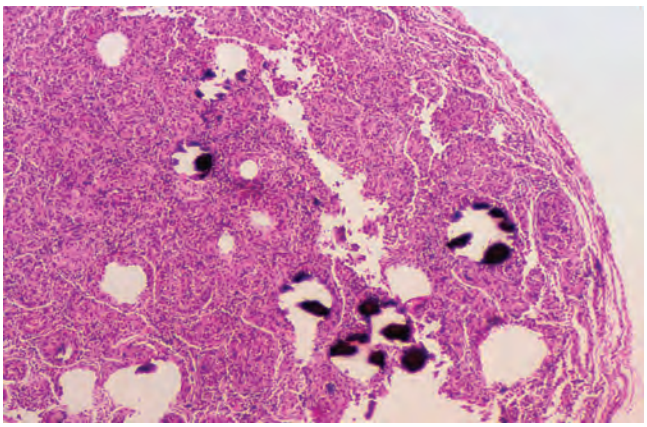

Figure 6.3 Multifocal testicular mineralization, the occasional end result of testicular degeneration or atrophy.

with furazolidone toxicity. Copper fungicides can cause atrophy, and mercury has been reported to cause reproductive dysfunction. Spermatoceles are cystic dilatations of the rete testis and/or epididymal tubules. Congenital spermatoceles are the result of failure of connection of one or more testicular or epididymal tubules to connect to the mesonephric duct (embryonal ductus deferens). Trauma or inflammation may lead to acquired spermatocele formation. Grossly the affected testicle/epididymis will have irregular nodular masses (Fig. 6.4) which will be fluctuant initially, but may become firm if a sperm granuloma develops. Histologically spermatoceles comprise dilated tubules containing large numbers of spermatozoa. Eventually the epithelium may atrophy and the basement membrane rupture, with extrusion of spermatozoa into the surrounding tissues. This results in a granulomatous inflammatory response.

Inflammatory disease

Inflammatory disease of the testicle (orchitis) is not commonly reported but has been associated with a variety of causes. The characteristics of the lesion depend on the underlying cause. Bacterial and fungal infections may be due to extension from the peritoneal cavity or the air sacs, or these infections may be hematogenous. Mycobacterial and chlamydial infections are also seen as a part of a more generalized problem. Grossly the affected testicle is enlarged, reddened, and may contain yellow-white foci.

Histologically there is necrosis and a variable inflammatory cell infiltrate. In acute infections, heterophils predominate, with macrophages and giant cells seen in more chronic bacterial problems. Granulomatous lesions are predominantly associated with fungal or mycobacterial infections. Finding the specific organism within the lesion is necessary for an accurate etiologic diagnosis (Fig. 6.5). In male chickens, infectious bronchitis virus (IBV) has been implicated in cases of low fertility and the formation of calcium calculi. Other than the formation of calculi, gross and histologic changes are usually not seen.

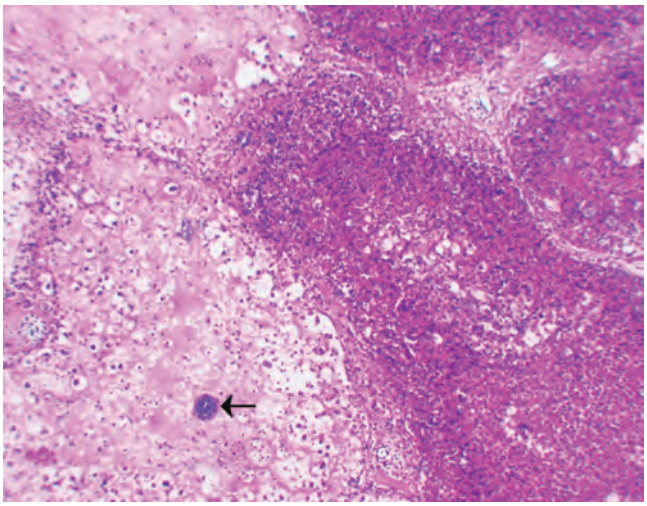

Figure 6.5 Severe necrotizing orchitis. There is marked necrosis, inflammation, and bacterial colony formation (arrow).

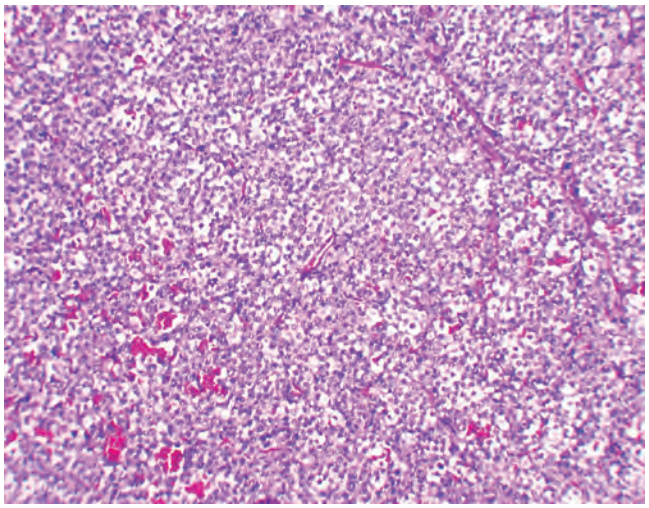

Figure 6.7 Effacement of normal testicular architecture by neoplastic cells in seminoma.

Neoplastic disease

Tumors of the testicle cause obvious enlargement and usually abdominal distension. Reported tumors include seminoma, Sertoli cell tumor, interstitial cell tumor, lymphosarcoma, undifferentiated sarcoma, and teratoma. We have seen testicular tumors in several avian species, but, in our experience and that of others, the highest incidence of testicular neoplasia occurs in the budgerigar.

Seminomas are tumors of immature germ cells. Grossly they are yellow-red and cause enlargement of the testis (Fig. 6.6). Occasionally they may be bilateral. On section, they are usually soft. Histologically the neoplastic cells are somewhat pleomorphic, with indistinct cytoplasmic boundaries and large vesicular nuclei (Fig. 6.7). There is minimal stroma, and there may be remnants of tubular architecture within the tumor. There is one reported case of metastasis to the liver.

Sertoli cell tumors are generally firm, gray-white neoplasms that may appear nodular on section. Cystic spaces are sometimes present. Histologically there are numerous tubules containing pleomorphic immature Sertoli cells (Fig. 6.8). These tubules are separated by abundant stroma. Clinical signs of feminization, including a change in cere color from blue to brown in budgerigars, are reported in birds with Sertoli cell tumors.

Interstitial cell tumors may be cystic and are often orange-red due to steroid hormones and areas of hemorrhage. These tumors are comprised of large polyhedral cells with vacuolated cytoplasm. The neoplastic cells form trabeculae and sheets (Fig. 6.9). There can be variable hemorrhage and necrosis.

Lymphosarcoma can involve the testicle, and both grossly and histologically these tumors may be confused with seminomas (Figs. 6.10 and 6.11). However, testicular lymphosarcoma is usually just one manifestation of a multisystemic disease.

Figure 6.6 Large seminoma that was displacing other abdominal organs. Note the smooth surface. Sertoli cell tumors are usually firmer and more nodular grossly.

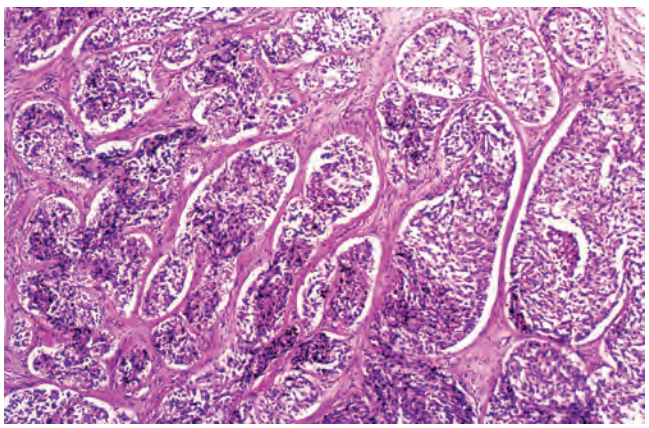

Figure 6.8 Sertoli cell tumor. Note the numerous tubular structures lined by neoplastic Sertoli cells. There is abundant connective tissue stroma, which results in the gross firmness and nodularity.

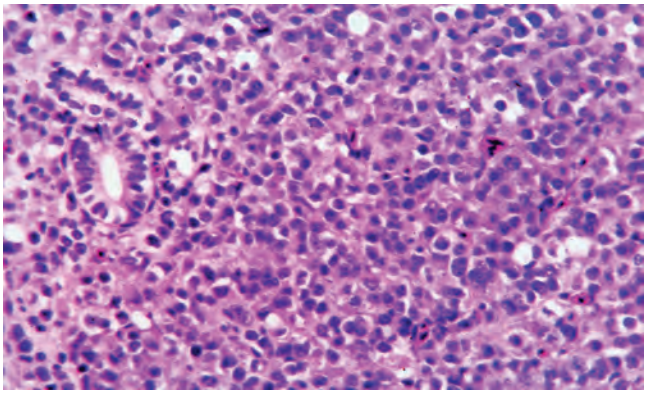

Figure 6.9 Interstitial cell tumor. Tubules are effaced by a sheet of neoplastic cells with abundant cytoplasm.

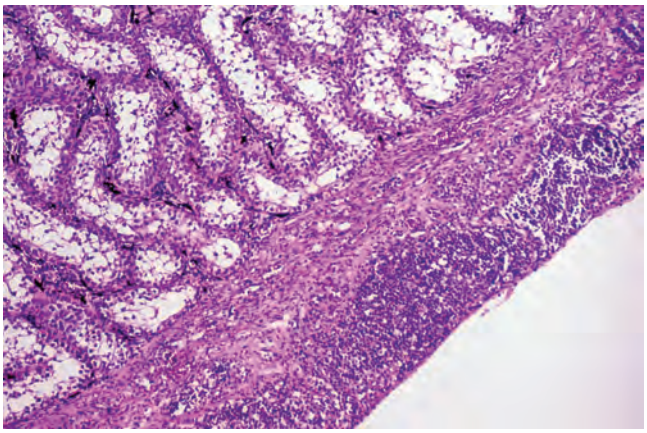

Figure 6.10 Infiltration of the thickened testicular capsule by neoplastic lymphoid cells in lymphosarcoma.

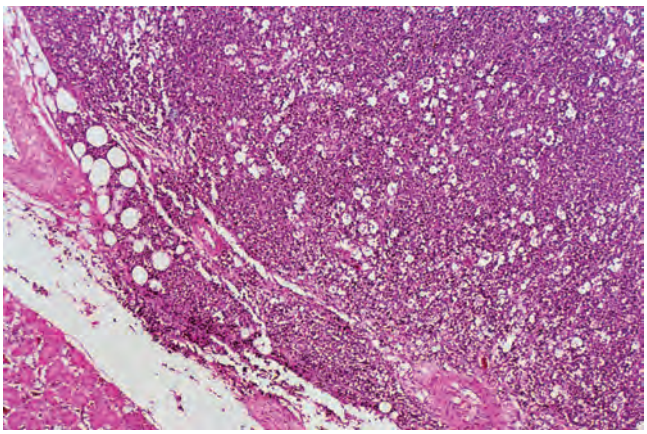

Figure 6.11 Replacement of testicular parenchyma by neoplastic lymphoid cells. Note the similarity to seminoma.

Figure 6.12 Prolapse of the phallus.

Undifferentiated testicular sarcomas may arise from connective tissue and are usually composed of fusiform cells forming interlacing bundles. Immunohistochemistry may be used to try to determine the exact cell type.

Teratomas do not have specific gross characteristics unless keratinaceous cysts or some other differentiated structures are seen. Histologically they contain a variety of structures comprising both epithelial and mesenchymal elements.

Diseases of the epididymis

Spermatoceles have been discussed previously. Inflammation and neoplasia are reported in the epididymis. Inflammation is generally due to the same causes as in orchitis. Both carcinomas and sarcomas can arise in the epididymis but are rare.

Diseases of the phallus

Prolapse of the phallus is infrequently reported in pet birds. It occurs sporadically in anseriformes and ratites (Fig. 6.12). It can either lead to, or be caused by, trauma, inflammatory disease, or frostbite. It is usually diagnosed clinically.

Female reproductive system

Normal structure

The ovary is located on the ventral surface aspect of the cranial division of the left kidney. In juvenile birds, the ovary is yellow, flattened, and somewhat triangular, with its apex pointing cranially. In contrast to the juvenile testis, the juvenile ovary has a granular surface. As a bird becomes sexually mature, secondary

and tertiary follicles develop, forming grapelike clusters prior to ovulation. The ovary is tightly adhered to the surface of the kidney but becomes pendulous as the tertiary follicles fill with yolk. It is suspended by the mesovarium from the abdominal wall. Only the left ovary is present in most species of birds. Exceptions include many birds of prey and the brown kiwi. Pigmentation of the ovary also occurs in some species of birds, including the white cockatoos and the blue and gold macaw.

The ovary has a defined cortex and medulla in juvenile birds, but this distinction is lost in the mature ovary. The outer surface of the ovary is covered by a cuboidal flattened peritoneal mesothelium. The cortical region consists of numerous follicles in various stages of development. Unlike in mammals, an antrum does not develop in the avian follicle. The medulla contains blood vessels, nerves, smooth muscle, and interstitial cells.

A stalk of smooth muscle containing blood vessels and nerves suspends an enlarged tertiary follicle, which comprises a primary oocyte enclosed by a six-layered wall. From internal to external, these layers consist of radial processes of the oocyte cytolemma and the radial processes of granulosa cells. The layers include the stratum granulosum, the theca interna (comprising fibroblasts and collagen), the theca externa, a connective tissue tunic, and the superficial "germinal" epithelium. The latter is essentially peritoneal mesothelium. Yolk, whose components originate in the liver, is supplied to the oocyte by the follicle. The follicle produces steroid hormones. Estrogen is produced within the thecal cells and progesterone within the granulosa cells. Thecal cells outside the follicle produce androgens.

Following ovulation, the follicle regresses and fills with granulosa cells that contain lipid. This is not a true corpus luteum as is seen in mammals, as there is no cellular multiplication. The thecal wall may rupture during this time, resulting in the escape of yolk into the ovary or the peritoneal cavity.

Oviduct

The oviduct is divided into five functional zones: the infundibulum, magnum, isthmus, shell gland or uterus, and vagina. The most cranial region, adjacent to the ovary, is the infundibulum. The funnel portion of the infundibulum, which receives the ovum, has a folded nonglandular mucosa and is lined by nonsecretory pseudostratified ciliated cells. The tubular region has a thickened wall and secretory epithelial cells. The tubular glands are present at its junction with the magnum. The lamina propria of the infundibulum is loose collagenous tissue. Diffuse lymphocytic cell accumulations may be noted. The ovum is fertilized in this region, and the chalaziferous layer of the albumen is produced.

The magnum is the longest and thickest portion of the oviduct. The wall is thickened due to numerous tubular glands that are lined by cuboidal columnar epithelium. Nonciliated and ciliated epithelial cells are present on the mucosal surface. In the caudal, few centimeters of the magnum are the mucous region. Glands in this region are reduced and contain abundant mucus. Most of the albumen and various minerals are deposited in the magnum.

The isthmus is shorter and has thinner walls and less prominent folds than in the magnum. Ciliated and nonciliated columnar epithelial cells line the isthmus. Branched tubular glands extend into the lamina propria. These glands contain sulfur-containing proteins. The outer and inner shell membranes are added in the isthmus.

The uterus or shell gland is a short region containing leaf-like lamellae. The mucosal epithelium is pseudostratified and intermittently ciliated. Coiled tubular glands are noted within the uterus. The shell is formed in the uterus.

At the junction with the uterus is the vaginal sphincter. The vagina is S-shaped due to its smooth muscle and connective tissue wall. It is thicker than any other part of the oviduct. Ciliated and nonciliated mucosal cells line the vagina. At the junction with the uterus are simple tubular glands lined by columnar epithelial cells containing lipid. These are so-called sperm-host glands that store and nourish spermatozoa.

Specific defects in abnormal eggs can sometimes be related to disease or dysfunction of a specific portion of the oviduct.

The length and diameter of the oviduct vary dramatically between the breeding season and the nonbreeding season. During the nonbreeding season, the oviduct is slender, pink, linear, and of uniform diameter. The oviduct of juvenile birds is thin and nearly transparent, making it difficult to find at necropsy. The oviduct of female birds that are in the process of laying will be greatly elongated, festooned, and will have a thickened wall and a greatly widened lumen. The oviduct may fill much of the left caudal coelomic cavity, displacing the intestines to the right.

Diseases of the ovary

A variety of congenital defects of the ovary is reported in birds. A retained right ovary is occasionally seen in birds that normally would have only a left ovary. Congenital ovarian cysts are most common in budgerigars and canaries.

Grossly they are fluid filled and thin walled (Fig. 6.13). Flattened cells line cysts caused by trapped surface mesothelium. Granulosa cells line follicular cysts (Fig. 6.14). Follicular cysts may either be acquired or congenital.

Hermaphrodism has been seen in some hybrid ducks but is not commonly reported in pet birds.

Oophoritis can be secondary to infection of the peritoneal cavity or air sacs or can be associated with hematogenous infection. Viruses, bacteria, fungi, and mycobacteria are possible causes. Grossly the ovaries are enlarged, discolored, and possibly hemorrhagic.

The histologic appearance depends on the cause. Herpesvirus infection leads to acute necrosis and hemorrhage of ovarian stroma. Intranuclear inclusion bodies are noted in syncytial cells (Fig. 6.15). Acute necrosis and heterophil infiltration predominate in most bacterial infections (Fig. 6.16). Organisms may or may not be seen. Mycobacteria and fungi tend to produce granulomas containing large macrophages and giant cells (Figs. 6.17

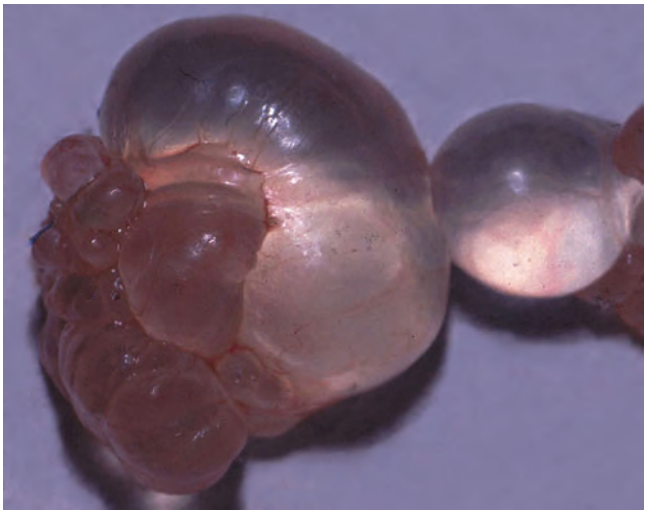

Figure 6.13 Large fluid-filled ovarian cyst.

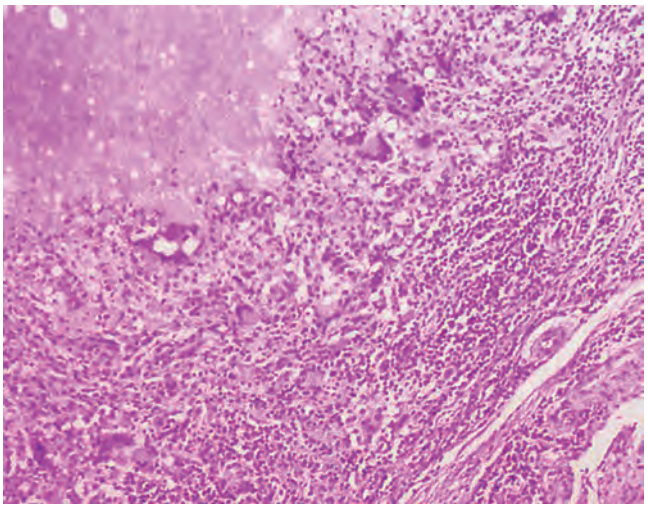

Figure 6.16 Bacterial oophoritis characterized by necrosis, inflammatory cell infiltrate, and fibrin deposition in the ovarian stroma.

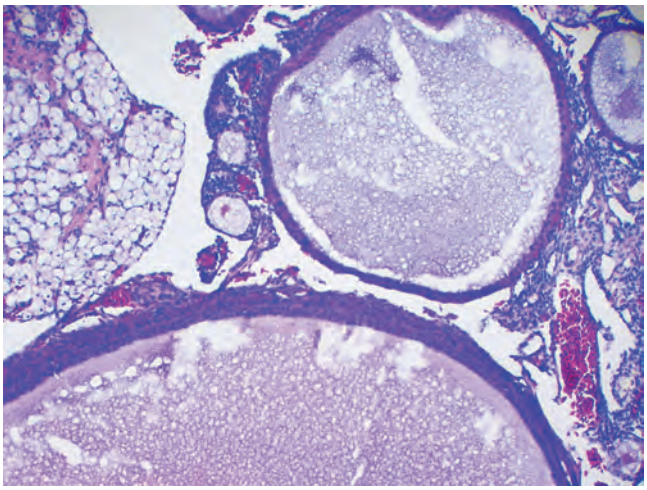

Figure 6.14 Fluid-filled follicular cysts of the ovary.

and 6.18). Fungal organisms may be seen with routine stains (Fig. 6.19), and acid-fast stains will confirm mycobacteria.

Noninfectious inflammation of the ovary is associated with rupture of follicles and extrusion of yolk material within the ovarian stroma. Grossly, affected ovaries may be slightly enlarged and contain variably sized yellow foci. Histologically the yolk material elicits a reaction initially composed of macrophages and lymphocytes. The macrophages usually have abundant foamy cytoplasm. Eventually giant cells are seen (Fig. 6.20).

Toxic agents may cause noninflammatory ovarian disease. Aflatoxin leads to cessation of egg production and ovarian atresia. Ovarian atresia/atrophy can also be the end result of a variety of insults, including inflammation of any cause and age. Affected ovaries will be small, and histologically there are primordial follicles, lutein cells, and collapsed stroma (Fig. 6.21).

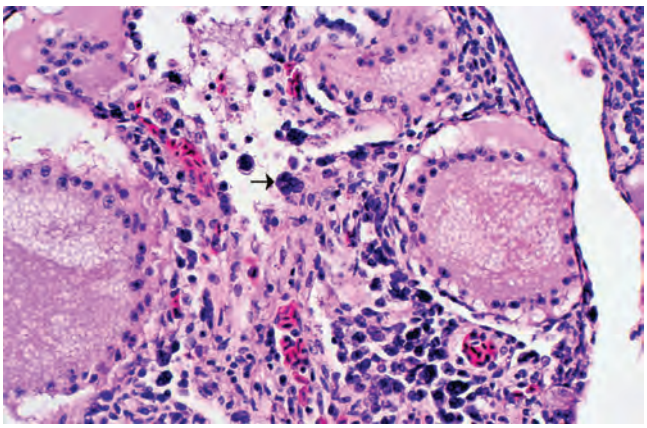

Figure 6.15 Herpesvirus-induced oophoritis. Note the numerous cells, including syncytial cells, with intranuclear inclusion bodies (arrow).

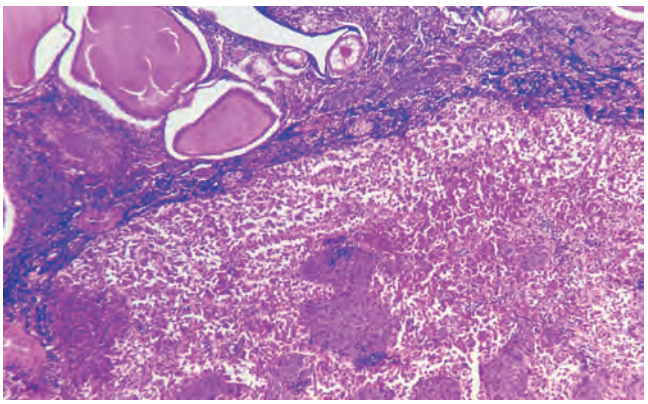

Figure 6.17 Granulomatous oophoritis due to mycobacteria. Note the diffuse infiltration of large macrophages with abundant cytoplasm.

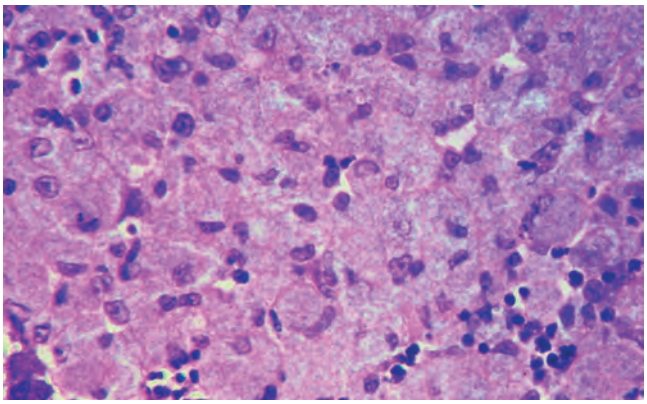

Figure 6.18 Detail of inflammation in mycobacteriosis of the ovary. The granular cytoplasm of the macrophages contains numerous acid-fast bacteria.

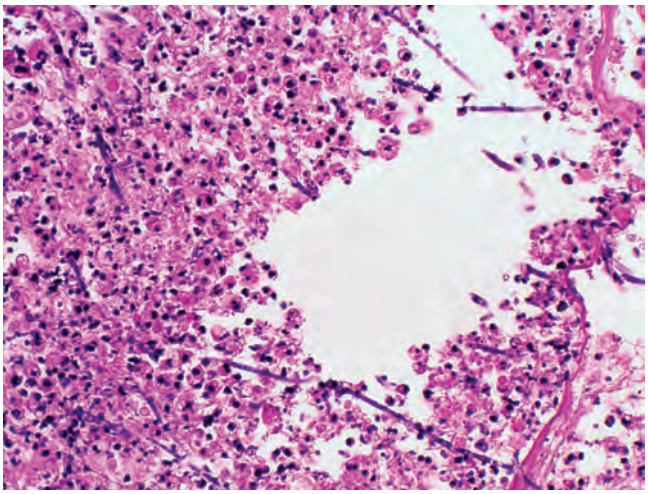

Figure 6.19 Mycotic oophoritis. Fungal hyphae are seen within an area of necrosis and inflammation.

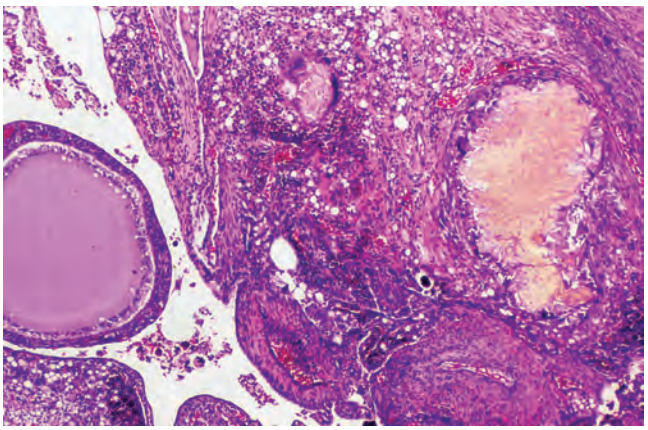

Figure 6.20 Yolk-induced oophoritis. A large mass of amorphous material is surrounded by macrophages and giant cells. Smaller granulomas are also seen.

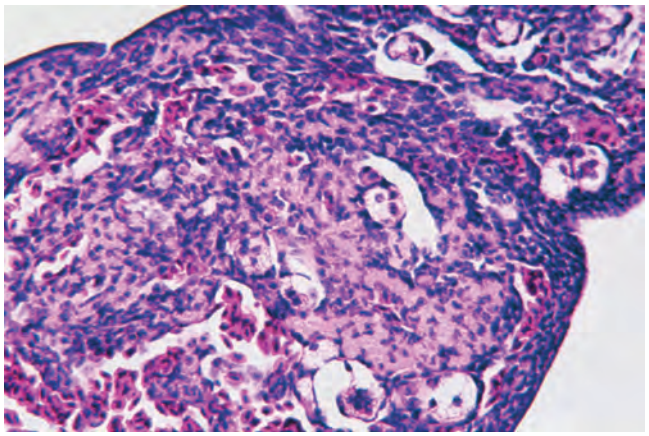

Figure 6.21 Atretic ovary with primordial follicles and collapsed stroma. A few cells resembling lutein cells have prominent eosinophilic cytoplasm.

Several types of ovarian neoplasms are seen in birds. Granulosa cell tumors, which are reported to be the most common but probably are not, are yellow lobulated irregular masses that are friable. They may become quite large and fill the abdominal cavity. Histologically the tumors are comprised of nests and trabeculae of slightly pleomorphic cells with eosinophilic cytoplasm and vesicular nuclei separated by variable amounts of stroma (Fig. 6.22). Occasionally structures resembling Call–Exner bodies are present (Fig. 6.23).

Ovarian adenomas are rarely reported in birds, but occasionally a small ovarian mass has the histologic characteristics of a benign tumor. In these tumors the cells are fairly well differentiated and form acinar or tubular structures (Fig. 6.24).

Ovarian carcinomas are variably sized, firm, gray-white, and multilobular. They may also implant on the serosal surfaces of adjacent organs, the mesentery, and body wall. They may also metastasize. Histologically carcinomas comprise poorly differentiated epithelial cells forming cords, acini, and papillary structures (Figs. 6.25 and 6.26).

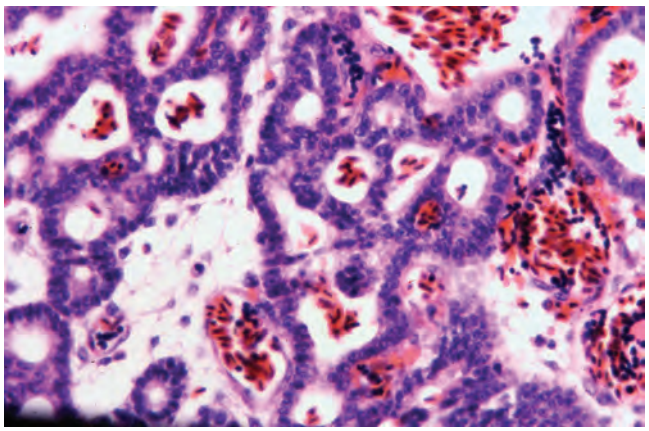

Figure 6.22 Granulosa cell tumor with predominant trabecular pattern.

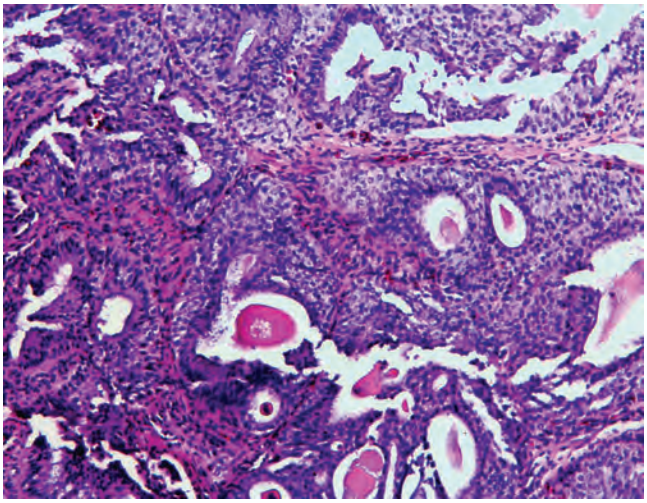

Figure 6.23 Granulosa cell tumor with scattered clear spaces containing fluid material and possible pyknotic nuclei.

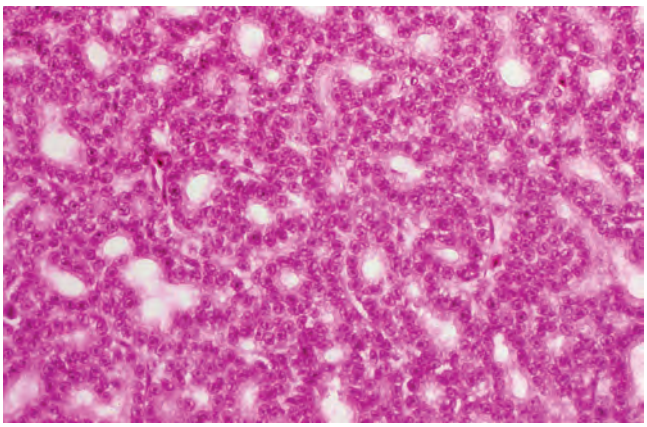

Figure 6.24 Probable ovarian adenoma comprising tubules and acini lined by fairly well-differentiated epithelial cells.

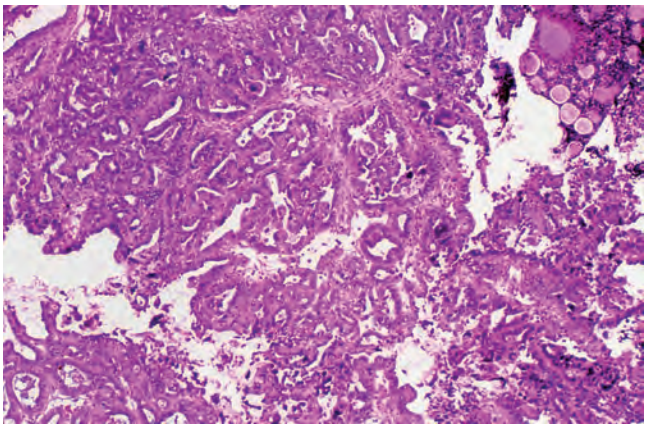

Figure 6.25 Ovarian carcinoma comprising tubules and cords of neoplastic cells.

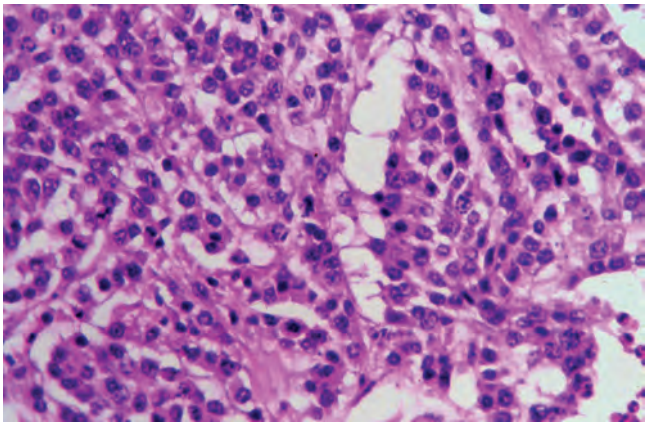

Figure 6.26 Cords and nests of anaplastic cells in ovarian carcinoma.

Dysgerminoma is the female analog of the seminoma and is infrequently seen. These tumors grossly are multilobular (Fig. 6.27), and histologically they comprise sheets of pleomorphic round or ovoid cells with abundant cytoplasm and vesicular nuclei.

Arrhenoblastoma is histologically similar to the Sertoli cell tumor. In mammals, these tumors are usually called ovarian stromal tumor, Sertoli pattern. In chickens, they are associated with masculinization, but masculinization is not seen in pet birds in our experience. The tumors are gray-white lobulated masses comprising structures resembling seminiferous tubules (Fig. 6.28).

Teratomas can become quite large and histologically comprise tissues of various types, including both mesodermal and epithelial elements (Figs. 6.29 and 6.30).

An unusual ovarian tumor seen in humans is the lipid (lipoid) cell tumor. We have seen a few examples in birds that appear to fall into this classification. The exact cell of origin has not been conclusively identified. The tumor cells are round or ovoid and may be in nests or diffuse sheets. There is moderate to abundant

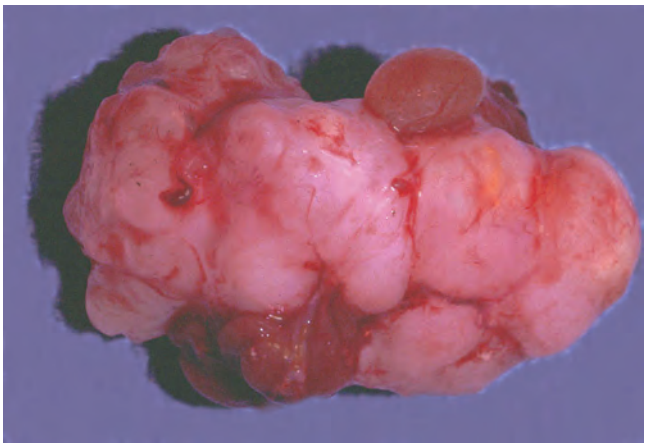

Figure 6.27 Multilobulated ovarian dysgerminoma.

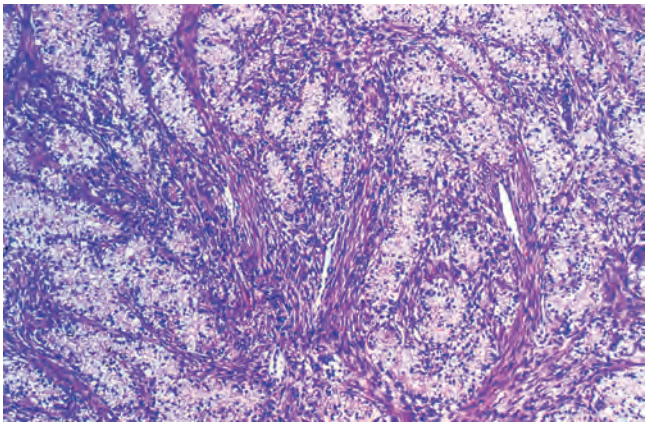

Figure 6.28 Ovarian stromal tumor, Sertoli's pattern (arrhenoblastoma). Nests and cords of neoplastic cells are separated by abundant stroma.

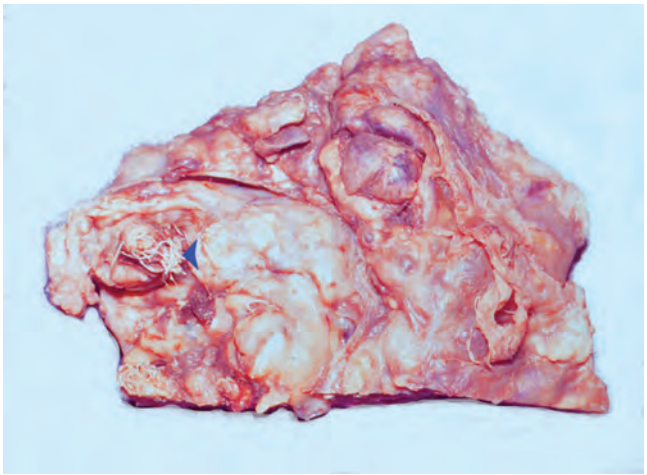

Figure 6.29 Ovarian teratoma. A large, irregular mass with an area of what appears to be attempted feather development (arrowhead).

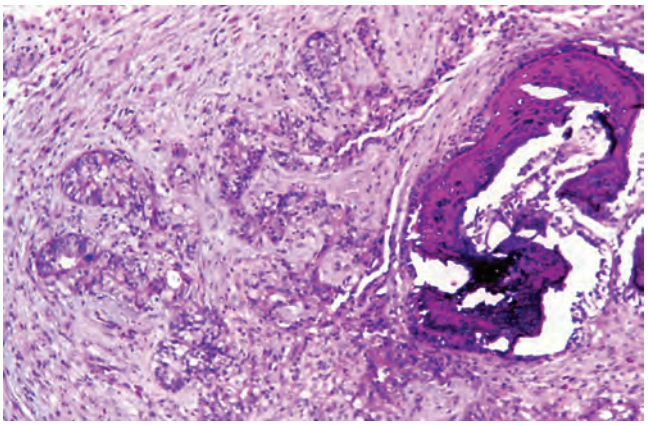

Figure 6.30 Irregular mixture of epithelial and mesenchymal elements in ovarian teratoma.

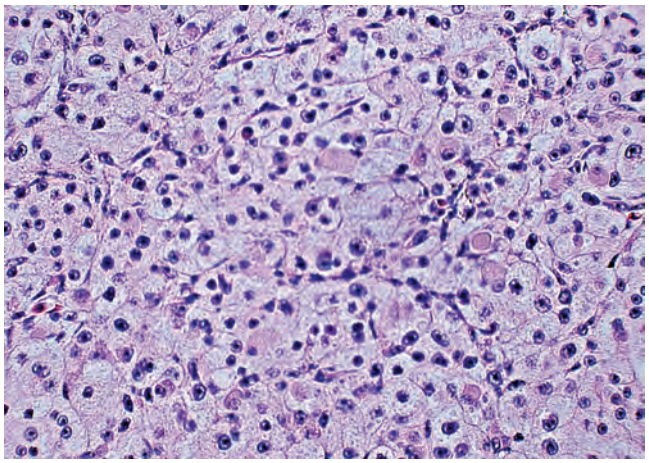

Figure 6.31 Unusual ovarian tumor resembling a lipid-cell tumor as seen in humans. The exact cell type is unknown.

granular cytoplasm that resembles lipid (Fig. 6.31). Differential diagnoses include lutein cell tumors.

Other tumors seen in the ovary include those of adipose tissue and connective tissue and hemangiomas/sarcomas, lymphosarcoma, and tumors of smooth muscle. As part of generalized tumor metastasis, malignant melanoma is occasionally seen in the ovary. The histology of these tumors is typical and is described elsewhere in this book.

Non-neoplastic proliferative disease is uncommon. We have seen a few cases of ovarian stromal hyperplasia.

Diseases of the oviduct/uterus

Congenital malformations of the oviduct include atresia, segmental aplasia, and congenital cysts. These lesions may be associated with the developed left oviduct or a retained or incompletely regressed right oviduct. The cysts are usually fluid filled and may collapse during surgery/necropsy. There may be multiple cysts in an affected oviduct (Fig. 6.32). Histologically they are lined by a flattened or low cuboidal epithelium (Fig. 6.33). Cysts can also be acquired in older birds. Morphologically they are similar to those described.

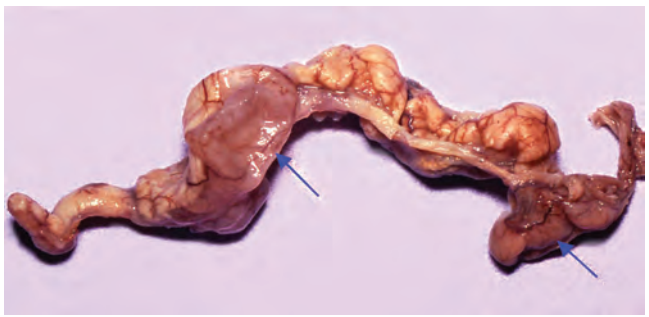

Figure 6.32 Multiple collapsed cystic areas in the oviduct (arrows).

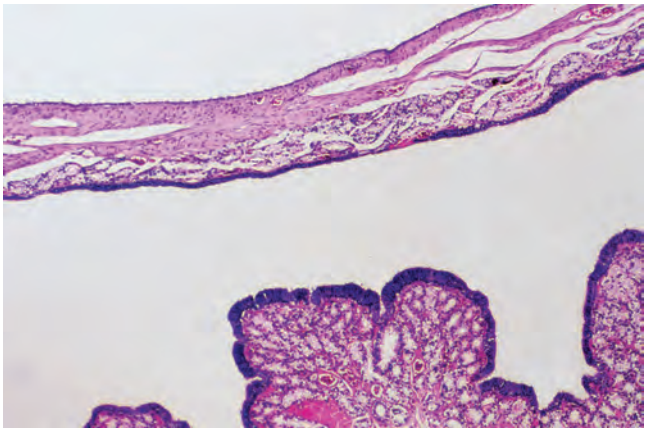

Figure 6.33 Area of oviductal cyst formation. The affected portion is lined by flattened epithelial cells.

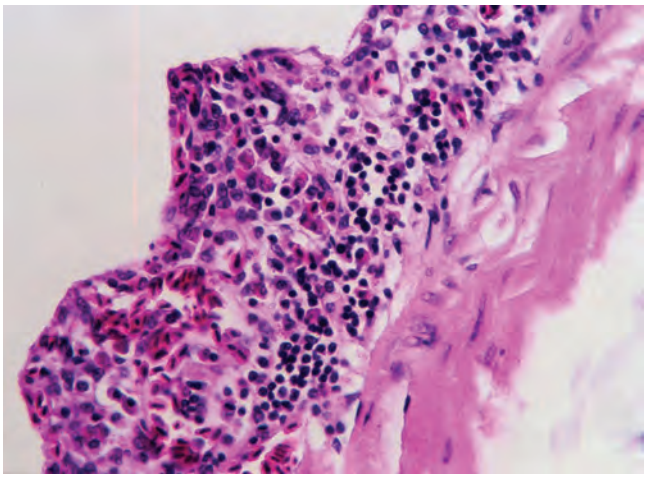

Figure 6.35 Bacterial salpingitis. Note the mucosal necrosis and diffuse inflammatory cell infiltrate.

Inflammation of the oviduct can be caused by either infectious or noninfectious etiologies. Infectious etiologies include viruses, gram-negative and gram-positive bacteria, mycobacteria, fungi, and parasites. The source of infection can be the result of an organism ascending from the cloaca, hematogenous spread, or extension of disease from the peritoneal cavity.

In chickens, infectious bronchitis virus (IBV) and avian metapneumonia virus (aMPV) may replicate in the epithelium of the oviduct leading to loss of cilia and necrosis of luminal and glandular epithelium. There may be no gross changes noted.

With other infections the oviduct is usually enlarged, reddened, and friable, and a variable amount of exudate may be present. The appearance depends on the exact etiology and duration of the disease. Histologically necrosis, hemorrhage (Fig. 6.34), inflammation, and fibrosis are all potential changes. Bacterial salpingitis is characterized by an infiltrate of heterophils, lymphocytes, and macrophages (Fig. 6.35). Eventually there can be giant cell formation (Fig. 6.36).

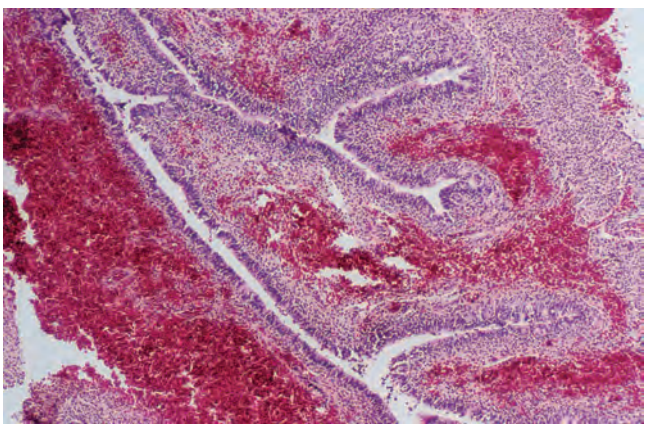

Figure 6.34 Hemorrhage due to herpesvirus infection within the oviduct wall.

Noninfectious causes of inflammation may be mechanical, secondary to improper egg maturation or formation. Inspissated yolk can elicit a chronic inflammatory response comprising lymphocytes and macrophages. Often the macrophages contain phagocytosed yolk material. Free yolk, in the form of round, variably sized, basophilic globules, is seen in the lumen and sometimes in the tissue (Fig. 6.37).

Peritonitis (Chapter 13) can be a secondary complication to either infectious or noninfectious salpingitis following penetration of the oviductal wall or rupture of the oviduct. Egg yolk peritonitis may result from internal ovulation or retrograde movement of the ovum back out through the infundibulum. Entire eggs may enter the abdomen either through a ruptured oviduct or by retrograde movement and expulsion through the

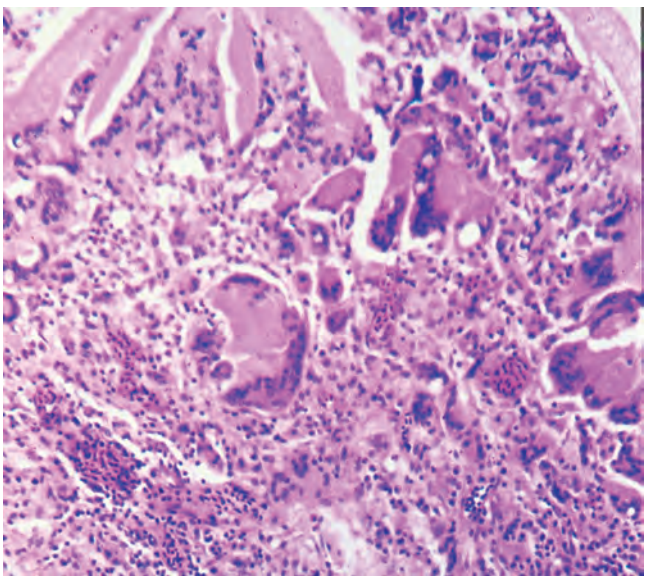

Figure 6.36 Chronic bacterial salpingitis with giant cell formation.

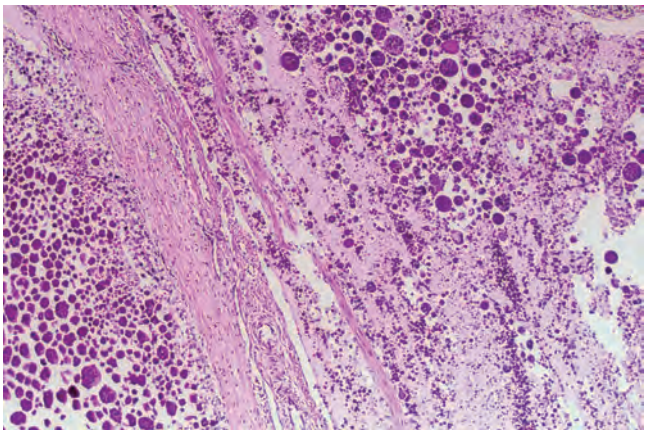

Figure 6.37 Salpingitis secondary to rupture of the forming egg and infiltration of yolk protein into the wall of the oviduct.

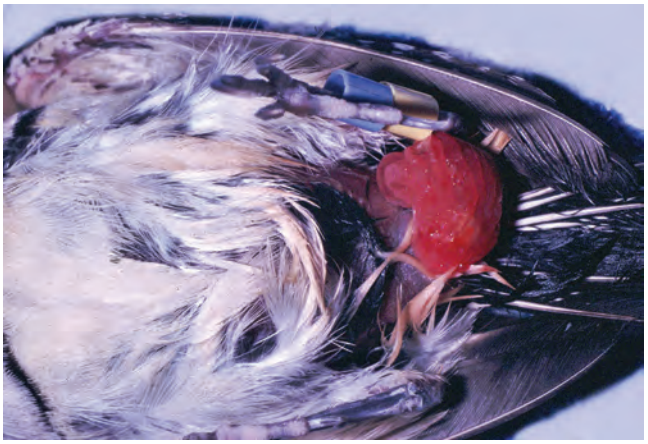

Figure 6.39 Oviductal prolapse. Differential diagnoses include prolapse of the cloaca.

infundibulum. If these eggs crack and leak their contents, they can also induce peritonitis.

Oviductal torsion/volvulus occasionally occurs and, if not diagnosed, leads to the death of the bird. There is often vascular compromise, and the oviduct will be edematous, red-black, and friable.

Impaction of the oviduct is almost always a sequel to salpingitis or egg binding. In addition to finding an impacted egg (Fig. 6.38), there may be free yolk material, excess mucin, and purulent material in the lumen. The impacted egg can lead to pressure necrosis of the oviductal wall. Large neoplasms may also be associated with impaction.

Secondary to anything that causes excessive abdominal straining, or possibly a mass within the coelomic cavity, the oviduct can prolapse into the cloaca and through the vent (Fig. 6.39). Differential diagnoses include cloacal prolapse and possibly mucosal proliferation near the mucocutaneous junction.

Proliferative and neoplastic changes of the oviduct include cystic hyperplasia and neoplasia. In hyperplasia, numerous cystic structures are seen grossly. These cysts may contain clear or cloudy fluid and are lined by proliferative mucosa of the particular portion of the oviduct involved. The condition is probably of endocrine origin, but an exact cause/pathogenesis has not been established.

Neoplasms can be either adenomas or adenocarcinomas. These are firm, nodular, gray-white masses (Fig. 6.40). Histologically cells of adenomas are arranged in acini, tubules, and sheets that resemble normal glands (Fig. 6.41). Carcinomas comprise less well-differentiated cells forming acini and tubules that are infiltrative into the oviductal wall (Figs. 6.42 and 6.43).

In severe chronic cases, these tumors can also implant on peritoneal surfaces. Grossly it may be difficult to differentiate tumors of oviduct origin from those of ovarian origin, and histologically there are similarities between carcinomas from either site. Careful necropsy examination is necessary for differentiation in advanced cases.

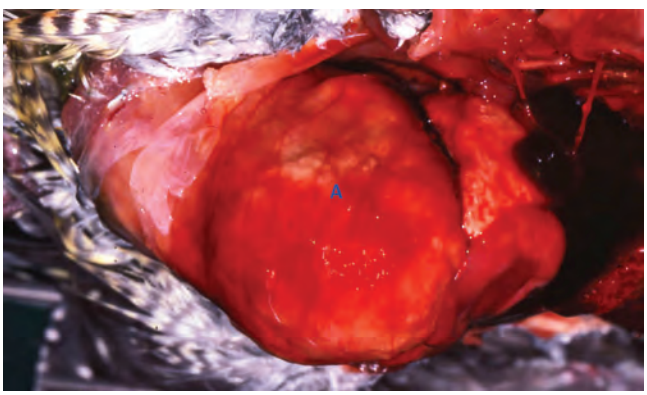

Figure 6.38 Enlarged, impacted oviduct associated with egg binding (A).

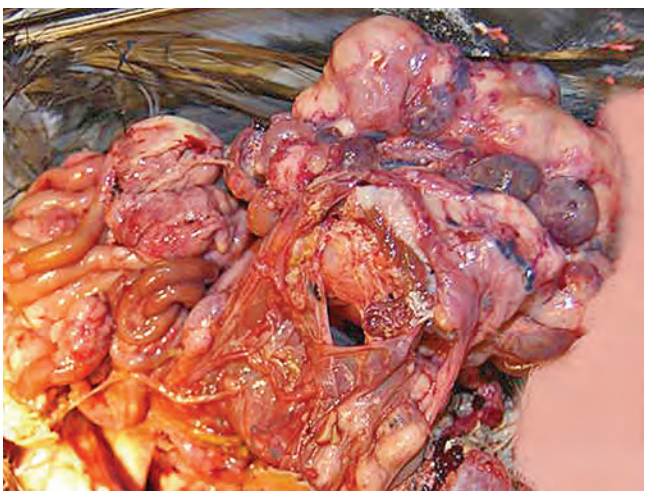

Figure 6.40 Oviductal carcinoma. Large, irregular mass with associated adhesions.

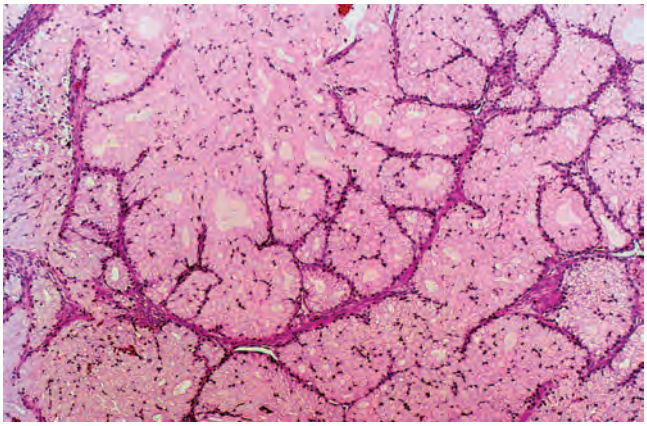

Figure 6.41 Oviductal adenoma. Numerous lobular structures comprise minimally undifferentiated mucosal epithelial cells.

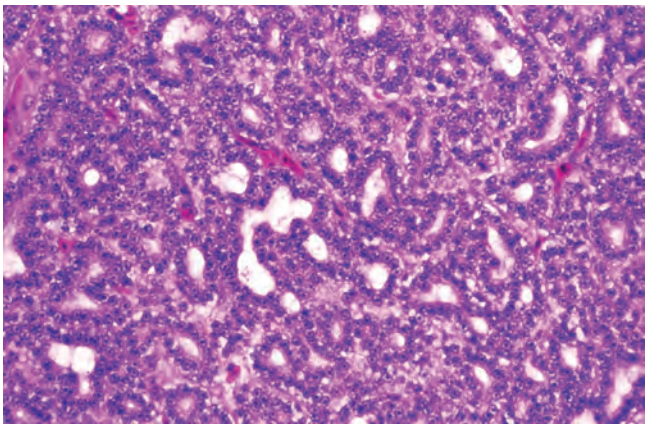

Figure 6.43 Nests and acini typical of oviductal carcinoma. Less well-differentiated tumors can be difficult to distinguish from ovarian carcinomas, particularly if implanted on serosal surfaces.

Leiomyomas are a common tumor of the oviduct of chickens. Grossly these are red-brown masses composed histologically of interlacing bundles of fusiform cells with oval or elongated nuclei.

Diseases of the cloaca

The cloaca is affected by a variety of inflammatory and neoplastic diseases that can lead to problems with fertility and/or egg laying. These disease processes may lead to fibrosis and stricture or blockage due to mass lesions. They are discussed in Chapter 3.

The morphology of egg binding/dystocia

Egg binding is the failure of eggs to pass through the oviduct at a normal rate. Dystocia is an egg obstructing the oviduct or causing oviduct prolapse. The most common cause of egg binding in companion birds is protracted egg laying. Birds naturally lay eggs and then brood the eggs and feed the young before beginning another cycle of egg laying if they lay at all again that year. Finches, budgerigars, lovebirds, and cockatiels that are kept as pets often lay clutch after clutch of eggs. Many of these birds are not provided with sufficient dietary calcium and, as a result, cannot mineralize their eggs properly and may become hypocalcemic. It is assumed that hypocalcemia may result in weakness of the muscle of the oviduct and its inability to contract.

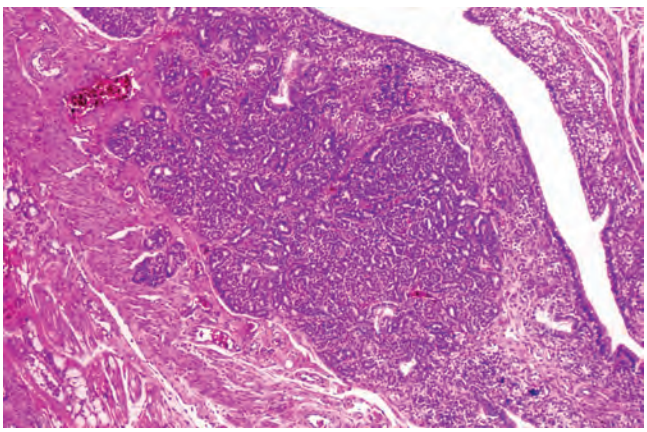

Figure 6.42 Focus of oviductal carcinoma formation. Note the infiltration of the oviduct wall by acini and tubular structures.

The retained egg then acts as a space-occupying mass placing pressure on the adjacent digestive organs and reducing the volume of the air sacs. The hypocalcemia, the mass effect, or both subsequently lead to the bird's death. Less commonly, adhesions form between the egg and the oviduct or rarely a portion of the oviduct is incorporated in the egg, preventing the egg from being passed. We have also seen egg binding in larger species of parrots that produce their first egg when they are older. The reason that these older birds become egg bound is not clear.

Other potential causes of egg binding are nutritional myopathies caused by a deficiency of either vitamin E or selenium, by obesity, and by a variety of environmental stressors.

Lesions associated with egg binding have been previously described. If there is dystocia, the oviduct may prolapse. If not corrected, the prolapsed oviduct may be found in the cloaca or extending from the vent at necropsy. Depending on the duration, affected tissue will be edematous, variably congested, and friable. Microscopically, necrosis, variable inflammation, congestion, and hemorrhage are seen.

Abnormal eggs

Soft-shelled eggs are sometimes a manifestation of vitamin A or D deficiency or calcium deficiency (Fig. 6.44). Infections with the avian bronchitis virus or an adenovirus also cause soft or thin-shelled eggs in poultry. Rough shells are sometimes a manifestation of salpingitis (Fig. 6.45). Organochlorine pesticides cause thin-shelled eggs. Other nutritional and toxic problems that can cause eggshell abnormalities include crude oil, nicotine, and furazolidone toxicity.

Ectopic eggs are sometimes an incidental necropsy finding but can also be a cause of mortality, particularly if associated with peritonitis. Oviductal rupture or reverse oviductal peristalses are

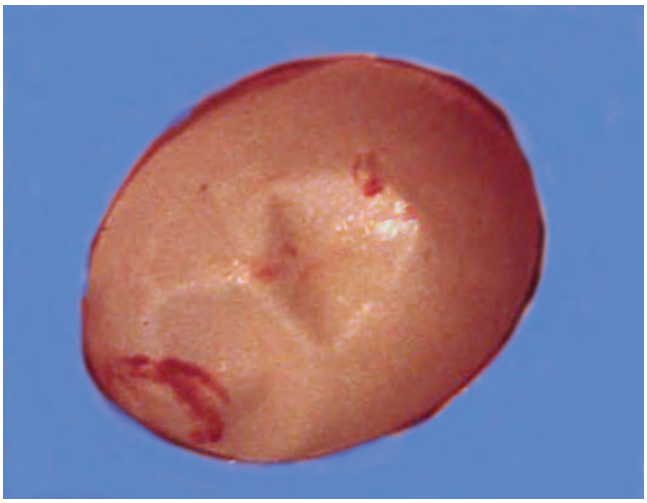

Figure 6.44 Inadequately calcified egg shell that can occur with nutritional deficiencies.

primary causes. At necropsy, the ectopic egg may have a complete normal shell, particularly if there is a rupture of the caudal oviduct. If the rupture is more cranial or if there was reverse peristalsis, the egg may be soft shelled or there may only be yolk and albumen present in the peritoneal cavity. There is usually some degree of peritonitis.

Infertility, dead in shell, and fetal necropsy

Investigation into hatching failure requires gross and histologic examination of the egg and its contents as well as the usual ancillary laboratory procedures. Egg necropsies are often disappointing. Aviculturists will often leave the egg in the incubator for an extended time after the embryo died because they are not aware of its death. As a result, many embryos are severely autolytic by the time they reach the pathologist. The pathologist must have some understanding of the environment of artificial incubation and what can go wrong that will eventually affect the developing embryo/fetus.

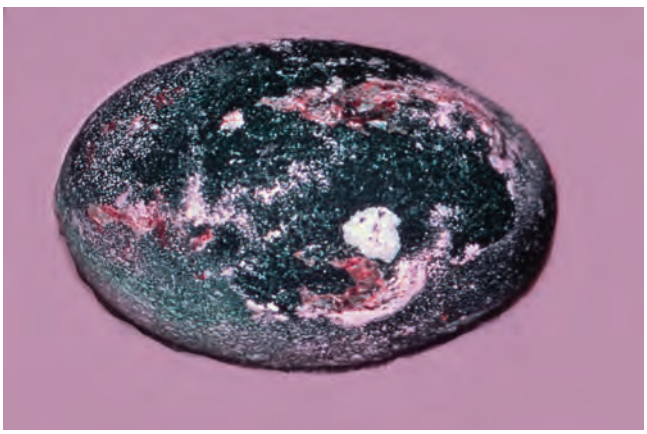

Figure 6.45 Roughening and discoloration of an eggshell secondary to bacterial salpingitis.

If there is failure to hatch, the first issue to be addressed is whether the egg is/was fertile. Fertilization of the ovum (yolk) initiates a series of cell divisions in the protoplasmic portion of the egg. This portion is seen grossly as a small white disc (blastodisc) present on the dorsal pole of the yolk. If there has been no fertilization, this small white area is all that is seen when the egg is examined.

Failure of fertilization is a potential reflection on a number of management issues. The most common cause of infertile eggs is pairing of two female birds. Other potential management problems include the use of inappropriate perches, inexperience of the male or the female parrot, immaturity of the male, improper nest boxes, and disturbances by other birds, wild or domestic animals, and caretakers. A properly formed egg usually implies that there is not a medical problem with the hen. The male, however, may not be producing sperm, or the sperm that he is producing may be abnormal.

A fertile egg will develop a blastoderm, which will appear as a small white area that enlarges and has a translucent center. Subsequently there is embryo formation and, by the end of the first third of incubation, organogenesis has usually taken place.

The first step of the egg necropsy is to evaluate the shell. If the shell is abnormal, then a problem with the hen should be suspected. Small or large cracks in the egg or small toenail punctures suggest rough handling by nervous or inexperienced parents. The egg should then be placed upright so that its widest end is up. The top of the egg should be cleaned and disinfected. A circular incision is made around the top of the egg with a sterile instrument, and the top is removed. This will expose the air cell. The underlying shell membrane can be cut with a sterile instrument and a culture taken through this opening. If bacteria are growing in the egg, the contents of the egg are typically fetid, and if the infection occurred early in incubation, the contents may be curdlike and/or discolored.

Approximately 30% of embryonic deaths occur during the first third of incubation. Causes of deaths during this period include incubators that are too hot or have excessive vibration and rough handling of the egg. A study comparing the relatedness of macaw parents found that infertility and early embryonic death are more likely if macaws are closely related. Bacterial infections of the egg can also cause early embryonic mortality.

Mortality during the second third of incubation is less common. Bacterial infections and incubator problems are the most likely cause of fetal death during this period. The most common incubator problems that affect embryos at this stage are improper turning techniques that include rocking rather than turning (parrots) and excessive turning.

Another 30% of fetal deaths occur within 1 or 2 days of hatching. Mortality during the last third of incubation can still be of bacterial origin but is most often the result of an improper incubation technique. For an egg to hatch, it is critical that it loses a specific amount of moisture. The target for many parrot species is approximately 15% weight loss over the entire incubation period. Either excessive moisture loss or insufficient moisture loss will result in a weak chick that may not hatch. One of

the main causes of late-term fetal death is failure to establish pulmonary respiration. If the incubator temperature is either too cold or too hot, weak and either dry or edematous chicks may be found. Weak chicks cannot penetrate the air cell with their beaks. Finally, airflow in the incubator is a critical factor. Insufficient airflow impacts chick development and moisture loss from the egg.

If the egg is near hatching, the position of the embryo should be examined carefully before it is removed from the egg. In the 2 or 3 days prior to hatching, the shell membrane contracts around the chick, making the air cell larger. At 1–2 days before hatching, the chick tears through the shell membrane, its head enters the air cell, and it begins to breathe air. Just prior to hatching, the chick should be positioned so that its tail is against the narrow end of the egg, the shoulders are against the air cell, and the head is tucked under the right wing. Seven abnormal positions are described. In position 1, the head is between the thighs. These chicks cannot hatch. In position 2, the head is at the small end of the egg. Some of these birds will pip, but others suffocate. In position 3, the head is to the left. This is a lethal position. In position 4, the body is rotated along the long axis of the egg, resulting in the beak not being near the air cell, and hatching is not possible. In position 5, the feet are over the head, and these birds usually fail to hatch. In position 6, the head is over the right wing. These chicks usually hatch. In position 7, the embryo is lying across the egg and cannot hatch. This position occurs if the egg is spherical and the embryo is small. With the exception of malformed eggs, an increase in the number of malpositioned chicks is often the result of improper turning techniques or possibly incubators with excess vibration.

Techniques of fetal necropsy vary. Small embryos and fetuses (finches) can be grossly examined, fixed, and processed for whole body sections. Larger chicks should be necropsied just as any posthatch bird. The yolk sac and other fetal and shell membranes should be examined histologically.

Gross and histologic lesions in chicks that are near hatching will be somewhat similar to those of posthatch chicks. Some things, however, are unique to developing chicks. Excessive humidity in the incubator can lead to a severely edematous fetus (Fig. 6.46). Inadequate humidity will have the opposite effect, and the fetus may be severely dehydrated (Fig. 6.47). Edema and dehydration are not, however, consistently this obvious.

Cockatiel and macaw late-term fetuses have a higher incidence of soft tissue, particularly renal, mineralization. This lesion may be the result of excessive vitamin D_3 in the diet of the hen, nutritional problems of the hen, or possibly improper incubation environments. The latter can lead to excessive loss of calcium from the shell and deposition of the calcium in the fetal soft tissues, particularly the kidney.

The yolk sac and chorioallantois mediate mobilization and transepithelial transport of mineral deposits from the egg. Mineral transport involves plasma proteins that bind minerals and are initially synthesized by the yolk sac and later by the liver. This change can be seen in developing fetuses and may appear grossly as white gritty foci in the kidneys. Typically there is variable tubular mineralization and no reaction histologically (Fig. 6.48). The underlying pathogenesis of the lesion cannot be determined based solely on its morphology.

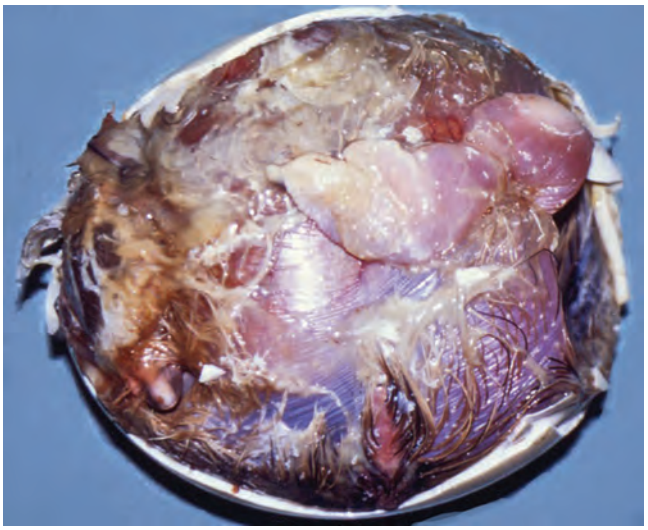

Figure 6.46 Severe fetal edema secondary to excessive humidity in the incubator.

Since fetal death is often associated with stress, examination of the bursa of Fabricius is very important in the fetal necropsy. Although not an etiology-specific lesion, the finding of severe bursal lymphoid depletion/necrosis or hypoplasia is indicative of stress to the developing chick.

Omphalitis and yolk sac problems

The yolk sac and umbilical tissues could be discussed with several systems, but will be covered in this chapter. Bacterial infections, often associated with poor husbandry/cleanliness, are the most common cause of lesions of the umbilical area, the umbilical stalk, and the yolk sac. Grossly the skin of the umbilical area may be swollen, reddened, and edematous (Fig. 6.49), and depending on the severity hemorrhage and necrosis may be present. If severe, the umbilical area may not be completely

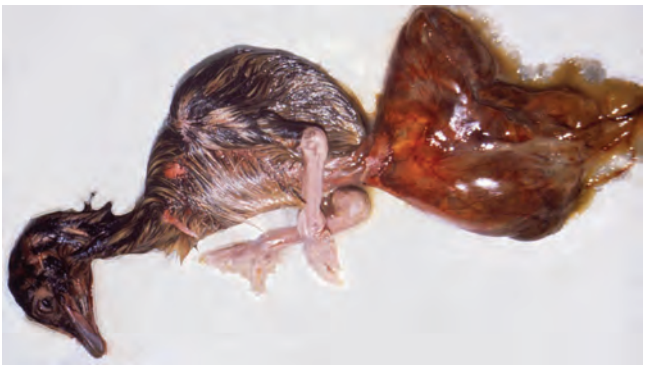

Figure 6.47 Fetal dehydration due to inadequate incubator humidity.

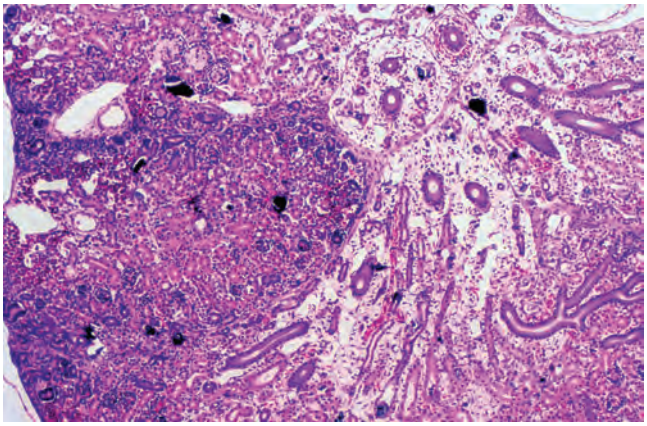

Figure 6.48 Fetal renal mineralization as a result of an improper incubation environment. If severe, this can lead to fetal death.

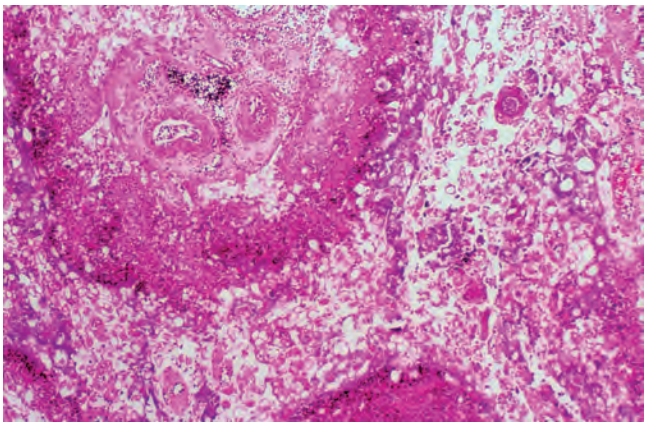

Figure 6.51 Necrosis, hemorrhage, inflammation, and bacterial growth typical of bacterial omphalitis.

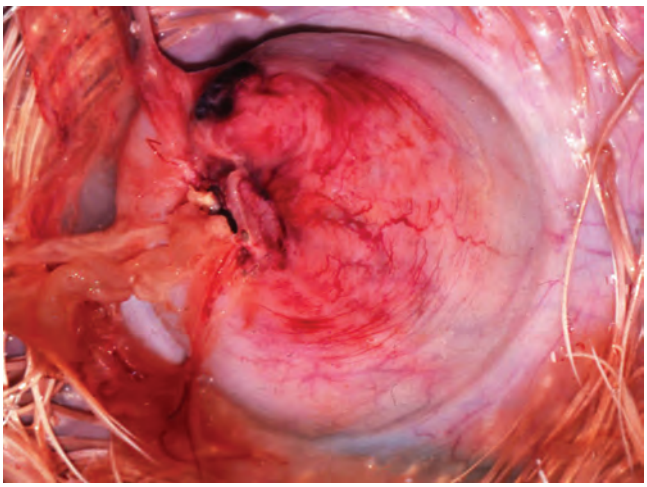

Figure 6.49 Inflamed umbilical skin associated with a bacterial infection.

closed due to problems with yolk sac involution. In chickens there may be involvement of a large area of the body wall which can be discolored and edematous. These chicks are often referred to as "mushy chicks." Virulent strains of *Escherichia coli* are a common cause. The morphologic changes can involve the entire stalk, and the yolk sac will often be darkly pigmented red to green (Fig. 6.50).

Microscopically there is necrosis of yolk sac membranes and yolk protein globules, heterophils and macrophages, and numerous bacteria are usually present (Fig. 6.51).

Infection/inflammation of the yolk sac must be differentiated from yolk sac retention. This condition is often due to problems with the environment, particularly in incubator-raised birds. Although there is no infection and grossly the yolk sac has normal color (Fig. 6.52), affected chicks usually do not thrive. If there was low humidity during incubation, the yolk sac may

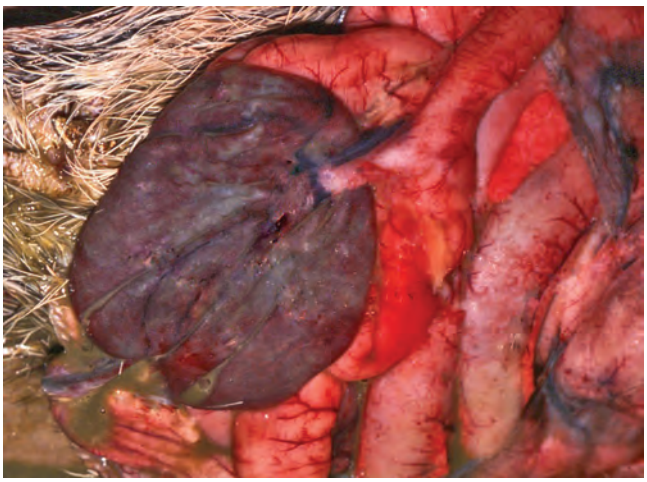

Figure 6.50 Discolored and necrotic yolk sac due to bacterial omphalitis.

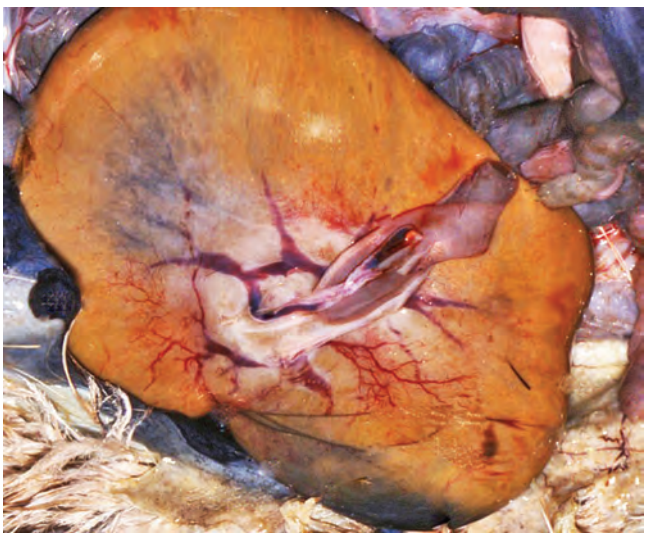

Figure 6.52 Retained yolk sac. There is no infection and the color is essentially normal. Compare with Figure 6.50.

adhere to the body wall and can be ruptured during hatching or with handling.

Additional reading

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7 Endocrine System

Pituitary gland

Normal structure

The pituitary gland is located in the sella turcica beneath the diencephalon and the optic chiasma. The pituitary is divided into the adenohypophysis and the neurohypophysis. The adenohypophysis consists of a pars tuberalis and a pars distalis, in contrast to mammals; birds do not have a pars intermedia. The pars tuberalis is further divided into cephalic and caudal zones. The acidophils of the cephalic zone stain lightly, while the acidophils of the caudal zone are more intensely eosinophilic. The pars tuberalis contains secretory cells that are arranged in cords. Capillaries and vascular sinuses separate the cords. The neurohypophysis (pars nervosa) is a direct extension of the hypothalamus at the base of the brain. Subdivisions of the neurohypophysis are the median eminence, the infundibular stem, and the neural lobe. Each has a three-layer structure of an ependymal layer that is in contact with the diverticulum of the third ventricle, a fiber layer, and a glandular layer.

Inflammatory disease

Infections of the oral cavity can become severe and extend to involve the pituitary. Grossly these lesions are yellow-white and often have the appearance of an abscess. Histologically there is necrosis of the pituitary gland and the surrounding bone, with a pleocellular inflammatory infiltrate whose composition may be affected by the particular etiologic agent. Bacteria, fungi, and protozoa such as *Trichomonas* sp. have been implicated and may be seen in the lesion.

The neurohypophysis may be affected by encephalitis involving the hypothalamus. Bacterial and viral infections are possible and their histologic appearance is similar to the lesion in nervous tissue.

Severe trauma can lead to hemorrhage and secondary inflammation of the pituitary. The gross and histologic appearance may be dominated by the hemorrhage, with necrosis and inflammation being more prominent if the bird survives the traumatic incident.

Neoplasms

Adenomas and carcinomas have been reported, particularly frequently in budgerigars. These tumors are usually soft, pink to red-brown, and may be extended outside of the sella tursica if large (Figs. 7.1 and 7.2). They may compress the optic chiasma and the bird may have a history of blindness. There can be associated bone lysis. Adenomas grow by expansion and there can be compression of adjacent brain. Adenomas are circumscribed while the margins of carcinomas are less well differentiated.

Histologically adenomas comprise large epithelial cells that are usually devoid of granules. These cells form nests and lobules with minimal stroma (Figs. 7.3 and 7.4). The individual cells may have variably indistinct margins and variable amounts of a pale eosinophilic cytoplasm. The cell nuclei are vesicular, oval, with variably prominent nucleoli. Bizarre and giant cell nuclei may be present. Rare tumors have been linked with functionality. Tumors immunoreactive for adrenocorticotropic hormone (ACTH) were associated with bilateral hyperplasia of the adrenal gland. The adrenal gland was composed of approximately 85% interrenal cells with abundant foamy eosinophilic cytoplasm and 15% of the chromaffin cells.

Budgerigars commonly develop chromophobic pituitary adenomas and less frequently carcinomas that will metastasize (kidney, liver, midbrain, and air sacs). These are generally young to middle-aged birds that present with neurologic clinical signs including inability to fly, ataxia, and blindness, as well as abnormal feathering and exophthalmos. Most adenomas extend beyond the gland into the brain, skull, and retrobulbar space. The tumors are strongly immunoreactive for growth hormone.

Cells making up carcinomas are more anaplastic and there may be mitotic figures seen. Tumor lobules and cords are infiltrative into surrounding tissue. Metastasis is rarely reported.

Thyroid gland

Normal structure

The thyroid glands are paired round to slightly oblong. They are found immediately lateral to the carotid arteries within the

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

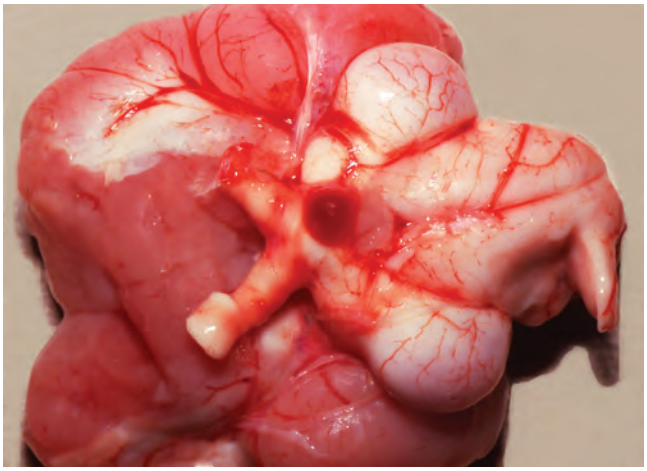

Figure 7.1 Pituitary gland adenoma. This tumor is most commonly seen in budgerigars.

thoracic inlet. They are red-brown, similar to the syringeal muscle, and the latter is sometimes thought to be thyroid gland by prosectors with minimal avian experience. Anatomically, they are very similar to the thyroids of other animals being composed of closely packed spherical follicles. A flattened single layer of epithelial cells lines the follicles in the adult bird. The epithelial cells, in young growing bird, are cuboidal and the follicles contain less colloid. Calcitonin-secreting cells are not present in avian thyroids except in doves and pigeons where they are within the follicular epithelium. In other birds they are in the ultimobranchial glands.

Congenital lesions

Partial persistence of the caudal portion of the thyroglossal duct can lead to cyst formation within or adjacent to the thyroid gland. These cysts are lined by epithelium similar to that of thyroid follicles.

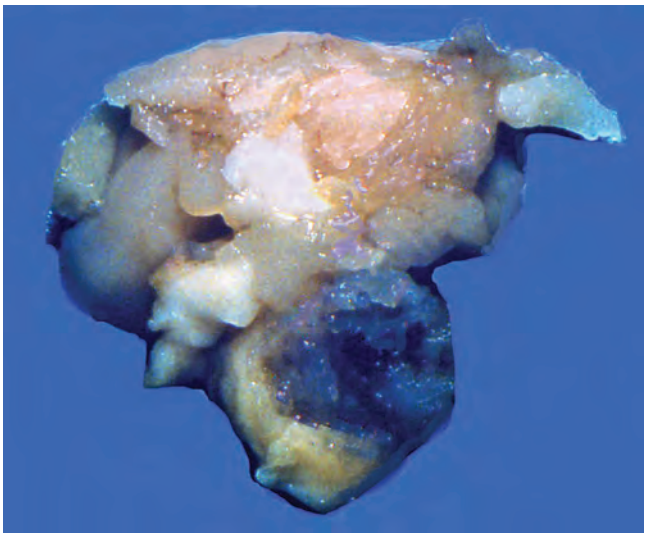

Figure 7.2 Pituitary adenoma that was compressing the adjacent brain. The tumor is necrotic and hemorrhagic.

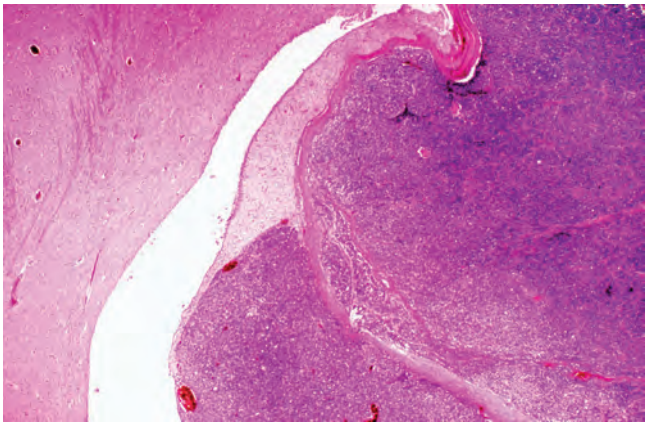

Figure 7.3 Pituitary adenoma growing by expansion and compressing the brain.

Inflammatory disease

Lymphocytic thyroiditis similar to autoimmune disease of humans and dogs has been seen in certain strains of chickens, and a morphologically similar lesion is seen sporadically in young African gray parrots. Affected glands are small, pale, and may be slightly irregular. Histologically there is a variable follicle degeneration and connective tissue proliferation associated with lymphoid cell infiltration and lymphoid follicle formation (Figs. 7.5 and 7.6). In chickens CD4+ and CD8+ T cells may be involved as treatment with murine monoclonal anti-CD4 leads to inhibition of the disease and anti-CD8 antibody leads to partial inhibition.

Disseminated mycobacteriosis may involve the thyroid. Grossly the glands are enlarged, yellow-white, and irregular. Histologically there is necrosis associated with an infiltrate of large histiocytes with blue-gray cytoplasm that contain acid-fast bacteria.

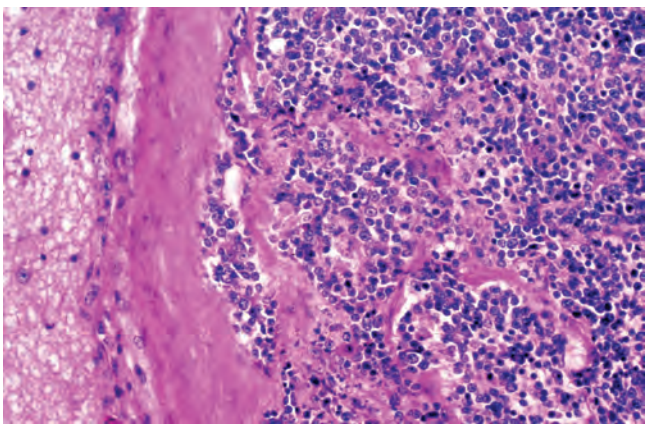

Figure 7.4 Pituitary adenoma. Note the nests of neoplastic cells separated by fine stroma.

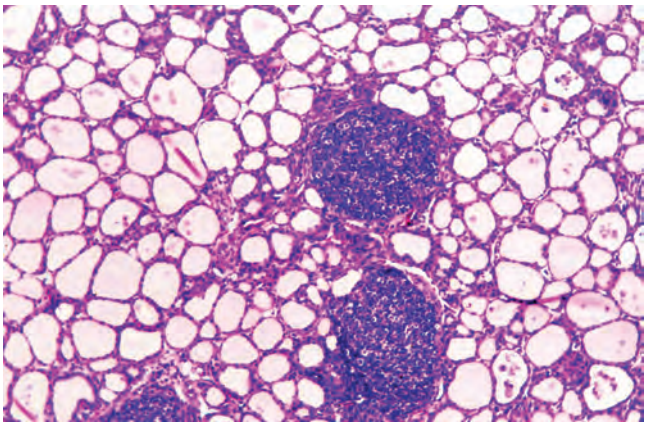

Figure 7.5 Multiple lymphoid follicles in the thyroid gland of an African gray parrot with thyroiditis histologically similar to autoimmune thyroid disease seen in other species.

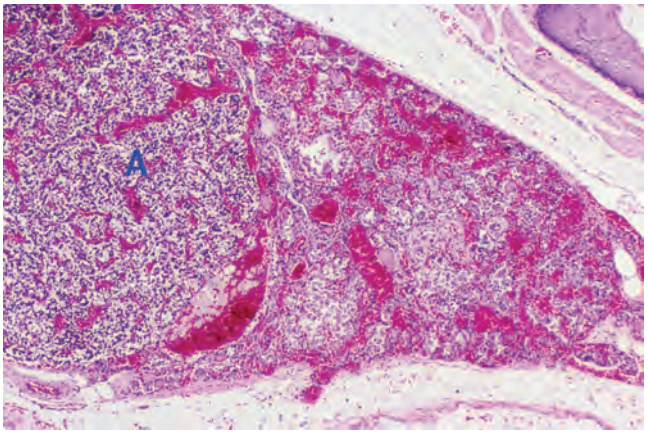

Figure 7.7 Thyroid degeneration, hemorrhage, and atrophy. Note the adjacent, histologically normal parathyroid gland (A).

Inflammation of the soft tissue of the neck secondary to trauma or infection that has spread may involve the thyroid glands. The specific changes depend on the underlying cause.

Noninflammatory disease

Apparent degenerative lesions are sporadically seen, particularly in budgerigars and cockatiels. Some older literature refers to the condition as dystrophy. Affected glands may be both slightly enlarged, pale and irregular, or occasionally slightly small. Foci of red-brown mottling may be seen.

Histologically variable follicular collapse and colloid loss characterize these glands. A few follicles may be cystic. Remaining colloid is usually granular and often discolored. Hemorrhage may be seen in follicles and interstitium (Fig. 7.7).

Experimentally, organotin compounds cause atrophy of the thyroid gland of chickens. Organotin compounds can be found in disinfectants, pesticides, and antihelmintics. Whether exposure to these compounds occurs in pet birds is not known, and if they cause some of the degenerative thyroid lesions described remains speculative. Atrophic glands, from whatever cause, will be small, flat, and dark red-purple, and associated parathyroid glands will appear enlarged (Fig. 7.8).

Amyloid deposition is occasionally seen in the interstitium of the thyroid and is just one manifestation of generalized amyloidosis.

Proliferative disease

Thyroid hyperplasia (goiter) has been most commonly reported in budgerigars, but occurs in a wide variety of pet and nonpet birds. Goiter in the budgerigar is common in parts of the world where the grain they are fed is grown on iodine-deficient soils. The soils of the midwestern United States are iodine deficient and budgerigars in the eastern and midwestern United States are at high risk for goiter. Goiters in budgerigars are readily preventable by supplying trace amounts of iodine in the diet or drinking water.

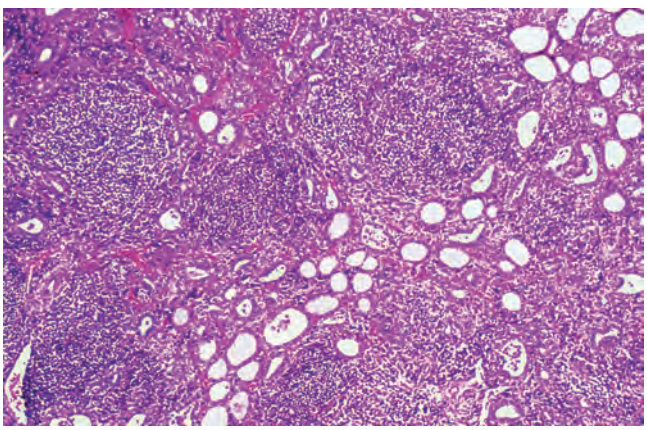

Figure 7.6 Severe lymphocytic thyroiditis and effacement of normal thyroid parenchyma.

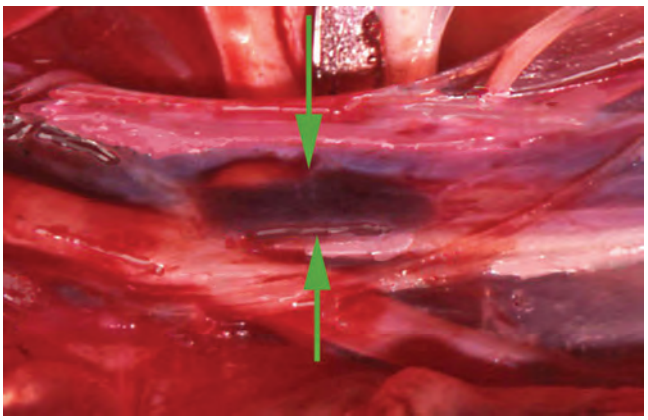

Figure 7.8 Atrophied thyroid gland that is difficult to delineate except for the dark coloration that is due to lipofuscin pigment deposition in the gland.

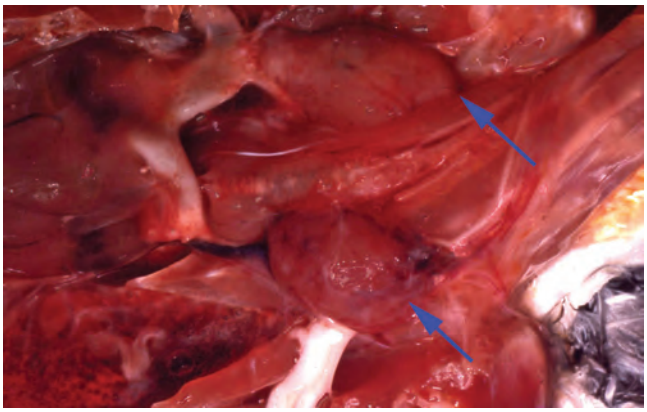

Figure 7.9 Enlarged thyroid glands typical of hyperplastic goiter (arrows). The enlargement is bilateral.

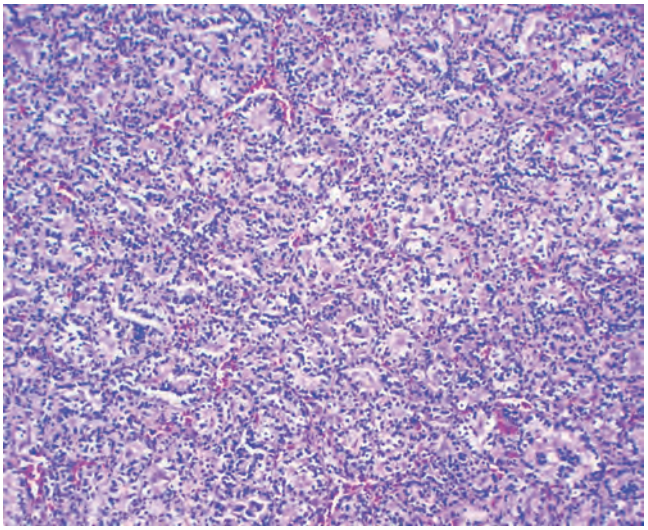

Figure 7.10 Thyroid hyperplasia. Follicles contain enlarged epithelial cells and minimal amounts of residual colloid.

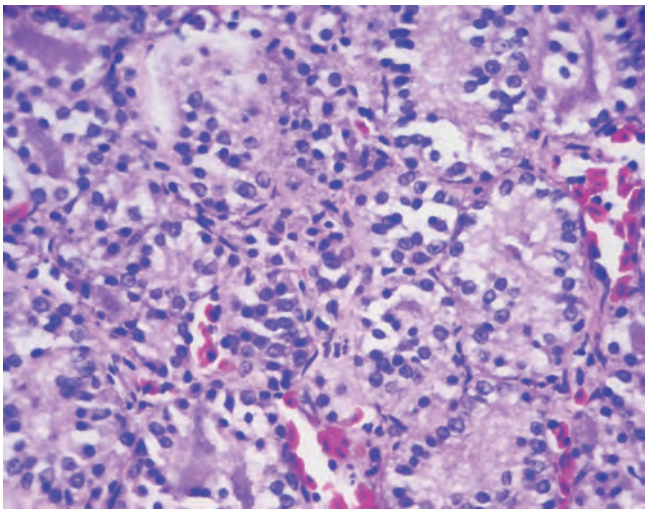

Figure 7.11 Detail of hyperplastic thyroid follicles.

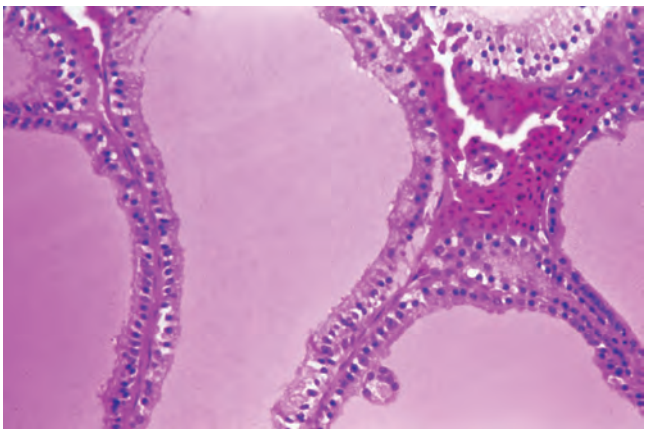

Figure 7.12 Early colloid goiter. Cuboidal or columnar cells line enlarged follicles.

The highest incidence in pet birds seen in our practice is in blue and gold macaws. The underlying cause of the condition has not been conclusively determined. Iodine deficiency or excess or ingestion of plant material containing goitrogenic substances are possible causes. Experimentally in Japanese quail it has been shown that hens deposit thyroid hormones into eggs in proportion to their own thyroid status, and if deficient, the chicks may also be deficient.

Congenital hyperplasia with a possible genetic link may also be possible. This genetic defect could result in loss of enzymes responsible for biosynthesis of thyroid hormone and a resulting decrease in T4 and T3, which stimulates production of thyrotropic hormone [TTH] and hyperplasia of follicular epithelial cells.

Thyroid hyperplasia is bilateral resulting in enlarged, red-brown, or purple glands that put pressure on the trachea, esophagus, and other soft tissues of the neck and collapse the interclavicular air sac. Hyperplastic glands have a smooth surface (Fig. 7.9). Histologically affected glands comprise numerous follicles lined by enlarged epithelial cells. There is no colloid and often no apparent follicular lumen (Figs. 7.10 and 7.11).

Colloid goiter is considered the involutionary phase of thyroid hyperplasia. Colloid is produced but endocytosis is decreased after T4 and T3 return to normal and TTH concentration is reduced. Affected glands are enlarged and red-brown and have a translucent or glassy appearance on section. Histologically the gland comprises large follicles containing colloid and lined by epithelial cells that may be cuboidal or columnar initially, but eventually become flattened atrophic cells having a smooth interface with the colloid (Figs. 7.12 and 7.13).

Thyroid gland neoplasia presents as a unilateral swelling of the affected gland. The highest incidence of thyroid neoplasia occurs in budgerigars and cockatiels, with thyroid adenomas the most common. In one study of pigeon neoplasms, 6% were adenomas. Thyroid adenomas are usually smooth, red-purple and may displace associated soft tissue (Fig. 7.14). Aspiration cytology is generally unrewarding and is usually a serosanguineous

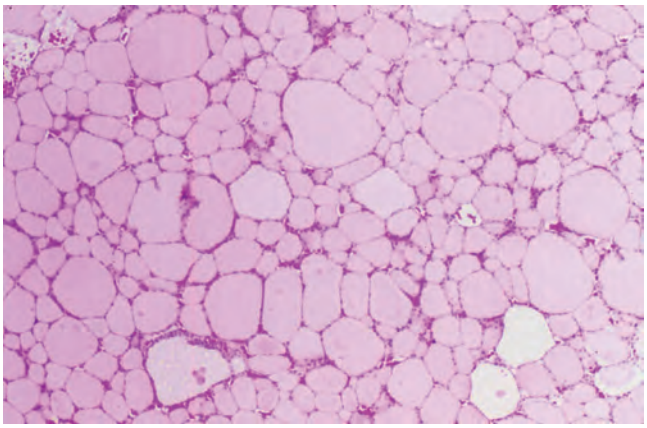

Figure 7.13 Diffuse colloid goiter with follicles lined by flattened atrophic epithelial cells.

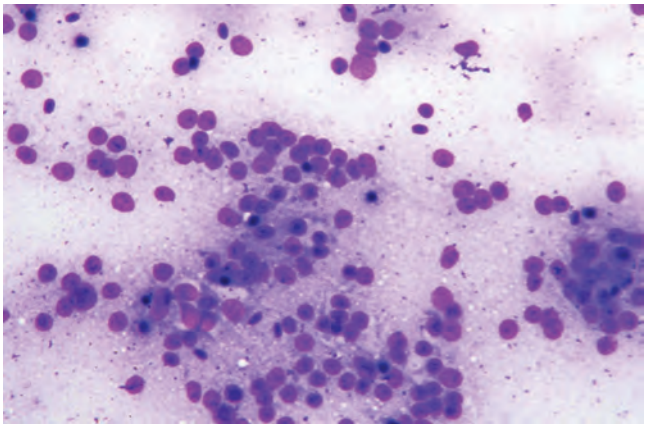

Figure 7.15 Cytology of a papillary adenoma of the thyroid gland. Cytoplasmic boundaries are indistinct, but nuclei are arranged in structures suggestive of follicles or acini.

fluid supporting primarily red blood cells. Impression cytology may indicate a follicular pattern (Fig. 7.15). Histologically several forms are noted. Follicles may be variably enlarged and lined by cuboidal or low columnar cells. Colloid is usually minimal or absent. In some cases cystic follicles with papillary projections are seen (Figs. 7.16 and 7.17). Some adenomas are primarily papillary with numerous papillae seen in dilated follicular structures. Carcinomas lead to distortion and enlargement of the thyroid gland. The mass may be firm and gray-white with indeterminate boundaries (Fig. 7.18). Histologically carcinomas comprise poorly differentiated cells that form irregular nests and trabeculae and infiltrate the capsule and surrounding tissue (Fig. 7.19). Papillary and cystic structures may be present in some tumors.

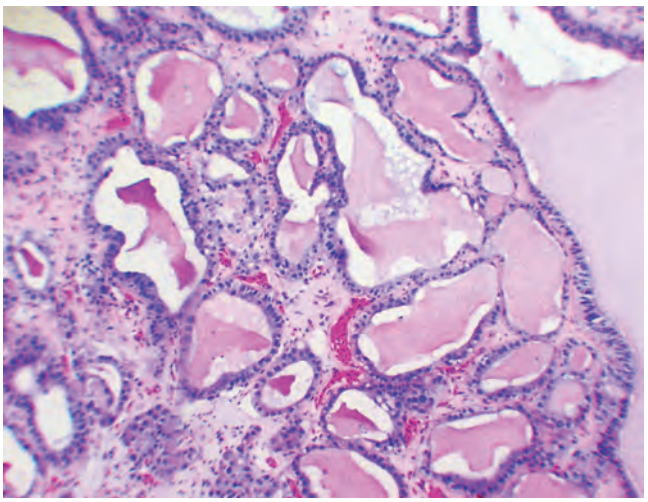

Figure 7.16 Thyroid adenoma with proliferative epithelium and irregular follicle formation.

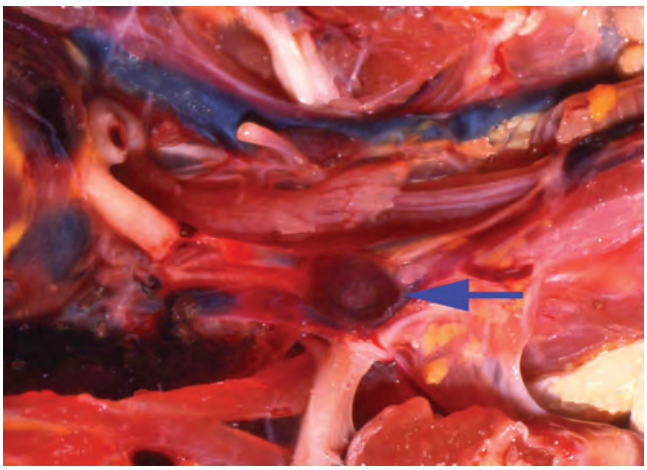

Figure 7.14 Thyroid gland adenoma (arrow). These tumors are usually unilateral, which is the only differentiation from hyperplasia grossly. The later is usually bilateral.

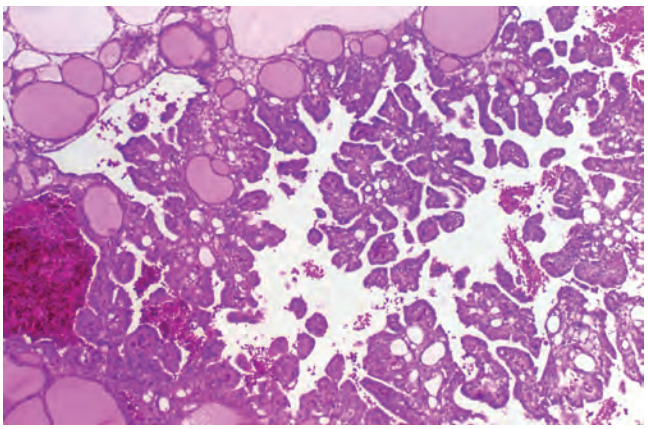

Figure 7.17 Cystic follicles adjacent to an area of cystadenoma formation in thyroid gland.

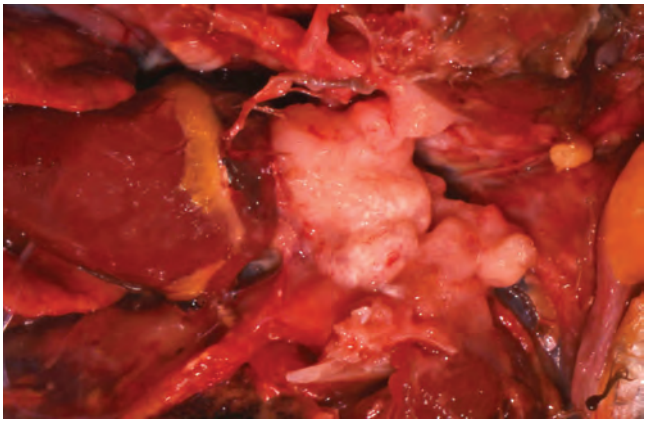

Figure 7.18 Large, irregular mass representative of a thyroid gland carcinoma. Essentially all normal architecture is lost.

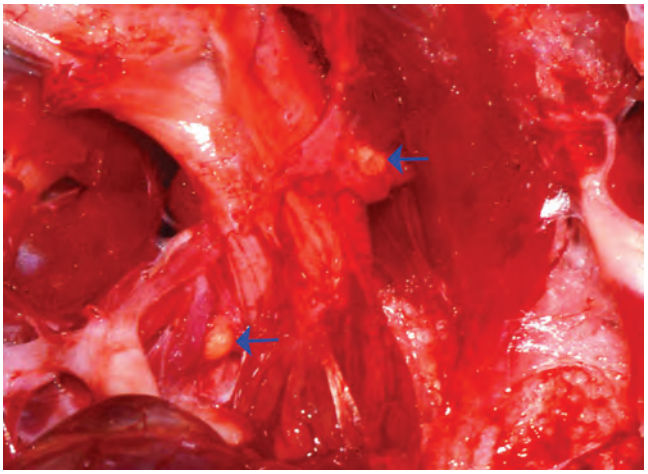

Figure 7.20 Marked bilateral enlargement of severely hypertrophied parathyroid glands (arrows).

Parathyroid glands

Normal structure

The avian parathyroid glands are paired structures that lie immediately caudal to the thyroid gland and immediately lateral to the carotid artery. They are ivory colored, round, and smooth. The parathyroids are often so small that they cannot be seen grossly if the bird is eating a diet with sufficient calcium. The parathyroids of birds that are in a negative calcium diet may reach 2–3 mm in diameter. Histologically, chief cells are in cords that in cross section appear as clusters of cells each surrounded by a thin layer of connective tissue. The chief cells in birds that are eating a diet that is sufficient in calcium are small round cells that are closely packed together. They have scant cytoplasm and a dense nucleus.

Proliferative disease

Hypertrophy and hyperplasia of the parathyroid may be obvious grossly (Fig. 7.20), but can be difficult to detect if minimal. The enlarged parathyroid is gray-white to yellow and the condition is bilateral. Affected birds may also have grossly observable bone problems (Chapter 9). Histologically chief cells are variably enlarged with granular cytoplasm that will become foamy to clear in severe cases. The chromatin of the chief cells becomes less condensed and the nucleus enlarges. The cells form trabecular structures and the entire gland is involved (Figs. 7.21 and 7.22).

Parathyroid adenomas can be unilateral or occasionally bilateral. Grossly they cannot be differentiated from severe hyperplasia in most birds. The histologic appearance of adenoma is similar to severe hyperplasia, but there will be compression of adjacent normal tissue and some indication of capsule formation.

We have not seen any example of parathyroid carcinoma.

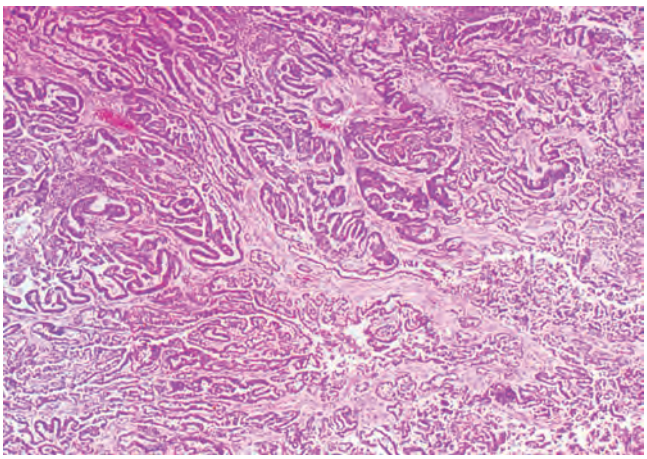

Figure 7.19 Irregular infiltrative structures in a carcinoma of the thyroid gland. Moderate amounts of stroma are also seen.

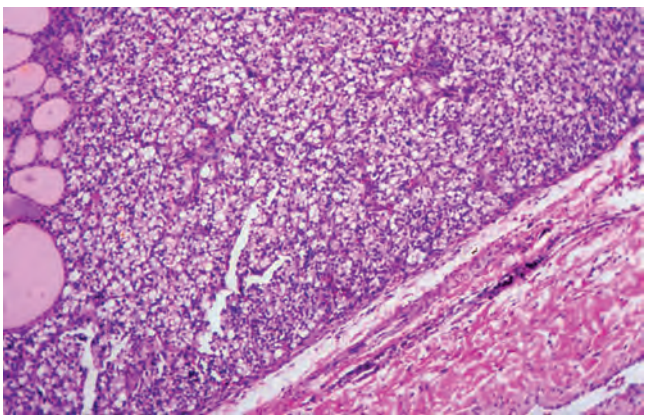

Figure 7.21 Parathyroid hypertrophy/hyperplasia. Affected cells have large amounts of clear cytoplasm.

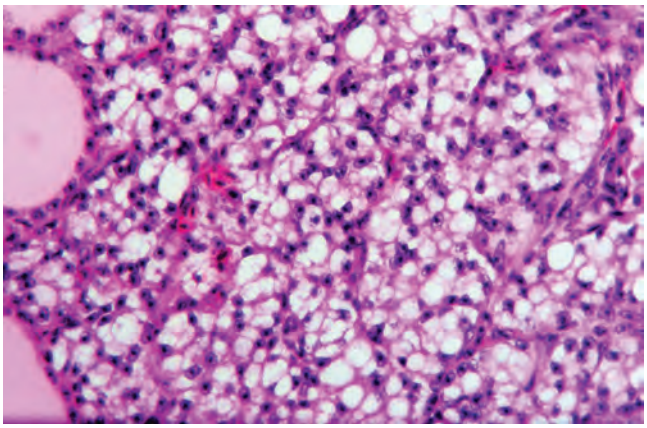

Figure 7.22 Detail of hypertrophied parathyroid gland cells.

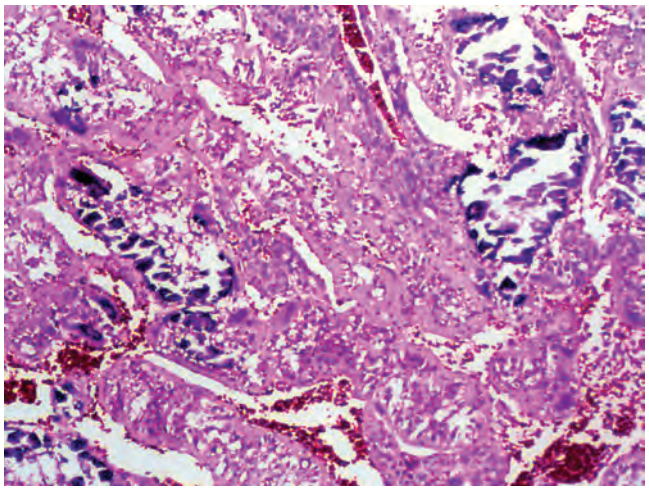

Figure 7.23 Severe mineralization and degeneration of the adrenal gland.

Adrenal glands

Normal structure

The avian adrenal glands are paired in most species, but in a few birds they may be fused. Jackdaws have several small accessory glands embedded in the epididymis. They are pink to orange, flattened, and lie at the medial and cranial aspect of the ventral surface of the cranial division of each kidney. Birds, unlike mammals, do not have a defined cortex and medulla to their adrenal glands. Instead, cords or islands of mesodermal-derived (interrenal or cortical) cells and neuroectodermal-derived (chromaffin or medullary) cells are intermixed within the adrenal gland.

Interrenal cells are rounded to polygonal, have substantial eosinophilic cytoplasm, and a small, dense, centrally located nucleus. These cells contain carotenoids, which impart the yellow color seen grossly. Chromaffin cells are of similar size and shape but have a densely basophilic and nearly granular cytoplasm.

Noninflammatory and inflammatory diseases

Generalized disease processes may involve any portion of the gland. Scattered foci of mineralization, which are usually only seen histologically, are sometimes found in the adrenal (Fig. 7.23). Amyloidosis occurs sporadically and when severe the affected gland may be enlarged and have a uniform pale appearance. Histologically amyloid is deposited primarily in interstitium near the basement membrane of medullary and cortical cords, which are thickened by a diffuse amphophilic or slightly eosinophilic material. There is a variable loss of both interrenal and chromaffin cells (Fig. 7.24).

Generalized inflammatory disease is usually the result of hematogenous extensions of systemic bacterial infections, or extension from bacterial or fungal peritoneal or air sac infections. The exact character of the lesion depends on the etiologic agent. Grossly, in bacterial and fungal disease of the adrenal, there may be hemorrhage and mottling with necrotic foci and exudate seen in severe cases. Histologically there is necrosis and an infiltrate of heterophils, macrophages, and variable numbers of lymphocytes and plasma cells. Finding the organism is often the only way to differentiate the type of infectious process. In chronic infections there can be giant cells.

Systemic mycobacteriosis may involve the adrenal glands. Grossly there is often no obvious change and the histologic lesion comprises infiltrating large macrophages with abundant lightly basophilic cytoplasm. These cells can be mistaken for normal chromaffin cells if not carefully evaluated. Aggregates of lymphocytes may be associated with the macrophages (Fig. 7.25).

A few lesions specific to the interrenal cells can be seen. Vacuolation of interrenal cells associated with no other lesion is seen in birds that die suddenly, particularly African gray parrots. The cause of the condition is not known. This lesion can be severe and may indicate that the bird was in adrenal failure, but as of yet antemortem tests that might confirm the possibility

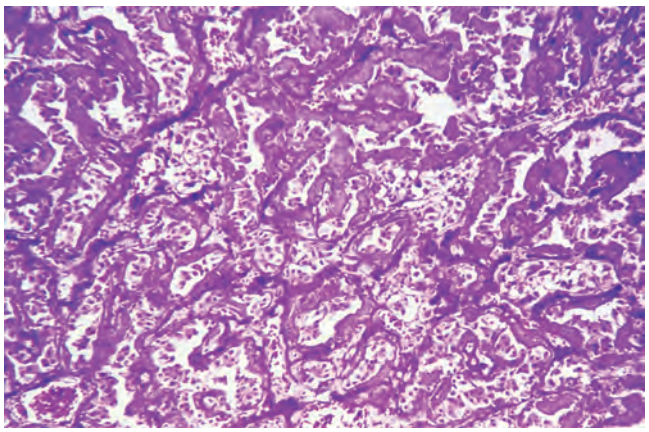

Figure 7.24 Generalized amyloidosis of the adrenal gland. Affected basement membranes are thickened by amorphous, darkly eosinophilic amyloid.

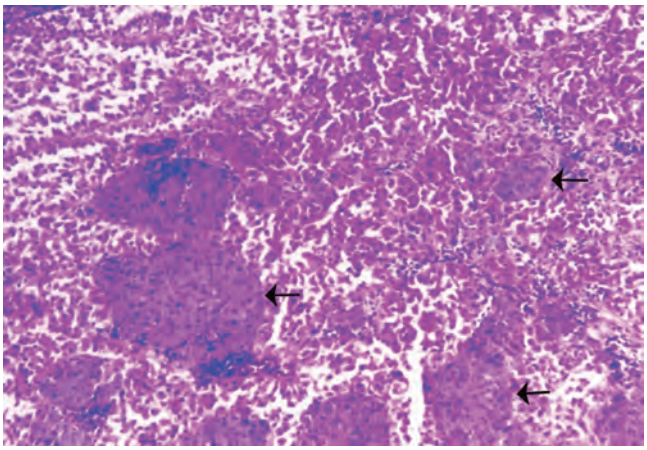

Figure 7.25 Mycobacterial infection of the adrenal gland. Numerous macrophages containing granular material are seen (arrows). This material represents acid-fast bacteria. There is degeneration of remaining gland cells.

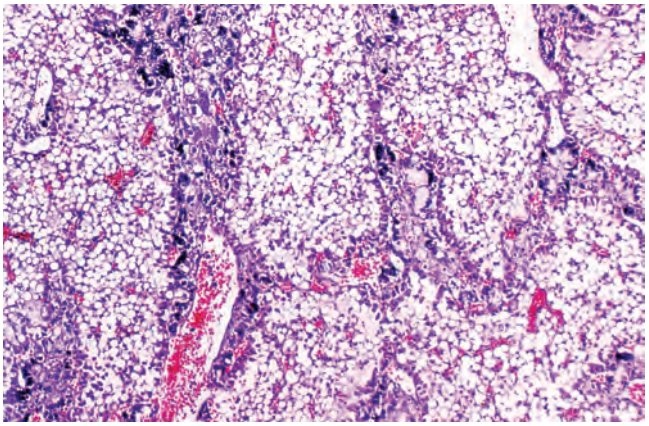

Figure 7.27 Severe swelling and vacuolation of interrenal cells that is typical of idiopathic adrenal degeneration.

have not been done. Grossly the gland may be yellow-brown and slightly mottled (Fig. 7.26). Histologically there is diffuse swelling and vacuolation of the interrenal cells (Fig. 7.27) With severe swelling and attempted compensatory hypertrophy of interrenal cells, nodular foci may be seen grossly. Fig. 7.28.

Several viral diseases affect the chromaffin cells. Polyomavirus inclusions may be seen in karyomegalic nuclei. The inclusions are amphophilic to clear and marginate the chromatin (Fig. 7.29). A novel APV (tentatively designated finch polyomavirus) has been sequenced from the adrenal gland of a European Goldfinch (*Carduelis carduelis*). Paramyxovirus inclusions have been noted in chromaffin cell cytoplasm. Both intracytoplasmic (Fig. 7.30) and intranuclear (Fig. 7.31) inclusions are possible.

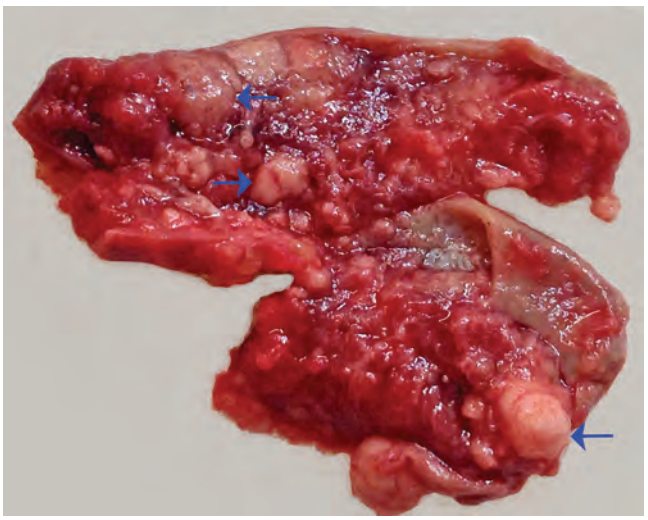

Figure 7.28 Multiple adrenal gland nodules (arrows) due to interrenal cell swelling and vacuolation. This change is often secondary to chronic stress.

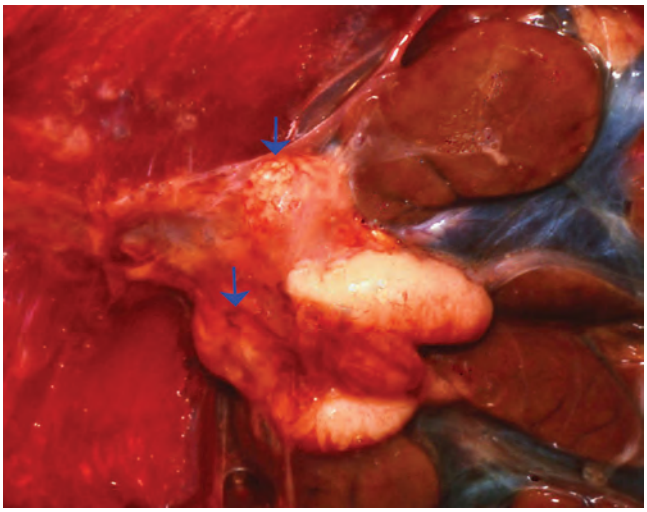

Figure 7.26 Degeneration of the adrenal glands. The glands are small and mottled (arrows).

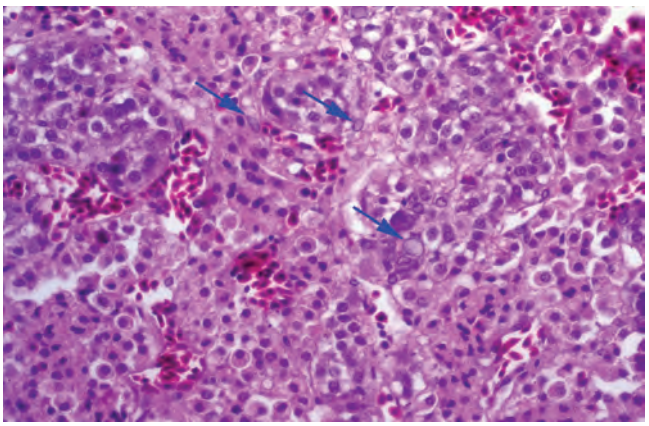

Figure 7.29 Large, clear, or minimally basophilic intranuclear inclusion bodies (arrows) in the adrenal gland of a bird with polyomavirus infection.

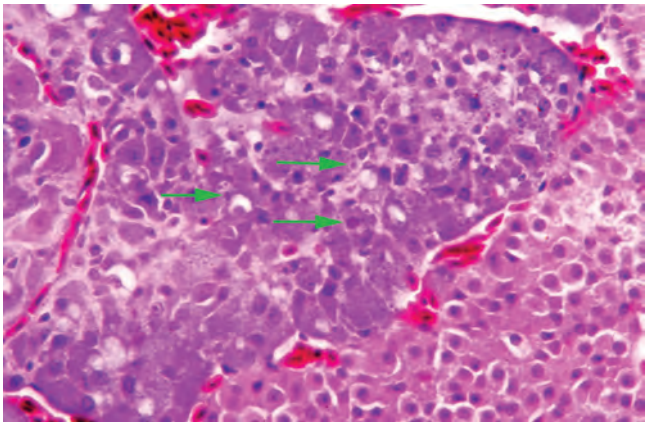

Figure 7.30 Necrosis of chromaffin cells and intracytoplasmic inclusion bodies (arrow) in the adrenal gland of a bird with paramyxovirus infection.

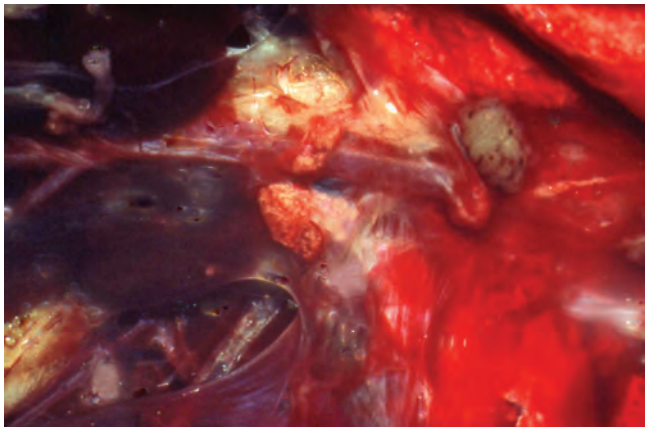

Figure 7.32 Bornavirus (proventricular dilatation disease) infection of the adrenal glands. The glands are slightly enlarged and mottled.

Birds with proventricular dilatation disease (PDD) may have adrenal gland involvement. Bornavirus is the causative agent for PDD and multiple genotypes have been identified. This virus is neurotrophic, infecting the central, peripheral, and autonomic nervous systems. The affected glands are slightly enlarged and may have mild red-gray mottling (Fig. 7.32). Microscopically there is a variable infiltrate of lymphocytes and plasma cells within the chromaffin portions of the gland (Fig. 7.33). In some cases the classic lesions of PDD within the digestive tract may be absent and the inflammation may only involve the central nervous system, heart, and adrenal glands.

Proliferative diseases

Hyperplasia as seen in the cortex of mammalian adrenal glands is not documented in birds. Hypertrophy of interrenal cells does occur, associated with vacuolar changes consistent with degeneration and may indicate chronic stress and eventual adrenal exhaustion. In a few severe cases necrosis of interrenal cells is seen.

Adenomas and carcinomas of interrenal cell origin are reported and occur sporadically. Grossly these tumors are lobulated and grey-yellow. Histologically adenomas comprise irregular cords of enlarged pale cells with amphophilic or eosinophilic cytoplasm (Fig. 7.34). Carcinomas contain pleomorphic anaplastic cells with vesicular nuclei and variable amounts of cytoplasm. These cells form poorly defined trabeculae separated by minimal stroma. There is moderate mitotic activity (Fig. 7.35). Stains for neurosecretory granules typical for chromaffin cells (Fontana–Masson and Grimelius) can be used to differentiate cell lines in the adrenal gland. Ultrastructural features of interrenal cells include numerous mitochondria, few lipid droplets, rare dense bodies, and no desmosomes. Occasional metastasis is seen, primarily involving liver or lung. Some tumors may be functional; however, measurements of plasma corticosterone need to be compared with healthy same species.

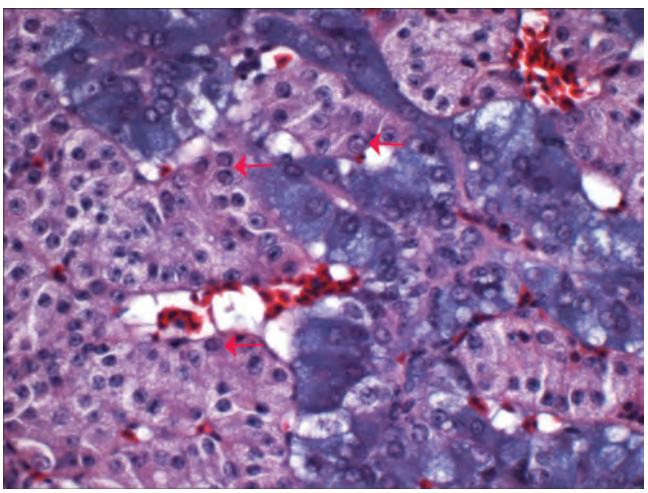

Figure 7.31 Intranuclear inclusion bodies in the adrenal gland of a bird with paramyxovirus infection.

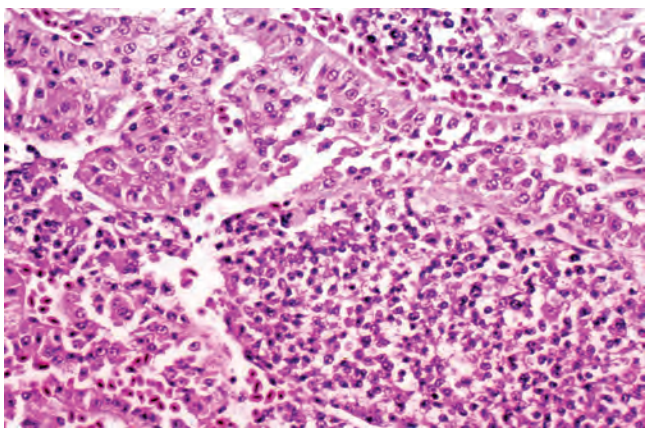

Figure 7.33 Proventricular dilatation disease. Diffuse infiltration of chromaffin portion of the adrenal gland by lymphocytes and plasma cells.

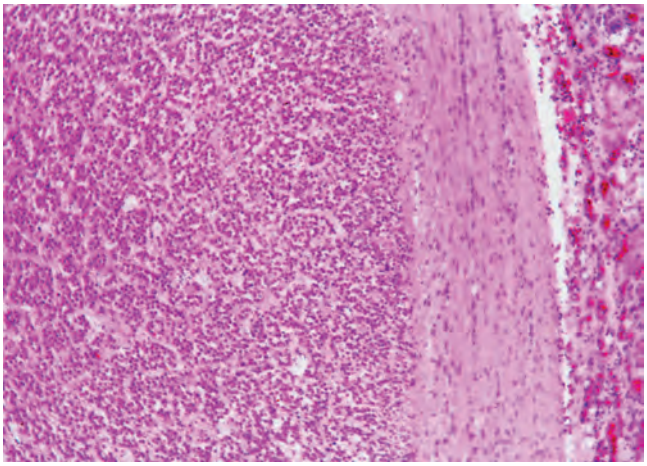

Figure 7.34 Adrenal gland adenoma comprising proliferative interrenal cells forming cords and nests and growing by expansion.

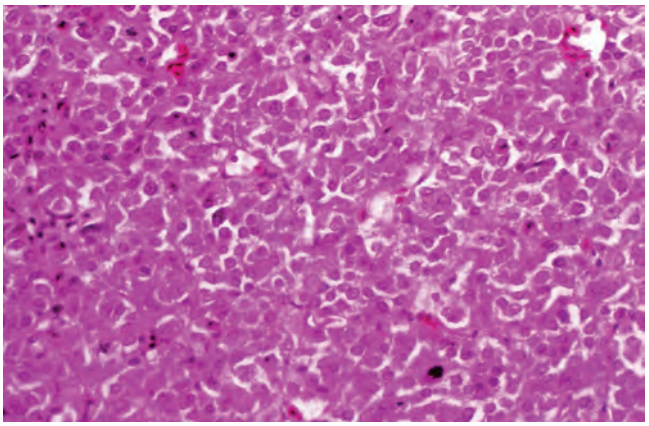

Figure 7.36 Sheet of neoplastic chromaffin cells in pheochromocytoma. Poorly defined trabeculae are seen.

Pheochromocytomas, endocrine tumors arising from the chromaffin cells, are not well documented in birds. Grossly the adrenal gland is enlarged. We have seen one case in a budgerigar in which the tumor was composed of small cells with minimal cytoplasm. Tumor cells formed nests and trabecular structures supported on fine fibrous connective tissue (Fig. 7.36). Another report of a pheochromocytoma in a budgerigar described metastasis to the liver and lung. A benign tumor has been described in a Nicobar pigeon (*Caloenas nicobarica*). A Churukian–Schenk stain, that detects neuroendocrine granules, highlighted numerous minute cytoplasmic granules in the cytoplasm of some of the neoplastic cells as well as in the cytoplasm of chromaffin cells adjacent to and displaced by the neoplasm.

Ganglioneuromas of the adrenal of birds are not distinctive grossly, presenting as a nonspecific enlargement adjacent to the gland or of the gland itself. Histologically they comprise large cells with basophilic cytoplasm resembling neurons. These cells form clumps and sheets, which are embedded in a stroma or ground substance that is lightly eosinophilic or amphophilic and resembles normal neuropil (Fig. 7.37).

Malignant melanoma

Malignant melanomas have been described as arising from the adrenal glands in several bird species, including a merlin, a red-tailed hawk, and a penguin. These neuroectodermal tumors frequently metastasize widely (liver, lung, spleen). Grossly the tumor is a black, rounded, well-demarcated, and firm mass. Histologically the tumor is unencapsulated with dense cellular nests and nodules of pleomorphic cells with variable amounts of cytoplasmic dark brown pigments. These are supported on fine fibrovascular stroma. Mitotic figures can be difficult to identify due to the dense pigmentation. Cellular atypia and prominent nucleoli may be predictors of malignancy.

The adrenal gland can be a site for tumor metastasis such as bile duct carcinomas (cholangiocarcinoma).

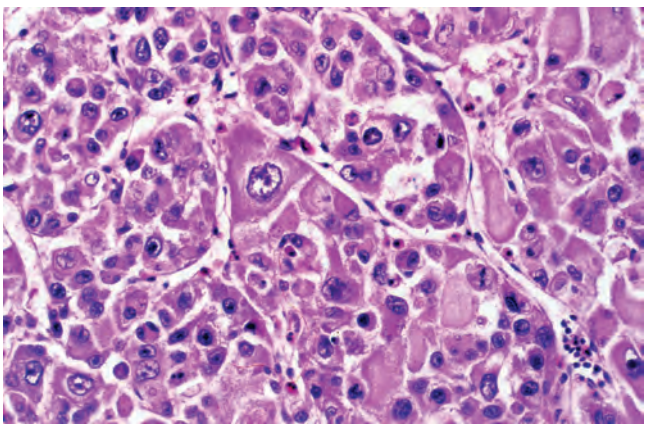

Figure 7.35 Anaplastic, pleomorphic interrenal cells typical of adrenal carcinoma.

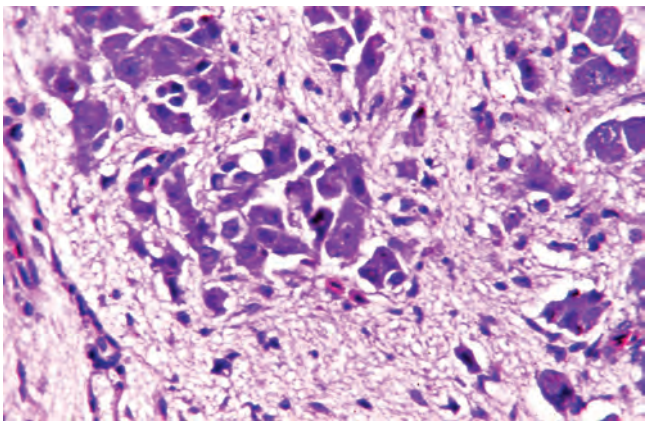

Figure 7.37 Portion of ganglioneuroma with neuropil-like substance and neoplastic cells.

Pancreatic islets

Normal structure

Avian pancreatic islets are of three types: light, comprises A and D cells; dark, comprises B and D cells; and mixed, which contain A, B, and D cells. A cells produce glucagon, B cells produce insulin, and D cells produce somatostatin. Histologically light islets blend with surrounding exocrine pancreas, while dark islets are separated by collagen. Islet distribution is not uniform in all species of birds so multiple sections of the pancreas should be evaluated.

Inflammatory disease

Paramyxovirus infections can cause pancreatitis in several pet avian species (see Chapter 3). The inflammation can be severe enough to involve the pancreatic islets in some cases. Additionally Psittacid herpesvirus-l was isolated from lesions of extensive chronic active pancreatitis in a cockatiel that resulted in hyperglycemia and glucosuria. The intranuclear inclusions were present in pancreatic acinar and ductal cells. Fibrosis isolated clusters of exocrine cells and islets were not identified.

Degenerative disease

Degenerative changes in the pancreatic islets usually lead to diabetes mellitus. This condition is seen in a variety of pet species, supposedly being somewhat more prevalent in toucans, although in our experience most cases are in psittacine birds. These birds have marked polyuria and blood glucose can be over 1000 mg/dl. No gross lesion of the pancreas is typically recognized. Histologically there may be hypoplasia, atrophy, and/or vacuolation of islet cells (Fig. 7.38). Inflammation is rarely reported, however, it is usually lymphoplasmacytic and centered on the islets. In rare cases, immunohistochemical evaluation of pancreatic islets has been negative for the presence of insulin but positive for glucagon. Most studies suggest that avian diabetes mellitus may be due to an excess of glucagon and not a deficiency of insulin, although rare cases have also identified low serum insulin. A common associated lesion is of variable vacuolar hepatopathy.

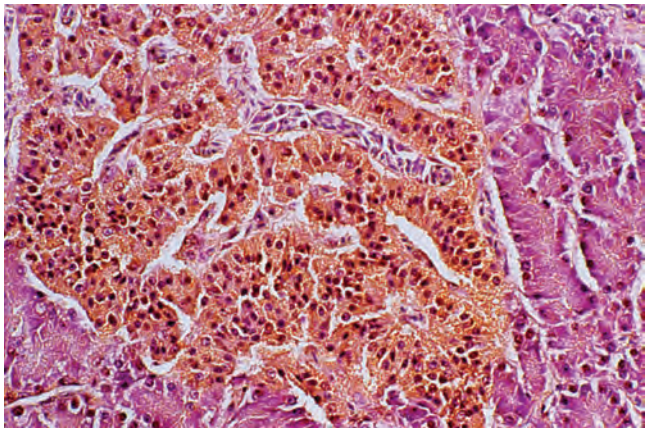

Figure 7.39 Marked hyperplasia of islets of Langerhans. Based on histochemistry, the brown granular material is glucagon.

Proliferative disease

Islet cell hyperplasia and hypertrophy are occasionally seen. In most of our cases it is due to proliferation and enlargement of A cells associated with vague clinical signs and death. There is no grossly observable change. Histologically the enlarged islets comprise large cells forming trabeculae (Fig. 7.39).

Islet cell tumors are rare in birds. Reported cases are described as nodular masses that comprise poorly differentiated epithelial cells with hyperchromatic nuclei. The cells form trabeculae that extend into surrounding pancreatic parenchyma (Fig. 7.40).

Foci of malignant melanoma have been seen in birds with disseminated disease. They appear grossly as small dark nodules and histologically are similar to the tumor in the skin (Chapter 11).

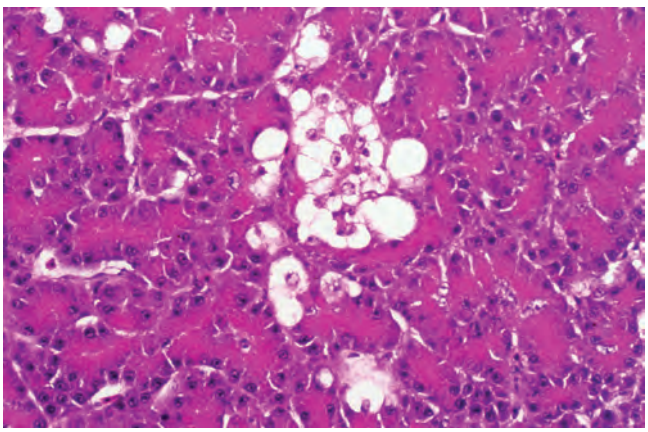

Figure 7.38 Typical swelling and vacuolation of islets of Langerhans seen in birds with diabetes mellitus.

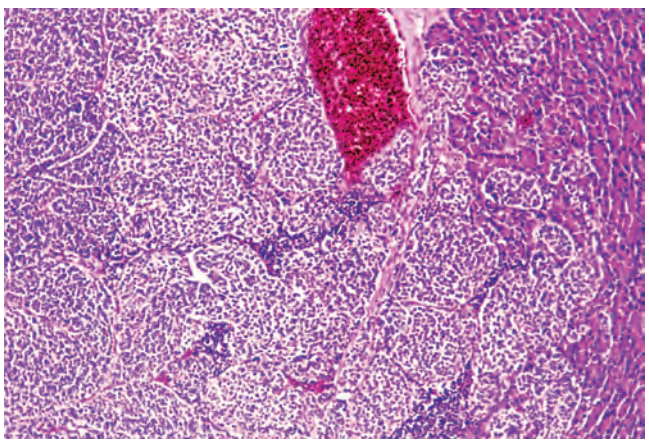

Figure 7.40 Infiltrative growth of low-grade islet cell carcinoma.

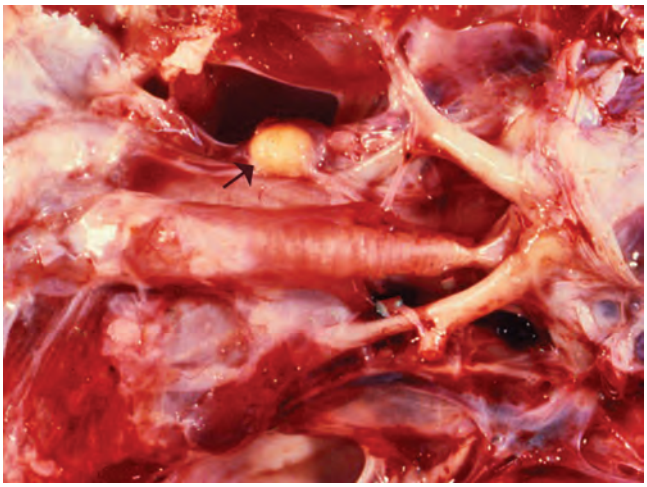

Figure 7.41 Yellow mass that is an ultimobranchial cyst. Depending on location, a parathyroid tumor would be a differential diagnosis.

Ultimobranchial body

Normal structure

Avian ultimobranchial bodies are paired structures posterior to the parathyroid glands and are immediately lateral to the carotid arteries. The ultimobranchial body in companion birds is typically 1.0–3.0 mm in diameter. The left body may attach to the parathyroid. They are difficult to locate in birds that have moderate or excessive amount of fat. The avian ultimobranchial body contains cords or islands of C cells, small vesicles, and parathyroid nodules in a loose connective tissue stroma. The C cells produce calcitonin.

Lesions

If there is long-term hypercalcemia there may be hypertrophy of the ultimobranchial bodies, and they can be greater than 3.0 mm and will be obvious grossly. Histologically the C cells are enlarged and have abundant cytoplasm. Cysts may develop in the ultimobranchial bodies. These cysts may be lined by C cells, or by squamous epithelium in some cases. Depending on location these cysts can resemble hyperplastic or neoplastic parathyroid glands (Fig. 7.41).

Carotid bodies, aortic body, pineal gland, and gastrointestinal endocrine system

Normal structure

The carotid bodies are paired at each side of the thoracic inlet in contact with the medial surface of the parathyroid glands. In some birds they may be embedded in the parathyroid gland. Accessory carotid bodies may occur in other sites including the adventitia of arteries. The cells of the carotid body are epithelioid with a round nucleus and a finely granular cytoplasm. A thick capsule surrounds the carotid bodies.

The aortic bodies are small groups of cells in the adventitia of the aorta near its base. As with the carotid bodies, these are not strictly endocrine organs but are considered here for want of a better place to include them.

The pineal gland is found between the cerebral hemispheres and the cerebellum. It is a dorsally divided projection of the diencephalon.

Cells of the gastrointestinal endocrine system are found in the mucosa of the GI tract, with the greatest concentration in the proventriculus.

Lesions

A chemodectoma has been reported in a budgerigar, but no detailed description was given. There is a report of an aortic body tumor in a duck. The tumor comprised lobules containing trabecular structures separated by vascularized stroma.

Pinealomas, both pineocytomas and pineoblastomas, are rarely seen. Pineocytoma is a circumscribed encapsulated cellular mass generally embedded between folia of the rostral cerebellar vermis. These benign tumors present as lobulated nodular growths of the gland. The lobules are composed of columnar epithelium and surrounding parafollicular cells. Histologically the cells have vesicular nuclei and form rosettes. Pineocytomas in poultry have been suggested to be functional resulting in ovarian inactivity.

Pineoblastoma is a friable suprathalamic gray mass located on midline that compresses adjacent structures. The tumor is composed of sheets and cords of cells having a round to oval nuclei and small to moderate amounts of vacuolated basophilic cytoplasm. Occasional rosettes may be found. Features noted on ultrastructural evaluation included cells with cytoplasmic dense core vesicles with no glial filaments. Neither cilia or microvilli nor apical vacuoles are described.

Lesions of the gastrointestinal endocrine system have not been reported.

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8 Lymphatic and Hematopoietic System

Immunity is defined as a state or power of resisting the development of a (given) disease (*Webster's Dictionary*). In birds, there are many redundant and integrated mechanisms to accomplish this. The innate immune system includes the epidermis, secretions into the gastrointestinal, urogenital, and respiratory tracts, inflammation, and cell phagocytosis. These systems function at birth and do not require antigenic stimulation. Adaptive resistance responds to antigens and combats pathogens that can evolve much faster than in any vertebrate immune system. This system can improve resistance upon repeated challenges.

Normal structure

The immune system is composed of two types of lymphoid tissue: primary and secondary. The thymus and the bursa of Fabricius are primary lymphoid tissues. The thymus, which is derived from the third and fourth pharyngeal pouches, comprises three to eight pale pink, flattened, irregularly shaped masses that extend along the length of both sides of the neck close to the jugular vein (Fig. 8.1). The thymus has both epithelial and lymphoid components. The epithelial tissue is present as both the onionskin layers of keratinized epithelioid cells called Hassall's corpuscles and the loose network supporting the lymphoid cells. In domestic fowl, the thymus will involute at around 4 months of age, at the onset of sexual maturity. The thymus can enlarge and regain function in adult chickens if they are exposed to thyroxine. The thymus of cage birds involutes at approximately the same time that the birds are weaned. Histologically the thymus is made up of lobes, each having a cortex and medulla. The junction between the cortex and medulla is less well defined in birds as compared with mammals. The thymus contains T lymphocytes (T cells) that are derived from stem cells produced in the para-aortic region that then migrate to the yolk sac before they enter the thymus. T cells mature and differentiate in the thymus. The thymus also contains a small number of B lymphocytes (B cells) that migrate to the thymus after hatching. Unlike in mammals, the thymus can function as a secondary lymphoid organ.

In most birds, the bursa of Fabricius is a dorsal median diverticulum of proctodeum that contains the bursal lymphoid follicles. It appears grossly as a light cream-colored saccular organ with inner folds (Fig. 8.2). Ratites are unusual in that the bursa of Fabricius is diffuse and contained submucosally in the dorsal wall of the cloaca and has a reversed cortex and medulla. The bursa of Fabricius reaches its maximum size before a bird is sexually mature and then undergoes involution. Each bursal follicle has a cortex of lymphocytes, macrophages, and plasma cells, and a medulla of lymphocytes, lymphoblasts, and plasma cells. In a normal bursa, the follicle-associated epithelium should be difficult to see (Fig. 8.3). Aggregates of granulocytic extramedullary hematopoiesis may be present between the follicles in young birds. Antigens from the cloaca move into the bursa of Fabricius by retrograde movement up the infundibulum and are presented to the developing B cells in the follicles. The bursa of Fabricius also functions as a secondary lymphoid organ for intestinal antigens.

The secondary lymphoid tissues include the spleen, Harderian gland, pineal gland, bone marrow, and a diffuse system of perivascular lymphoid aggregates. Solitary and aggregated lymphoid nodules are more numerous in the digestive tract, with scattered nodules in the oropharynx around the choanal opening and the pharyngeal opening of the auditory tubes. These nodules are nonencapsulated aggregates of lymphocytes and small numbers of plasma cells and macrophages. Ducks have an esophageal tonsil that is located at the terminal part of the thoracic esophagus and is an aggregate of lymphoid nodules. In some birds, prominent lymphoid nodules called cecal tonsils are found in the wall of cecum, near the junction of rectum. In nestling budgerigars, and possibly other nestling psittacine birds, there are extensive areas of lymphocytes and plasma cells in the lamina propria of the isthmus of the stomach. These likely represent normal gut-associated lymphoid tissue.

The spleen, which is located at the right side of the junction of proventriculus and ventriculus, is round to oval in most psittacines, elongated with a slight curve in passerines, triangular in ducks and geese, and spherical in many poultry species. The spleen has a thinner capsule compared with the spleen in mammals and does not have a distinct red-and-white pulp.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

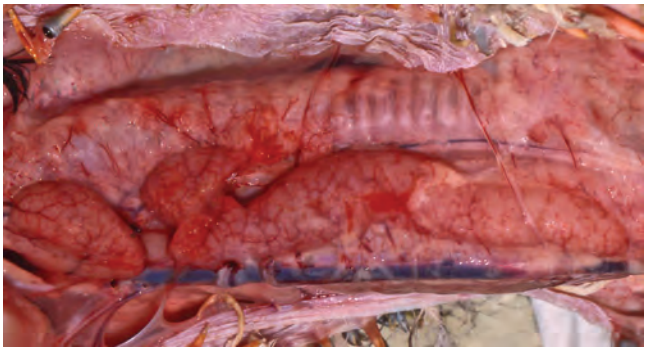

Figure 8.1 Normal thymus in a psittacine bird. Thymic tissue extends almost the entire length of the neck.

Birds have distinct sheathed arterioles, which are surrounded by the histiocytic reticular cells. These are very prominent structures in the spleen of owls. In birds, the spleen is not a significant reservoir of blood. The splenic circulation is open, with no direct vascular connection between arteries and veins. Within the spleen, worn-out erythrocytes are phagocytosed, and lymphopoiesis and antibody production occur.

The Harderian gland, which is located ventrally and posteromedially to the globe of the eye, is infiltrated with plasma cells and is a site of immunoglobulin A (IgA) production. The pineal gland, which contains B lymphocytes and T lymphocytes and has germinal centers, contributes to the granulocytic extramedullary hematopoiesis of hatched chickens.

The bone marrow is the main source of granulocyte production in late embryonic life and after hatching. Histologically erythropoiesis and possibly thrombopoiesis occur within the vascular sinuses (intravascular), whereas granulopoiesis is outside the vascular sinuses (extravascular). Some long-lived IgM-secreting lymphocytes are found in bone marrow. The precise role of the bone marrow in avian immunology is unclear, although it is not a primary organ as in mammals.

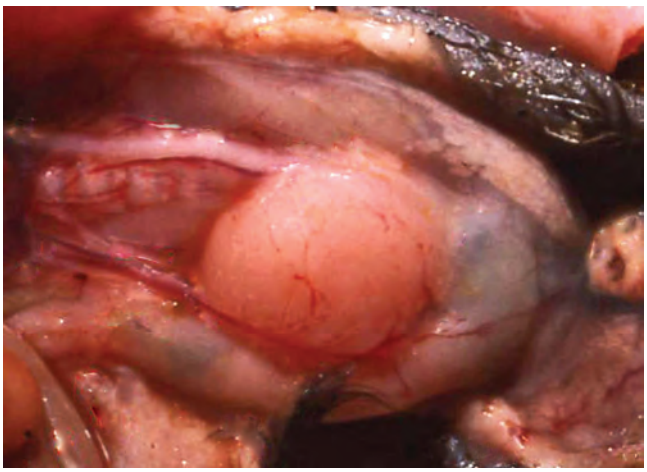

Figure 8.2 Normal-sized bursa of Fabricius in a young psittacine bird.

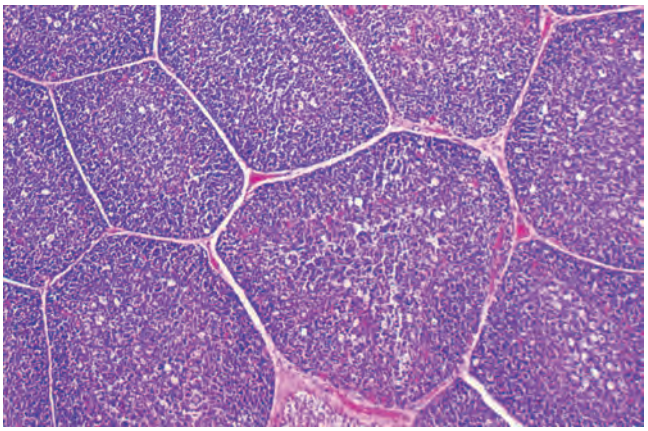

Figure 8.3 Normal psittacine bursa. The follicle-associated epithelium is barely visible.

Immunity

Innate immunity

This is a static immunity, where the organism responds to immunologic stimulation the same way each time. The components of the innate system include complement proteins, acute-phase proteins, iron-binding proteins, natural killer cells, and phagocytes. The avian phagocytic cells are the macrophages/monocytes, heterophils, and thrombocytes. An example of an innate system is the chicken respiratory system-resident macrophages. In chickens, there are low numbers of these macrophages present in the respiratory system. However, when stimulated by a pathogen, there is a preventive activation of the respiratory phagocytes, resulting in an induced influx of phagocytes to the area and enhanced phagocytosis.

Adaptive or acquired immunity

The adaptive immune system of all vertebrates (including birds) can be divided into two arms: humoral immunity and cellular immunity. Humoral immunity develops in the bursa of Fabricius and is characterized by antibodies secreted by B cells. The bursa of Fabricius is a primary lymphoid organ unique to birds and not found in mammals. The cellular immune system develops in the thymus. The thymus is essential for the maturation of T lymphocytes, the principal cells of cellular immunity.

Humoral immunity

Adaptive or acquired immunity has a memory with a primary and a secondary response. In the primary response, there is a lag time of approximately 10–15 days before there is measurable serum antibody. The predominant antibody generated is IgM. With sustained antigenic stimulation, there is a transition to IgG secretion, and high antibody titers will develop. The secondary response occurs if a bird is subsequently exposed to the same antigen. In this case, antibody production occurs more quickly because of the presence of a population of memory cells.

IgG is the primary antibody. In the secondary response, the B-lymphocyte receptors also have a higher affinity for antigen, and the T lymphocytes adhere more strongly to other cells to transduce extracellular signals more efficiently.

The avian antibody is structurally similar to mammalian immunoglobulins. There are five classes in mammals, but only three classes have been completely described in birds: IgG (this may be listed as IgY in some literature), IgM, and IgA.

IgM, a pentameric molecule, is the predominant immunoglobulin until 20 days of development in the chicken. It is confined to the vasculature and is an efficient agglutinin (the clumping of bacteria or other immunologically reactive material) and cytolytic antibody.

IgG, which is the major serum immunoglobulin, forms the largest class. It functions to enhance phagocytosis, neutralize toxins, and inactivate some viruses. In ducks and chickens, there is passive transfer of IgG through the egg yolk. The intestinal lamina propria lymphocytes are rich in cells secreting IgG.

IgA, generally a trimer molecule, is the most common immunoglobulin found in external secretions. Both the intestinal lamina propria and the lungs are relatively enriched in cells actively secreting IgA. As in mammals, a secretory polypeptide that is synthesized by epithelial cells attaches to the IgA before secretion. In the chicken embryo, IgA and IgM are found in low concentrations in egg white and are believed to be derived from oviduct secretions. IgM and IgA that are swallowed by embryos via amniotic fluid during development are believed to provide some protective immunity to newly hatched chicks.

The immunoglobulins in nonpoultry species have only recently been examined. In ostriches, both IgG and IgM classes have been identified. They are distinct from chicken classes by both molecular weight and structure. Pigeons have all three groups: IgG, IgM, and IgA. IgA is transferred to squabs via crop milk. It appears that in the crop milk it exists in a dimeric state and probably does not have a secretory component.

Maternal IgG is present in the egg yolk and reaches the embryo via the circulation of the yolk sac as in chickens. The maximum values of IgG resorption are reached on the second day of life. In psittacine birds, monoclonal antibodies made to the IgG heavy chain of IgG from the blue and gold macaw cross-reacted with the sera of other macaws, conures, and a few other New World psittacines, but did not cross-react with IgG from African and Australian psittacines. There is some evidence, from studies showing protection from circovirus in hatchlings and low levels of hemagglutination inhibition activity in psittacine chicks, that maternally derived antibody is passed to psittacine chicks. In budgerigars, although maternal IgG is present in the yolk sacs, the antibody does not reach the nestling circulation in measurable amounts.

Cell-mediated immunity

Cell-mediated immunity, which is mediated by T cells, includes the cytotoxic, helper, and suppressor responses. The T lymphocytes are different from B lymphocytes in that they have a lower affinity to antigen, interact with other cells, do not produce antibody, and recognize digested foreign peptides on cell surfaces. These actions help them to protect the host primarily from viruses by mediating the destruction of virus-infected cells. They also have actions against intracellular bacteria, parasites, fungi, and some tumor cells.

Antigen receptors on chicken T cells are described as CD3/TCR complexes. T-cell receptors (TCRs) define the lymphocytes as T cells and function to recognize foreign antigen when displayed on the surface of a target cell. TCR1 and TCR2 correspond to the mammalian counterparts, and TCR3 is unique to birds. The T cells have coreceptors that do not bind antigen and are invariant and nonpolymorphic. The receptors in poultry are designated CT1, that is, different molecularly from the mammalian CD1, but appears to have the same functions. CD4 receptors bind to MHC2 (major histocompatibility complex 2) and are expressed in helper T cells. CD8 receptors bind to MHC1 and are expressed in cytotoxic T cells.

Chickens have a unique T cell. CD3/TCRs are not expressed on its surface, but it does have CD3 in the cytoplasm. It is designated as TCR0 and can be found in spleen, bursa, thymic medulla, and intestine. These may be natural killer cells. The TCR genes are rearranged and gain diversity in the hematopoietic precursor cells in the thymic microenvironment along with T-cell differentiation and proliferation in chickens.

Immune suppression

Direct immune suppression can occur with drug toxicity, aflatoxicosis, and lead poisoning. Fenbendazole and related drug, albendazole, have been associated with adverse effects and death in some sensitive avian species (solitary lories, rock doves, barefaced ground doves, southern picui doves, and cockatiels). The inhibition of microtubule polymerization by benzimidazoles is suspected of interfering with mitosis. Damage to rapidly dividing cells is the hallmark finding within the avian gastrointestinal tract and bone marrow. They usually exhibit a rapid heteropenia and then anemia.

Aflatoxin depresses complement activity, decreases phagocytic activity, and impairs cell-mediated immunity through inhibition of thymic-associated lymphocytes in chickens. All fungal toxins interfere with protein synthesis, which affects both T and B cell immunity. In poultry, tetracycline, tylosin, and gentamicin are immunosuppressive and decrease antibody production. Lead poisoning may have immunosuppressive effects in birds. Poisoned mallards have decreased hemagglutinating antibody as compared to normal controls.

Stress-induced immunosuppression is mediated through the adrenal gland. Corticosteroids are reported to inhibit antibody-forming cells and inhibit the production and action of immunoregulatory cytokine interleukin-1 in mammals. Acute feed restriction or fasting elevates plasma corticosterone dramatically in chickens. Injectable dexamethasone reduced serum IgG in ducks. It also suppressed the humoral response in

other species of birds. In pigeons, a single oral dose or ocular dose of glucocorticoids caused suppression of the pituitary–adrenocortical system.

Nutrition plays a critical role in maintaining the immune system. In humans, chronic malnutrition, particularly protein malnutrition, suppresses the immune system preventing a response to immunogens. A calorie-deficient diet suppresses the antibody responses in chickens. The weight of the bursa of Fabricius is reduced in vitamin A-deficient chickens.

Disease

Bursa of Fabricius

Atrophy

The bursa of Fabricius normally involutes as the bird matures. It becomes grossly smaller (Fig. 8.4). During this process the lymphocytes of both the medulla and cortex undergo apoptosis. Medullary cysts may form, and these may contain mineralized material. The follicular-associated epithelium becomes more prominent and is transformed into a pseudostratified layer separating the cortex from the medulla (Fig. 8.5). There will be variation in the size and shape of the follicles with increased interfollicular connective tissue separating the follicles. Histologically there are only a small number of follicular remnants (Fig. 8.6). Nonspecific stresses, such as malnutrition, poor management, or infection, can result in premature atrophy of the bursa and potential immunosuppression.

Viral disease

Psittacine circovirus disease

The psittacine beak and feather disease virus (PBFDV) is a 14- to 16-nm nonenveloped virion belonging to the family Circoviridae. All psittacine species are considered susceptible to infection by this virus, but disease is predominantly confined to parrots of African and Australasian distribution and is most common in birds less than 3 years of age. Unique circoviruses infect doves, racing pigeons, and other pigeon varieties, canaries, finches, geese, the Australian raven, and the Southern black-backed gull.

Four main clinical presentations exist. A common presentation occurs in wild and recently imported wild-caught cockatoos, several other species of Australasian parrots, and, rarely, New World parrots. This chronic form of the disease is insidious in its development and progression. Typically, dystrophic feathers gradually replace normal ones as they are molted. Affected birds are usually 8 months to 3 years of age. An acute form of the disease also occurs in nestling cockatoos, lorikeets and, less commonly, other parrot species. In these birds, all growing feathers are affected simultaneously; the birds show generalized signs

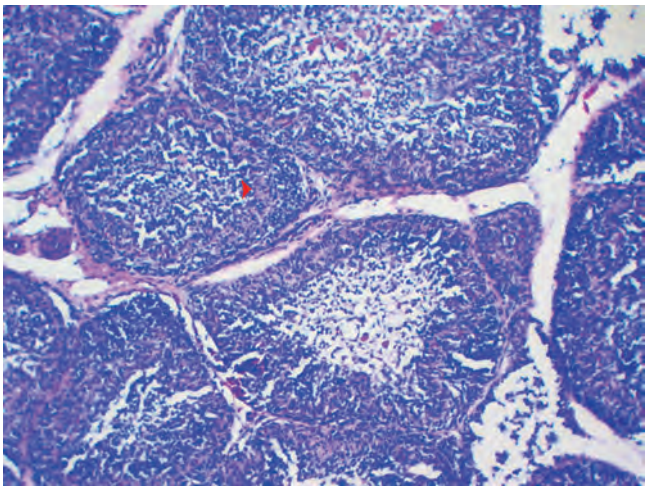

Figure 8.5 Nonspecific bursal atrophy. Follicles are irregular, there is loss of lymphoid cells, and the follicle-associated epithelium is easily seen (arrowhead).

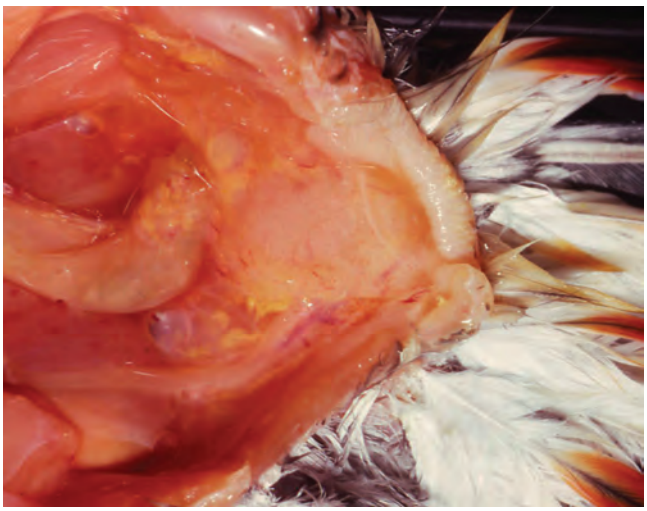

Figure 8.4 Bursal involution in a psittacine bird. The bursa is small and difficult to see. Compare with Figure 8.1.

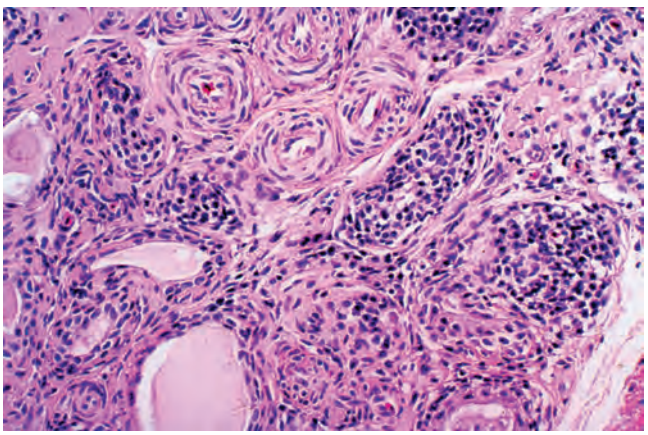

Figure 8.6 Severe atrophy and involution of psittacine bursa. It may take over a year for this to occur.

of disease and die within a few days to weeks. Nestling budgerigars also show generalized feather dystrophy, but it may not be fatal. Another acute form of PBFDV infection may not result in feather lesions, or the feather lesions may be localized and minimal. These birds generally die from secondary infections due to virally induced immunosuppression. In budgerigars, wild rainbow lorikeets, and in a range of other Australian parrot species fledglings present that are unable to fly because they have dystrophy to varying degrees of their primaries, secondaries, and tail feathers.

Primary PBFDV replication occurs at the portals of entry in the bursa of Fabricius and/or gastrointestinal tract lymphoid tissue. Secondary virus replication occurs in the liver, thymus, and probably other tissues. A common target organ is the epidermis, where the virus attacks cells in developing feathers.

Atrophy of the primary lymphoid organs is the typical finding on gross examination. The thymus and bursa of Fabricius may be difficult to find. The bone marrow can appear pale and yellowish. In pigeons with pigeon circovirus infection, spleens are typically small and little reactivity is observed even in the face of systemic infections.

Histologically, if the PBFDV attacks B cells prior to bursal regression, there will be extensive necrosis of the lymphoid follicles, with lymphocytolysis. Proteinaceous fluid and cell debris may accumulate within medullary cysts, and the follicular-associated epithelium will be prominent. Bursal hemorrhage may also be prominent. Inclusion bodies both intranuclear and intracytoplasmic can be found in macrophages and lymphocytes (Fig. 8.7). The intracytoplasmic inclusions that are more common in macrophages form clumps of globular basophilic to magenta pigments (Fig. 8.8). Eosinophilic intranuclear inclusions are characteristic of epithelial cells. In chronic cases, the bursa of Fabricius is greatly distorted by loss of lymphoid follicles and severe lymphocytic depletion (Fig. 8.9).

Young African gray parrots have a specific presentation of peracute PBFDV infection characterized by severe leukopenia, anemia, or pancytopenia and liver necrosis often in the absence of feather and beak abnormalities. The liver will be enlarged and pale orange, with necrotic foci. Splenomegaly and mycotic pneumonia are also common. The definitive viral inclusions are generally restricted to the bursa of Fabricius.

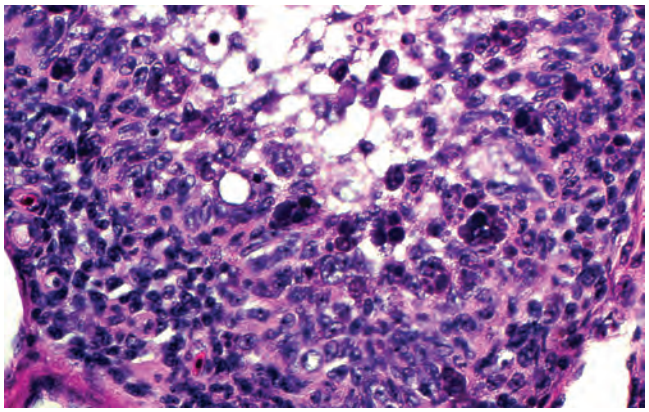

Figure 8.8 Detail of circovirus inclusions in the cytoplasm of bursal reticular cells.

Circovirus in other avian species

Circovirus infections have been reported in finches, pigeons, doves, ducks, geese, the Australian raven, and the black-backed gull. As with psittacines, circoviral infections are associated with secondary diseases due to the immunodeficiency caused by the virus. Nonspecific clinical signs are generally a failure to thrive, lethargy, and uncommonly feather abnormalities. Histologically there is a variable severe lymphocytic depletion of the thymus, spleen, and the bursa of Fabricius with eosinophilic, globular intracytoplasmic inclusions within mononuclear cells. In situ hybridization (ISH) can confirm circovirus DNA in the lesions. Underlying circovirus infections should be suspected in pigeons when multiple diseases such as trichomoniasis, salmonellosis, and columbid herpesvirus are present in young birds.

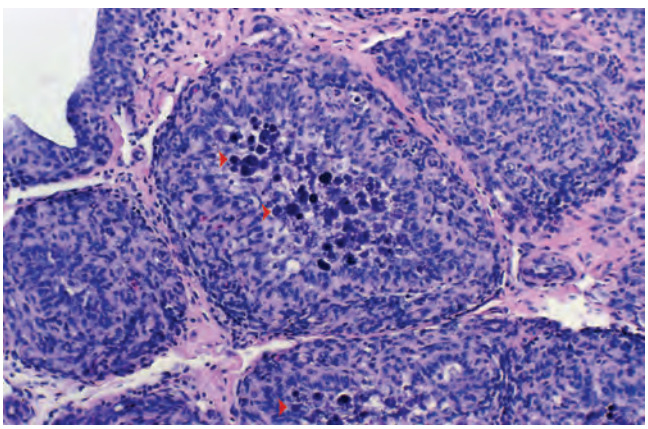

Figure 8.7 Bursal lymphoid depletion due to circovirus infection. Inclusion bodies can be seen in some follicles (arrowheads).

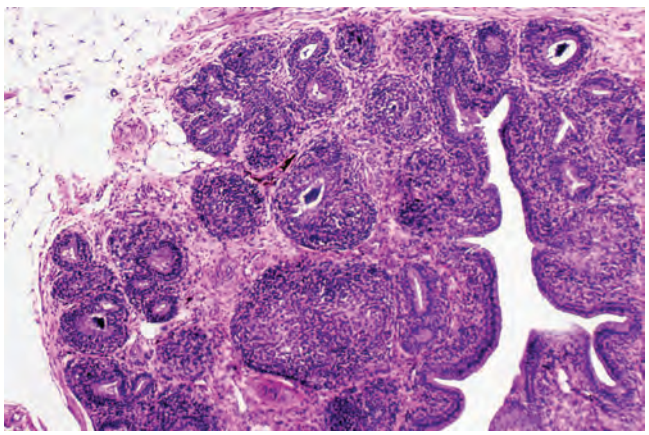

Figure 8.9 Severe bursal depletion and loss of follicles in chronic circovirus infection.

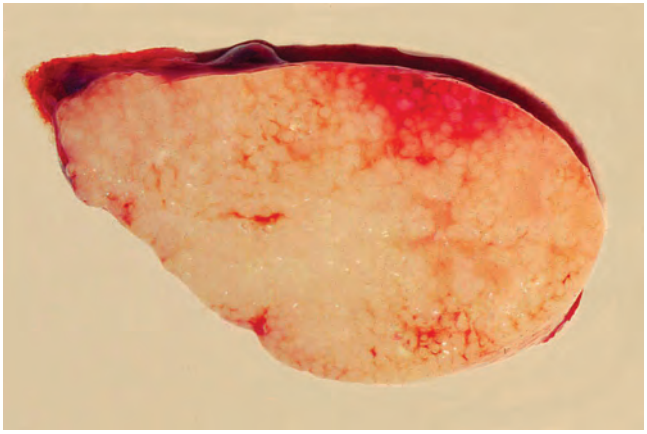

Figure 8.10 Hemorrhage in the bursa of Fabricius from a bird with polyomavirus infection. The disease was acute and the bursa is essentially of normal size.

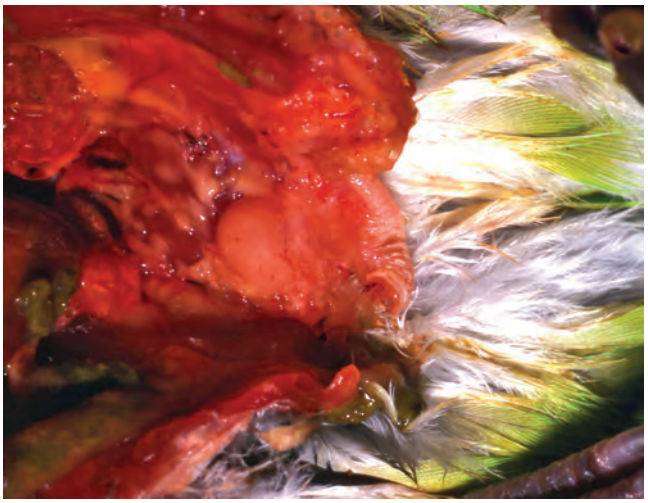

Figure 8.12 Premature lymphoid depletion in the bursa of Fabricius of a bird with vitamin D toxicity resulting in gross atrophy.

Avian polyomavirus

Avian polyomavirus disease (APV) is described extensively in Chapter 4. Nestlings dying of APV disease will have swelling and often hemorrhage of the bursa of Fabricius (Fig. 8.10). Depletion and necrosis of lymphocytes in medulla of bursa of Fabricius are seen histologically. Karyomegaly with typical clear to lightly basophilic intranuclear inclusion bodies is occasionally seen in lymphocytes within the bursa of Fabricius.

Other viruses

Many of the common bird viral infections will result in damage to the lymphoid follicles of the bursa of Fabricius. These include psittacid herpesvirus-1 infection (Pacheco's disease, PsHV-1) (Fig. 8.11), parvovirus of ducks and geese, avian influenza, and adenovirus in poultry, psittacine birds, and pigeons. Intranuclear inclusion bodies may be found in bursal reticular cells in PsHV-1. Infectious bursal disease virus of chickens has a direct cytopathic effect on immature B cells. There will be extensive necrosis characterized by lymphocytolysis. Chickens infected with this virus are often subsequently immunocompromised. We have recognized a similar virus by electron microscopy in the bursa of Fabricius of ostriches. Canary poxvirus has been identified in the thymus, bursa of Fabricius, spleen, and bone marrow. Severe mononuclear inflammatory cell proliferation containing eosinophilic, intracytoplasmic inclusion bodies was present effacing many of these organs.

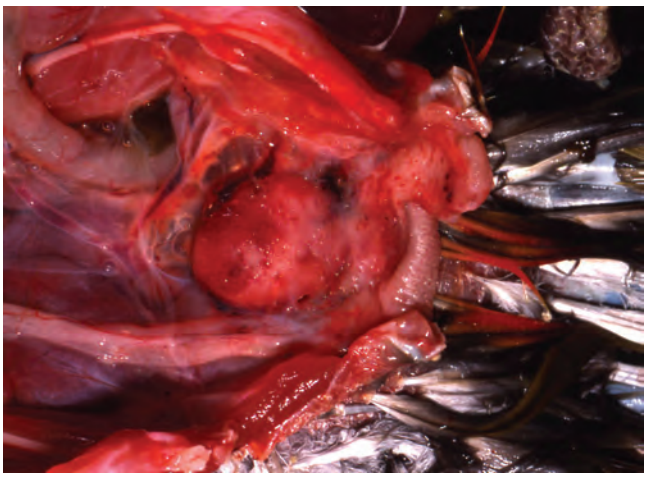

Figure 8.11 Hemorrhage within the bursa of Fabricius in a bird with systemic herpesvirus infection.

Bacteria

Bacterial infections of the bursa of Fabricius are uncommon. They may represent localization of a systemic disease or an extension from a cloacal infection. The bursa of Fabricius may be enlarged and irregular and have caseous foci. Usually the follicles are diffusely and severely depleted of lymphocytes. Multiple foci of necrosis and microabscesses with intralesional bacteria are seen. The abscesses may be surrounded by macrophages and giant cells, some containing intracytoplasmic bacteria.

Yeast

Yeast infections of the bursa of Fabricius are very uncommon. They are most likely a localization of a systemic disease and are more commonly recognized in young cockatiels. The bursa of Fabricius may be difficult to identify grossly. Usually the follicles are diffusely and severely depleted of lymphocytes. Multiple foci of necrosis with intralesional yeast and pseudohyphae are seen. Mixed inflammation of heterophils, lymphocytes, plasma cells, macrophages, and giant cells may be present.

Protozoal disease

Cryptosporidia are 2- to 5-μm intracytoplasmic, apicomplexid coccidian parasites that parasitize the apical portions of the occulorespiratory, gastrointestinal, and genitourinary epithelia.

Infections are rare in pet birds. The majority of cases described have been confined to the gastrointestinal tract. The intestines will have excessive intraluminal fluid and gas. The proventriculus will also have intraluminal fluid and a thickened mucosa. The bursa of Fabricius may appear edematous. The spherical to ovoid cryptosporidia proliferate within the epithelium of the bursa of Fabricius and mucosa epithelium of the proventricular glands and intestinal mucosa. These gram-negative organisms have a foamy, pale eosinophilic cytoplasm with a distinct basophilic nuclei and occasional periodic acid-Schiff-positive (PAS) internal structures. Many cryptosporidial infections occur in birds that are concurrently infected with PBFDV.

Toxins

A number of toxins have resulted in severe lymphocytic depletion and lymphocytolysis of the bursa of Fabricius in wild birds and poultry. These have included crude oil, excessive vitamin D (Fig. 8.12), selenium, mycotoxins, and organotin compounds used as pesticides, stabilizers, disinfectants, molluscicides, antihelminthics, and antitumor agents.

Nutrition

Calorie-deficient diets and hypovitaminosis A will result in atrophy of the bursa of Fabricius of young birds.

Neoplastic disease

Tumors of the bursa of Fabricius are rare in birds. There is a single report of a spindle cell sarcoma arising within the bursa of a budgerigar. Lymphoma has been identified in an African gray parrot, Senegal, two Amazon parrots, and a cockatiel. All were young birds (less than 4 years) except the Amazon parrots. The African gray parrot tested negative by polymerase chain reaction (PCR) for Marek's disease virus, avian leukosis virus, and reticuloendotheliosis virus. Lymphoma is the classic poultry tumor of the bursa of Fabricius that is induced by a chicken retrovirus.

Thymus

Cysts

Thymic cysts are rarely found as incidental lesions in birds. The etiology of the cystic development in birds is unknown; however, thymic cysts may be dilations of persistent thymopharyngeal ducts. Another possibility is that they develop during thymic involution from clefts forming in the condensed thymic epithelium. The cysts may be lined by a columnar or stratified squamous epithelium of variable thickness and filled with a colloid-like material (Fig. 8.13).

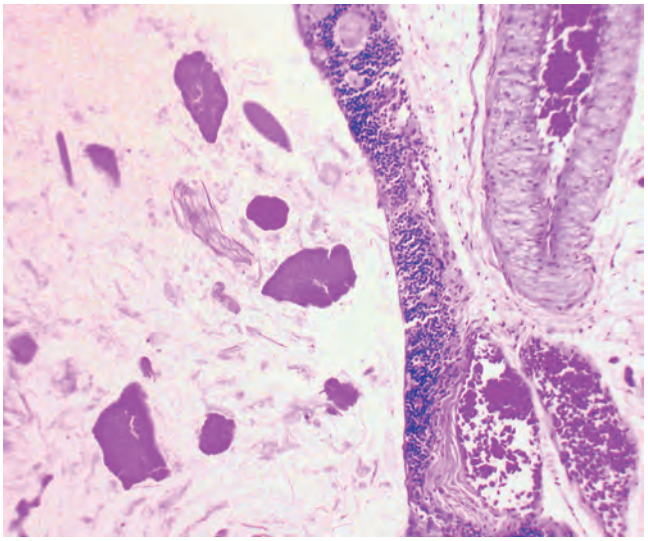

Figure 8.13 Thymic cyst containing amorphous debris.

Atrophy

Premature thymic atrophy is characterized by loss of the lymphocyte population and a loss of cortex and medulla differentiation. In psittacine birds, the viral diseases commonly associated with the atrophy or widespread lymphocytolysis of the thymus include circoviruses and psittacid herpesvirus (PsHV-1). Avian influenza, Marek's disease virus, and some strains of infectious bursal disease virus cause similar lesions in poultry. Nutritional stress and exposure to corticosterone hormone can also induce thymic atrophy. An atrophic or involuting thymus is characterized by scattered solitary nodules in the cervical region (Fig. 8.14).

Inflammatory/infectious

The eosinophilic intranuclear inclusions of PsHV-1 have been recognized in the epithelial reticular cells and Hassall corpuscles of the thymus.

Neoplastic disease: thymoma

Neoplasms of the thymus may arise from the epithelial cells or lymphocytes. The epithelial tumors are classified as thymomas, and the lymphoid tumors are thymic lymphosarcomas. The

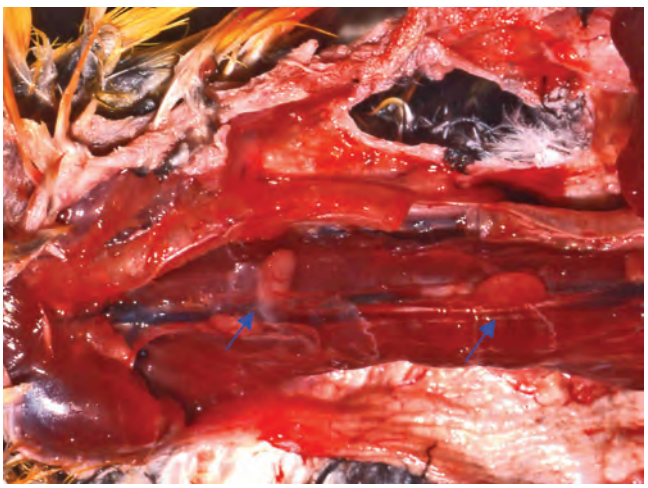

Figure 8.14 Involuted thymus in a Caique. Several foci of tissue are present (arrows). Compare with Figure 8.1.

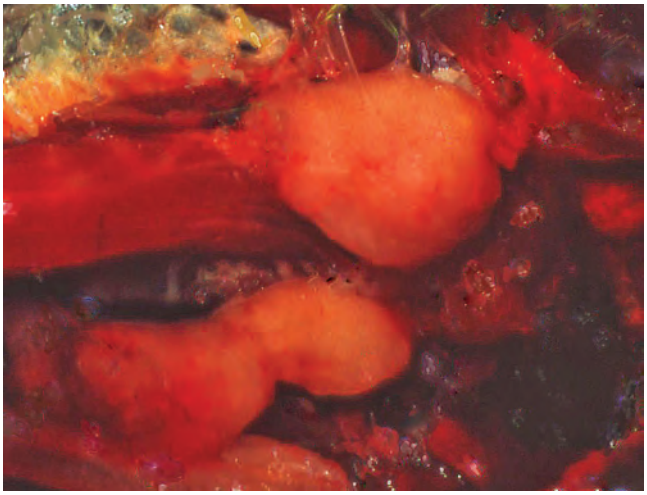

Figure 8.15 Lymphosarcoma involving several lobes of the thymus.

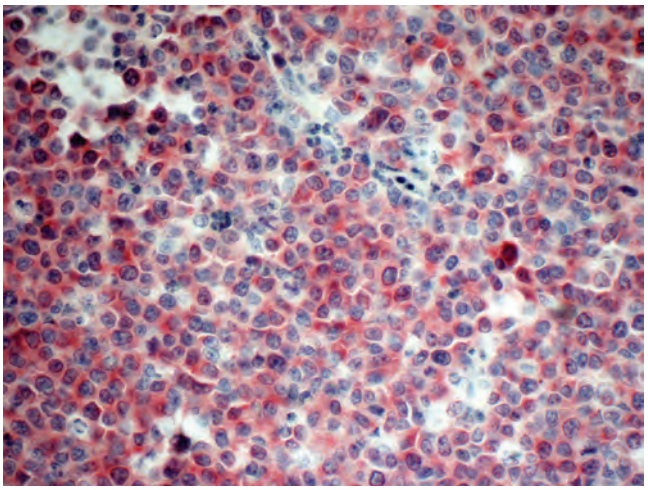

Figure 8.17 Thymic lymphoma. The cells are CD3 positive (red cytoplasm).

tumor masses may form anywhere in the subcutis of the neck from the mandible to the thoracic inlet. These masses may be cystic and hemorrhagic (Fig. 8.15).

Thymomas comprise a pleomorphic population of small to moderately sized lymphocytes, lymphoblasts, and large reticular cells. The reticular cells are arranged in sheets with large, round to oval vesicular nuclei, and a strongly eosinophilic cytoplasm. Mitotic figures are common. These cells may be positive for cytokeratin and proliferating cell nuclear antigen. Scattered lymphocytes and fewer plasma cells may be present throughout the tumor. Behaviorally most are benign. Thymic lymphosarcomas are typical lymphosarcomas and are composed of sheets of neoplastic lymphocytes effacing the normal architecture of the thymus (Fig. 8.16). In cases where immunohistochemistry has been applied, the lymphocytes have been CD3 positive (T cells) (Fig. 8.17). Scattered clusters of Hassall's corpuscles may be found throughout. Thymic lymphomas often metastasize by the time the primary mass is recognized. These have been described in birds as young as 2 months.

Spleen

Viral disease

Avian polyomavirus

Birds with APV disease typically have an enlarged and often hemorrhagic spleen. Histologically there is multifocal splenic necrosis (Fig. 8.18). Karyomegaly with typical lightly basophilic to clear intranuclear inclusions are usually prominent and may be massive (Fig. 8.19), particularly in macrophages of the splenic periarteriolar sheaths (Fig. 8.20). Impression smears of an affected spleen may contain numerous inclusions and provide the prosector with a tentative diagnosis (Fig. 8.21). Karyomegaly can also be prominent in splenic reticular cells. A

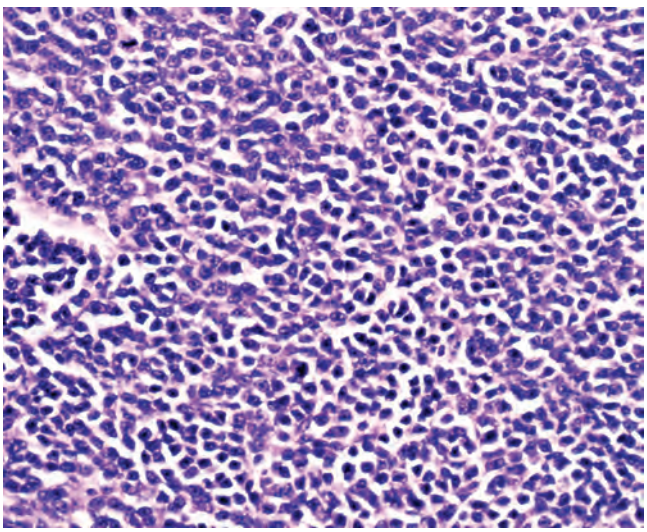

Figure 8.16 Sheet of monomorphic neoplastic lymphoid cells effacing the thymus.

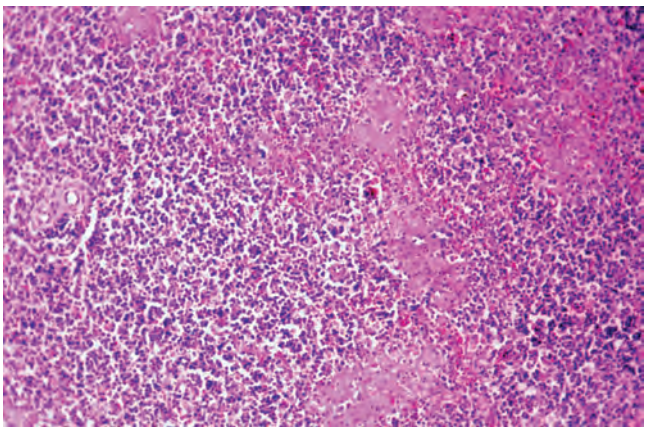

Figure 8.18 Multifocal splenic necrosis in a bird with polyomavirus infection.

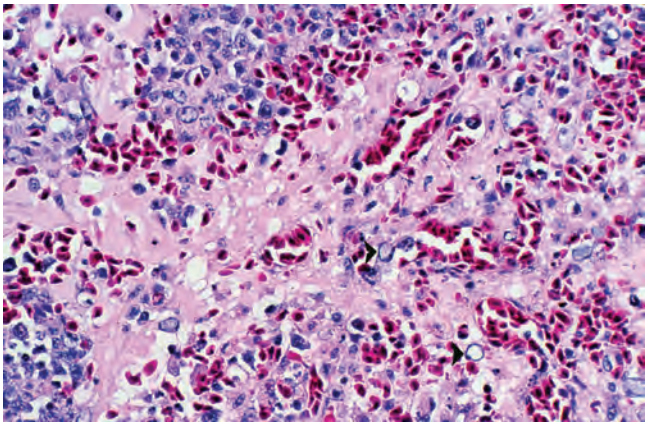

Figure 8.19 Detail of splenic necrosis and minimal inclusion body (arrowhead) formation seen in many large psittacine birds with APV.

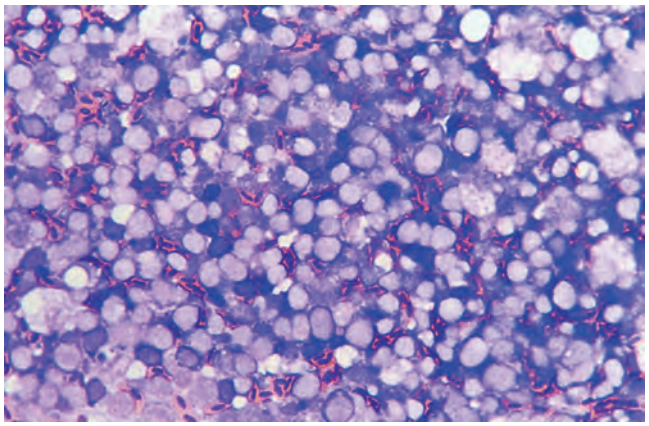

Figure 8.21 Splenic impression smear with numerous cells with karyomegalic nuclei containing pale azurophilic inclusion bodies.

nonspecific lymphocytic depletion may also occur. Rarely a bird will survive APV disease. These birds may have little functional tissue remaining in their spleen.

Herpesvirus (Pacheco's disease)

Psittacid herpesvirus-1 disease viruses commonly cause lesions of the spleen. Often there is splenomegaly, although this may be absent in birds with peracute disease (Fig. 8.22). Necrosis of the cells in the periarterial lymphatic sheaths and of the mononuclear cells and lymphocytes is common. Pale to deeply staining eosinophilic intranuclear viral inclusions are generally common. Syncytial cell formation is rare (Fig. 8.23). Pacheco's disease is described in more detail in Chapter 4. Columbid herpesvirus-1 infections in hawks, falcons, and owls have similar lesions in the spleen including loss of the lymphoid tissue with deposition of abundant fibrin and cellular debris. Histiocytes and some lymphocytes contain eosinophilic intranuclear inclusion bodies.

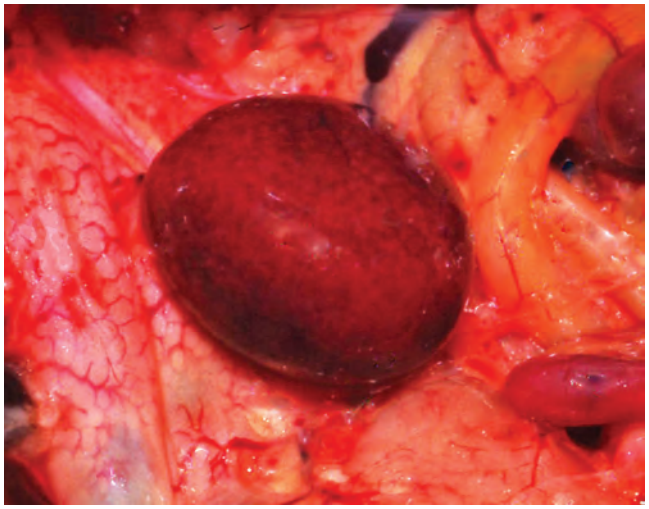

Figure 8.22 Enlarged, mottled spleen in a psittacine bird with Pacheco's disease.

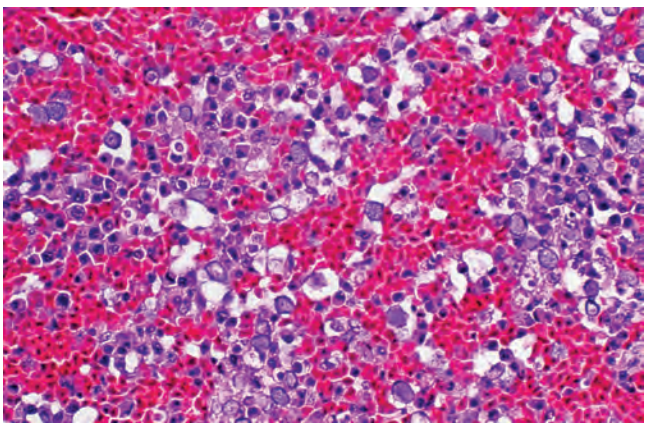

Figure 8.20 Numerous intranuclear inclusion bodies in reticular cells of spleen typical of the presentation in budgerigars and some eclectus parrots.

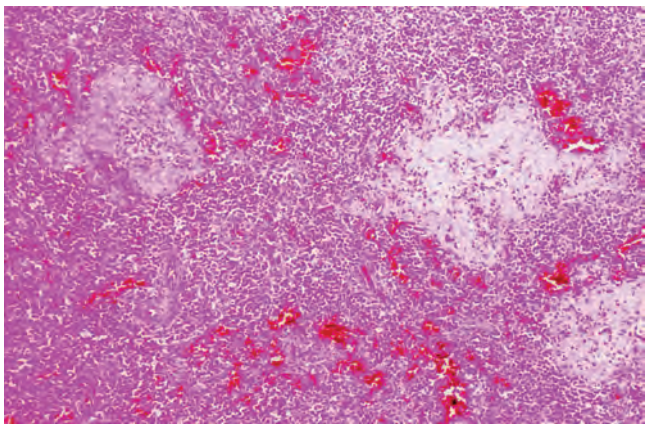

Figure 8.23 Splenic necrosis and mononuclear cell infiltrate in Pacheco's disease.

Avian adenovirus (aviadenovirus)

The adenovirus infections in avian species are undergoing classification changes. Group I aviadenoviruses have been isolated from various avian species (chicken, duck, goose, quail, pigeons, psittacines). Avian siadenoviruses, formerly Group II avian adenoviruses, contain the hemorrhagic enteritis virus of turkey, the marble spleen disease virus of pheasants, and the avian adenovirus group II splenomegaly of chicken. Avian atadenoviruses (previously Group III) is the egg drop syndrome of chickens.

Adenovirus infection in psittacines, pigeons, and raptors is associated with splenic necrosis, lymphoid depletion, and basophilic intranuclear inclusion bodies. PCR should be considered to determine specific classification for further understanding of these infections in birds.

Avipoxvirus

Avipoxvirus infection can result in a systemic disease, as well as the classic cutaneous infection. The systemic disease, which is more common in house sparrows, canaries, and other finches, is characterized by a proliferative rhinitis, bronchopneumonia, air sacculitis, and necrosis of the liver and heart. Splenomegaly has been described (Fig. 8.24), although commonly there will be marked lymphocytic depletion. An unusual lesion of marked splenic lymphoid proliferation has been associated with systemic canary pox infections (Fig. 8.25).

Paramyxovirus

As the Eurasian collared doves (*Streptopelia decaocto*) expand their range across the United States, they have experienced mortality events of pigeon paramyxovirus (PPMV). PPMV is considered endemic in domestic pigeons in Europe and the United States. Histologically, fibrinoid necrosis of the spleen and degenerate lymphocytes in the bursa of Fabricius. In addition mild hepatic necrosis and nephrosis with mild to moderate interstitial lymphocytic inflammation similar to that of PPMV infections in pigeons occurs in these doves.

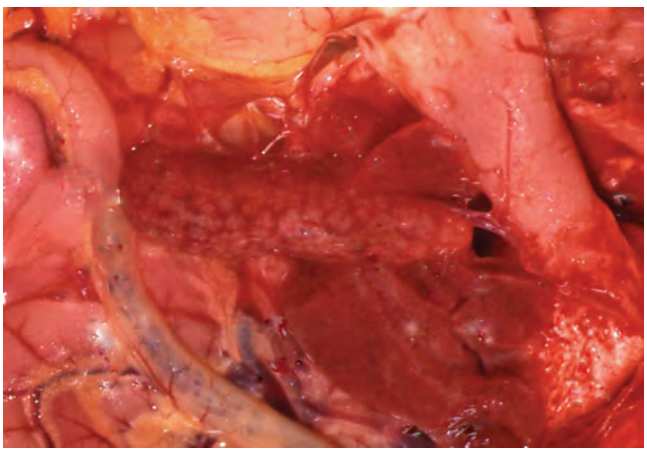

Figure 8.24 Enlarged, mottled spleen in a canary with systemic poxvirus infection.

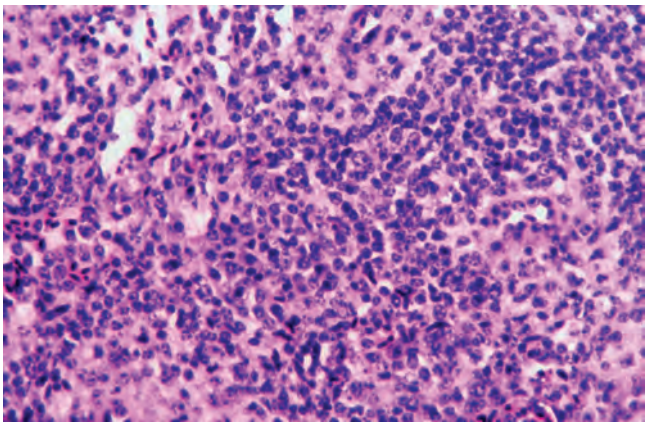

Figure 8.25 Marked lymphoid proliferation typical of systemic canary pox infection. The proliferation can have a "pseudolymphomatous" appearance.

Acute splenic necrosis with variable fibrin deposition in periarteriolar areas has been noted in cases of West Nile virus infections of susceptible avian species. Another common lesion is of severe depletion of lymphoid tissue and an increased number of macrophages in the red pulp.

Bacterial disease

Salmonella

This gram-negative bacterium is a member of the large family Enterobacteriaceae and is cosmopolitan in distribution. *Salmonella* is considered a primary pathogen, with some serotypes able to penetrate the mucosal barrier. Noninvasive serotypes may result in the carrier state. Domestic poultry is the single largest reservoir for *Salmonella*. *Salmonella typhimurium* is the most common psittacine and free-living avian isolate.

The disease progression in birds depends on the number of organisms present, the serotype, and the age, species, and condition of the host. It ranges from peracute, to acute, to chronic, to a subclinical infection.

The classic lesions are hepatomegaly, splenomegaly (Fig. 8.26), pneumonia, and a catarrhal to hemorrhagic enteritis. Salmonellosis may also result in meningitis and osteoarthritis. In most cases, there is a multifocal to coalescing necrotizing splenitis with nodular aggregates of lymphocytes, macrophages, and heterophils (Fig. 8.27). Bacteria may be present within these foci (Fig. 8.28).

Yersinia

Yersinia pseudotuberculosis, which is a gram-negative, nonspore-forming, rod bacterium with a zoonotic potential, is indigenous to Europe and the Soviet Far East but has a worldwide distribution. The organisms can be found in water and on vegetables and fish. Free-living birds and rodents that have access to aviaries are considered to be significant reservoirs of *Y. pseudotuberculosis*. Toucans are reported to be very susceptible. It has been incriminated in major epornitics in canaries, lorikeets, and mynahs.

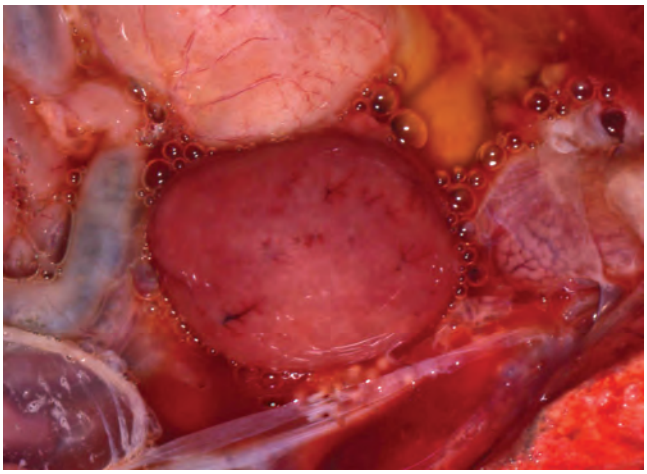

Figure 8.26 Splenic enlargement and variable pallor in a macaw with salmonellosis.

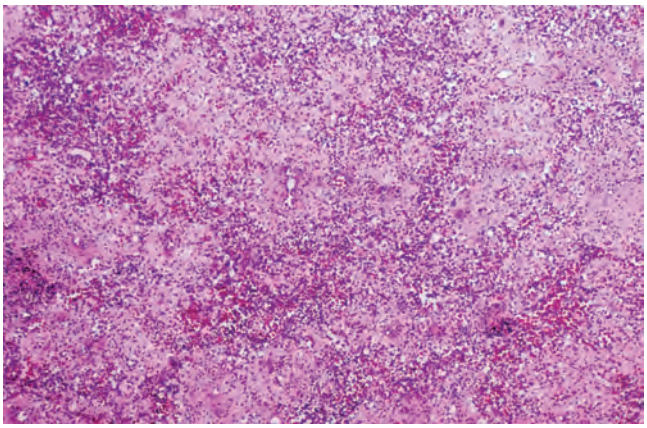

Figure 8.27 Multifocal to confluent splenic necrosis in a bird with salmonellosis.

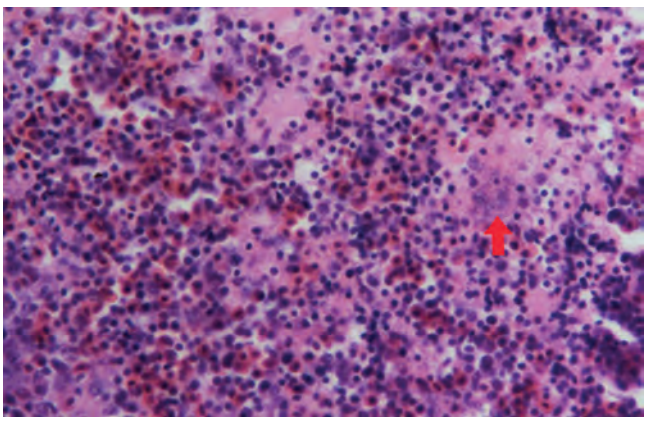

Figure 8.28 Detail of necrotic area containing clumps of bacteria (basophilic material, arrow).

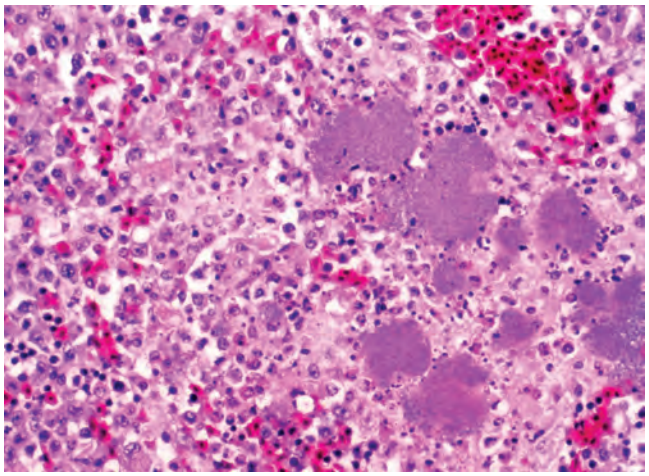

Figure 8.29 Splenic necrosis and numerous large bacterial colonies typical of *Yersinia* infection.

The disease in birds is an acute septicemia, followed by a chronic focal infection, with caseous swellings and nodules resembling avian tuberculosis.

Postmortem lesions include focal necrosis and miliary abscesses of the liver and spleen, as well as a severe catarrhal or hemorrhagic pneumonia. In canaries and related passerine species, there is an impressive swelling of the spleen. Histologically the spleen has irregular multifocal to coalescing areas of necrosis characterized by central cores supporting large numbers of bacteria in a granular eosinophilic matrix and surrounded by a band of degenerate macrophages and cell debris (Fig. 8.29).

Coxiella burnetii. *Coxiella burnetii* is an obligate, intracellular, gram-negative bacterium that typically replicates within phagocytes of the host. It is zoonotic being the causative agent of Q fever in humans. The organism is resistant to drying and able to survive in the environment for long periods of time and it can be transmitted through arthropod vectors such as ticks and lice. Outbreaks with high morbidity and mortality are recognized in a variety of psittacines and a toucan. Progressive neurological signs such as hemiparesis and seizures with weakness and lethargy are common clinical presentations. Grossly both the liver and spleen are greatly enlarged and pale. The histologic lesions are lymphohistiocytic microgranulomas and mixed inflammation in multiple organs: liver, spleen, heart, and brain. These histologic lesions resemble chlamydial infections. Gimenez and variably PAS stain will highlight multiple 1–4 μm intracytoplasmic inclusions within macrophages. The microbes do not stain with Fite acid fast, Warthin–Starry, Brown and Brenn, or Giemsa. Coxiella IHC assays do not react with avian samples. The organisms within macrophages are round to rod-shaped prokaryotic organisms with a trilaminar cell wall by electron microscopic examination. A peripheral zone of loosely arranged electron dense material is present beneath the membrane (Fig. 8.30).

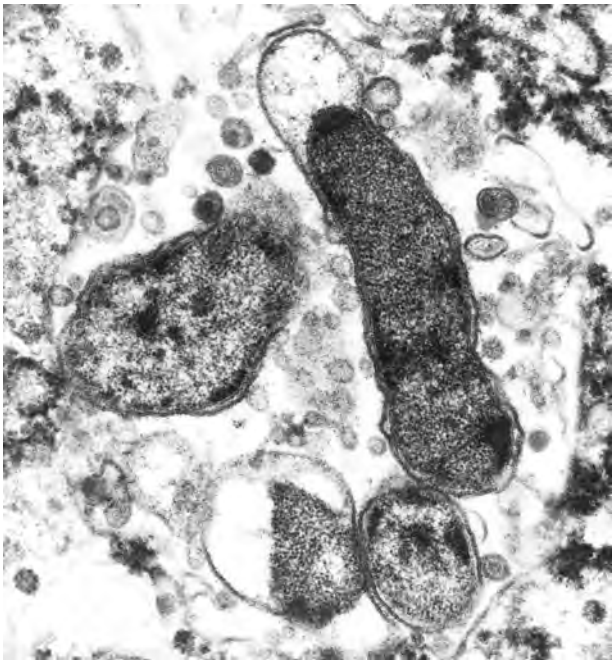

Figure 8.30 *Coxiella burnetii* in a macrophage. Electron microscopy may be one of the few ways to make a conclusive diagnosis.

Other bacterial splenitis

Both systemic and localized bacterial disease may affect the spleen. With bacteremias, the spleen will enlarge and appear deep red with vascular congestion. The bacteremia usually results in peracute to acute lesions with the bacterial organisms confined to the vascular spaces. Peracute lesions may result in perivascular edema and fibrin deposition, and an associated vasculitis characterized by numerous heterophils transmigrating across necrotic vessel walls. The acute lesions will include random foci of acute necrosis characterized by cell debris supported in lacy to homogeneous eosinophilic matrix that may be infiltrated with small numbers of heterophils. Erythrophagocytosis and histiocytic hemosiderin may be present.

Lymphocytic depletion or lymphoid hyperplasia with a plasmacytosis may occur. Heterophils may be a prominent cell type in spleens from birds with systemic bacterial disease. Bacteria may be present within multifocal areas of acute necrosis composed of pools of homogeneous eosinophilic material that represent hemorrhage, fibrin, edema, and cell debris.

Some bacterial organisms will produce more chronic lesions of granulomas. These will have a central core of bright granular material that is proteinaceous fluid or fibrin-supporting cell debris and surrounded by variable numbers of macrophages, degenerate heterophils, and occasional multinucleated giant cells (Fig. 8.31).

Mycobacteria

Mycobacteria are acid-fast and weakly gram-positive rods. The typical gross lesions are of organ enlargement, especially the liver

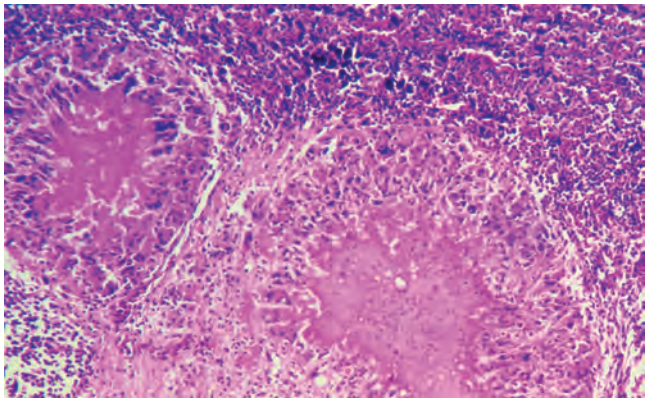

Figure 8.31 Chronic bacterial splenitis with granuloma formation.

and spleen (Fig. 8.32), and variably a regional thickening of the intestines. Multiple focal to large coalescing firm, white masses may develop through the coelomic body cavity. In pet birds, the nodular masses (tubercles) do not calcify. The granulomas and granulomatous inflammation are commonly found in the liver, intestine, spleen, lung, air sacs, and, uncommonly, bone marrow and kidney.

The splenic parenchyma will be effaced by proliferation of macrophages, lymphocytes, and plasma cells, with granulocytic extramedullary hematopoiesis (Fig. 8.33). Mott cells with numerous intracytoplasmic globular pale eosinophilic pigments are not uncommon within the cell population. Multifocal granulomas and/or foci of necrosis within the splenic parenchyma are characterized by central cores of granular eosinophilic background matrix-supporting cell debris and surrounded by vacuolated macrophages as well as infiltrates of mixed inflammatory cells. Multinucleated giant cells may surround a number of these granulomas (Fig. 8.34). Outlines of rod-shaped bacteria may be

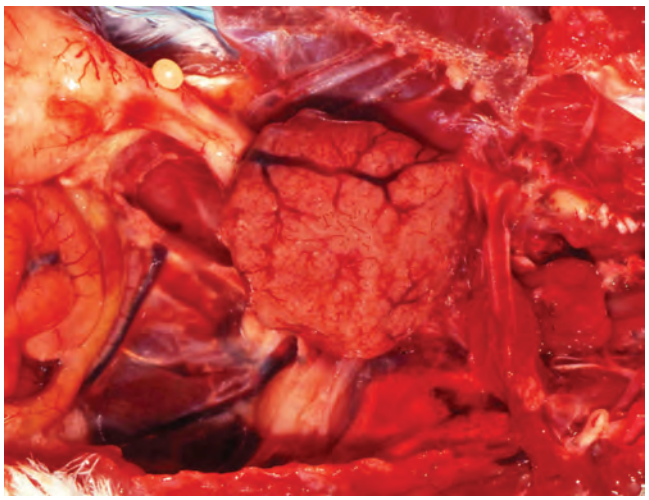

Figure 8.32 Markedly enlarged, pale spleen from a bird with avian mycobacteriosis.

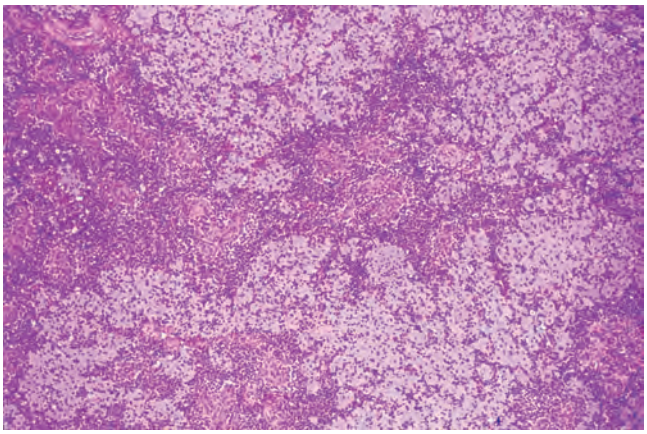

Figure 8.33 Early mycobacterial infection with lymphoid depletion and macrophage infiltration. Organisms may not be found on special stains in early inflammatory lesions.

recognized within the cytoplasm of macrophages as well as identified within the core of the granulomas on hematoxylin–eosin preparations.

Chlamydia psittaci

Chlamydial infections in birds commonly cause splenomegaly. The spleen may range from dark red to purple, a change characteristic of a congested spleen. Alternatively the spleen may be pale as the result of increased numbers of histiocytes and plasma cells (Fig. 8.35). On histologic examination, the single most consistent lesion is histiocytosis. There will be hyperplasia of histiocytes of the perivascular sheaths and a diffuse proliferation of plasma cells. Occasionally chlamydial organisms can be recognized as punctate basophilic structures within the cytoplasm of macrophages. Special stains are often necessary to demonstrate these bacteria. Fluorescent antibody and Gimenez staining of impression smears of the spleen are sensitive and rapid means of identifying this infection. PCR assays of splenic swabs

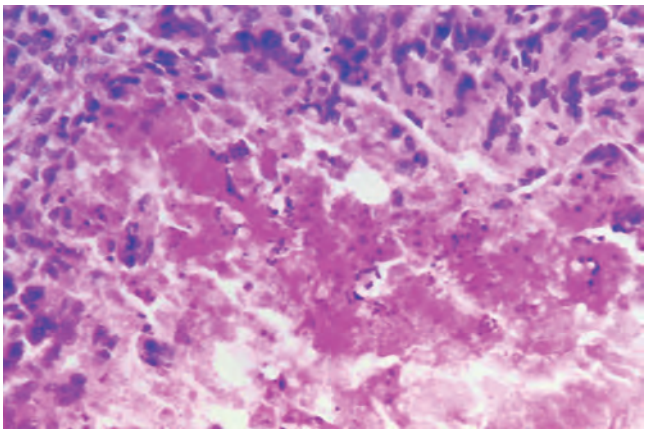

Figure 8.34 Chronic avian mycobacteriosis with granuloma formation. Organisms will be seen on special stains at this stage of the infection.

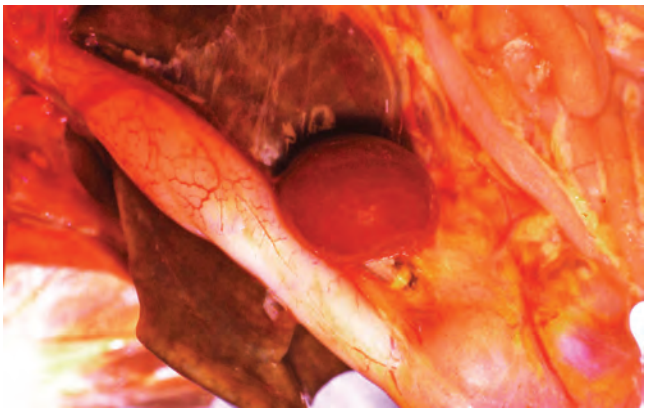

Figure 8.35 Splenic enlargement and minimal necrosis (small white foci) as a part of systemic *Chlamydophila* infection.

are also valuable diagnostic tools. The differential diagnosis for the lesions can include chronic bacterial infections and *Sarcocystis*.

Protozoal disease

Atoxoplasmosis

Atoxoplasma is an apicomplexa coccidian with a prolonged life cycle involving the reticuloendothelial system and intestinal epithelium. It is more commonly recognized as a pathogen of passerines. Asexual reproduction (merogony) occurs in the intestinal and blood cells and in the lymphocytic/histiocytic system. Sexual (gametogony) reproduction occurs in enterocytes. The primary gross lesion is the great enlargement of the spleen (Fig. 8.36) and occasionally the liver. The small intestines may be edematous and congested. The spleen will have a profound

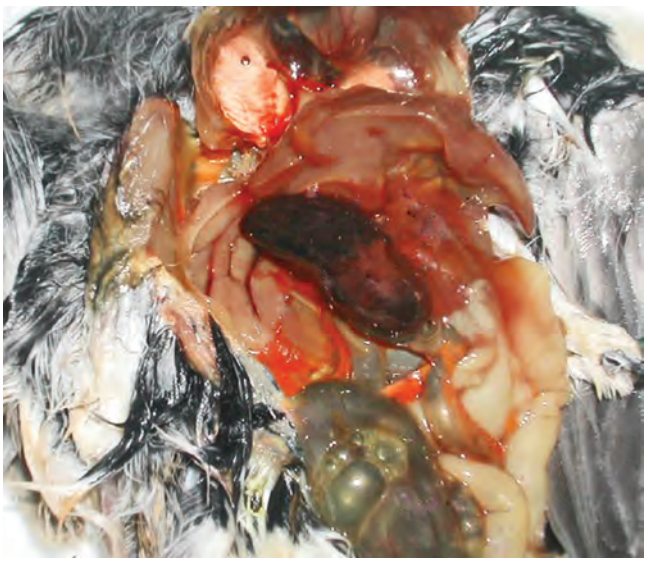

Figure 8.36 Canary with atoxoplasmosis. The spleen is enlarged and congested.

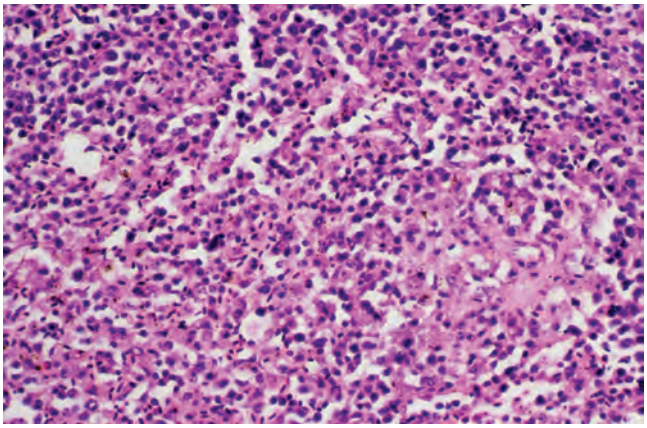

Figure 8.37 *Atoxoplasma* infection with splenic lymphoid depletion and histiocyte infiltration. Organisms are usually difficult to see.

lymphohistiocytic inflammatory response. Mononuclear infiltrates will be present in the liver and lamina propria of the intestines. Oocysts may be recognized in epithelial cells of the intestinal mucosa. Macrophages within the spleen that have an intracytoplasmic, 3- to 5-µm diameter, poorly stained organism indenting the host nucleus can occasionally be found by careful examination (Fig. 8.37). *Atoxoplasma* organisms are readily identified on exfoliative cytology imprints of the spleen and lung (Fig. 8.38). A PCR assay for this organism is commercially available.

Malaria (Plasmodium)

Plasmodium is one of the three avian blood parasites that have life cycles with a schizogenous tissue phase and gametogenous sexual phase in host erythrocytes. It has an additional asexual replication phase in erythrocytes, where invading merozoites develop into trophozoites and then undergo schizogony and produce hemozoin. Briefly the life cycle includes a female mosquito that bites a bird and releases sporozoites, which form cryptozoites at the point of entry. The first-stage exoerythrocytic schizogony (asexual reproduction) occurs in tissue macrophages adjacent to the mosquito bite. From here, the merozoites develop into metacryptozoites and can infect erythrocytes and other cells such as endothelial cells (*P. relictum*) and hematopoietic cells (*P. elongatum*). In erythrocytes, the merozoites round up, form trophozoites, and undergo schizogony, during which they incompletely catabolize hemoglobin, leaving a brown pigment, hemozoin, within food vacuoles. Trophozoites can produce more merozoites as well as differentiate into gametocytes. Merozoites will continue on to infect other cells. With infections of nonadapted hosts, the exoerythrocytic schizogony is more prominent, and merozoites from erythrocytic schizonts are able to infect cells of the reticuloendothelial system.

Although there are 25 *Plasmodium* species of birds, these parasites rarely cause disease in psittacines. Some *Plasmodium* can be associated with significant disease in gyrfalcons, peregrines, penguins, and canaries. The liver and spleen can be black in some infected birds, particularly raptors (Fig. 8.39). Hepatosplenomegaly and pulmonary edema are common gross lesions. The most striking histologic lesion is exoerythrocytic schizogony in the lungs, spleen, liver, and other organs. The parasitic hemozoin pigment, which is dark brown and coarsely granular, can be identified in Kupffer cells and histiocytes of the spleen along with intracellular schizonts (Fig. 8.40). The pigment is birefringent and iron negative. A marked histiocytic and plasmacytic splenitis develops. In some species pigment is minimal and there is no gross color change.

Sarcocystis

Sarcocystosis is predominantly a disease involving the skeletal muscle and lung. An extensive description of this disease is

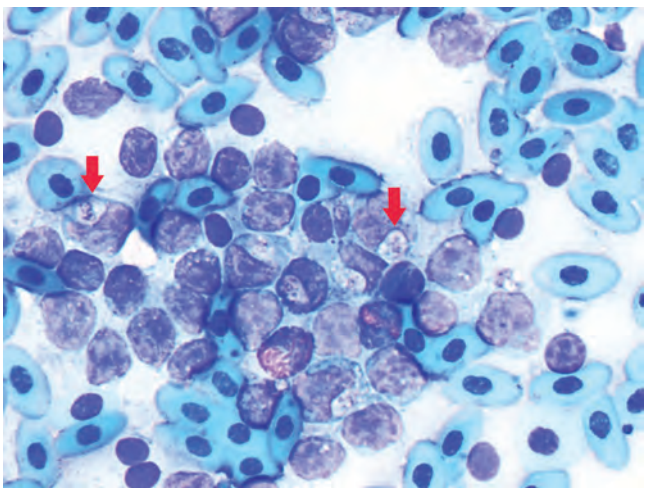

Figure 8.38 Splenic impression smear illustrating *Atoxoplasma* organisms indenting the nuclei of macrophages (arrows).

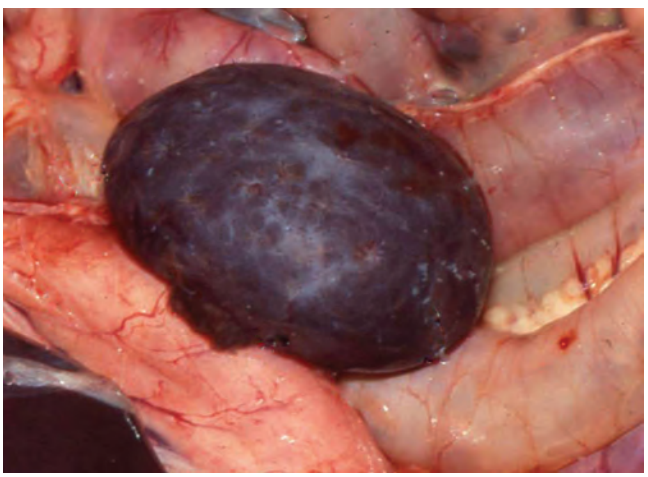

Figure 8.39 Enlarged dark spleen from a falcon with malaria (*Plasmodium* sp.).

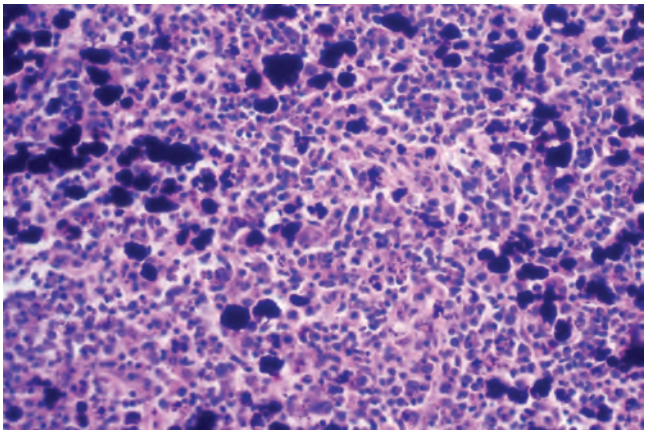

Figure 8.40 Macrophages containing malaria pigment in the spleen. The pigment is seen primarily in raptors but not in small passerines with the infection.

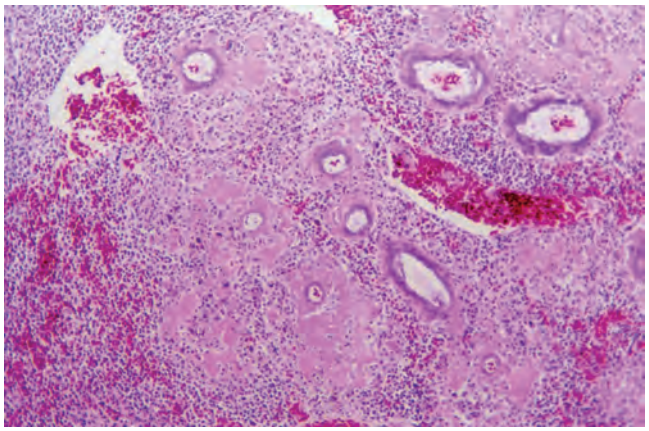

Figure 8.42 Mild splenic amyloidosis primarily involving the walls of blood vessels.

provided in Chapter 2. Birds surviving the acute pulmonary disease develop a histiocytic, plasmacytic splenitis (Fig. 8.41).

Degenerative disease

Amyloid

This is an insoluble pathologic proteinaceous substance deposited between cells in various tissues and organs of the body. In birds, the amyloid is usually considered to be secondary. This amorphous, eosinophilic, hyaline, extracellular substance encroaches on, and results in, pressure atrophy of adjacent cells. Systemic amyloidosis has been reported in finches, in captive domestic and wild Anseriformes especially of the Anatidae family (swans, geese, and ducks), and in gallinaceous birds (domestic fowl and turkeys). The incidence in Pekin ducks ranges from 5% to 40%. Amyloidosis is less common in psittacine birds but, when it does occur, generally involves both the spleen and the kidney. In finches, amyloid deposition is more common in the liver and spleen. The presence of amyloid can be confirmed with special stains (e.g., Congo red) and by examination under polarized light.

Grossly the spleen will appear pale and will be firm when sectioned. Amyloid is a homogeneous, pale, eosinophilic to amphophilic material. It may be found randomly within the splenic parenchyma expanding and filling spaces. Deposits may thicken the basement membranes of blood vessels (Fig. 8.42) or accumulate around the periarterial sheaths and extend into the surrounding parenchyma (Fig. 8.43).

Hemosiderin

The accumulation of this iron-containing pigment is typically due to previous hemorrhage (including hemolytic anemia) or severe tissue congestion resulting in breakdown and phagocytosis of the red blood cell debris. Impaired use of iron, such as from systemic bacterial infections or from anemia of chronic disease, also leads to the increased presence of hemosiderin.

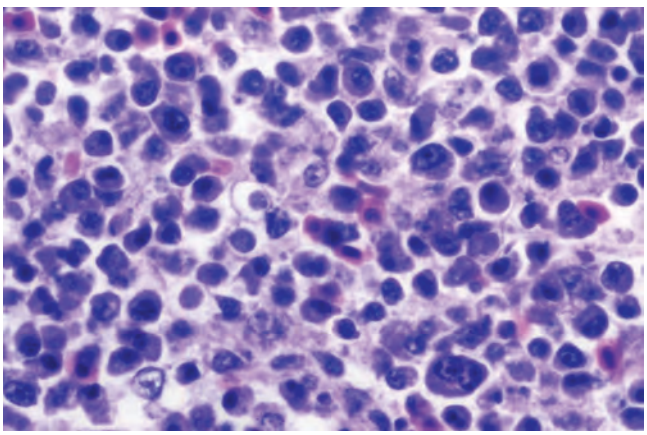

Figure 8.41 Mixed mononuclear infiltrate in the spleen of a bird with systemic sarcosporidiosis. The infiltrate is similar to that seen in *Chlamydia* infection, and organisms are usually not seen.

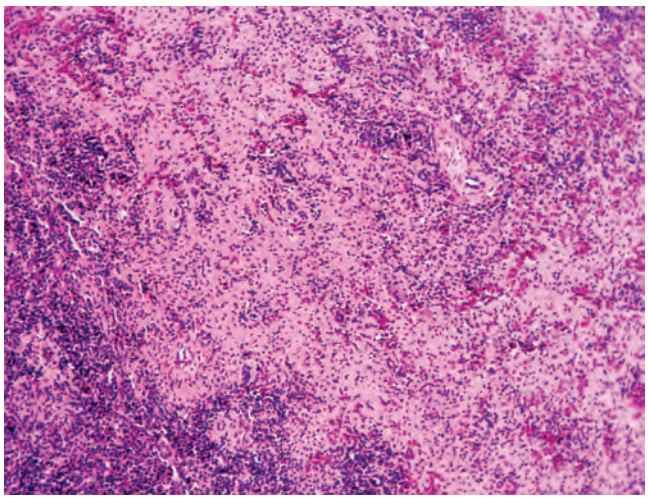

Figure 8.43 Severe splenic amyloidosis with marked tissue effacement.

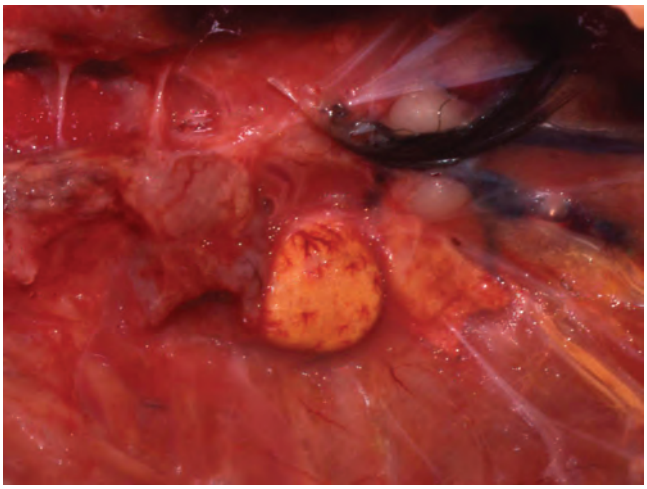

Figure 8.44 Severe splenic lipidosis (fat accumulation) in a bird with severe liver disease.

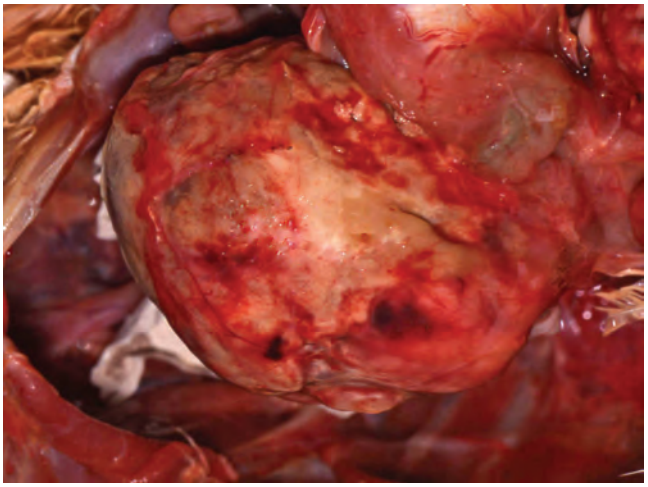

Figure 8.46 Extremely enlarged and discolored spleen due to systemic malignant lymphoma.

This is a common mechanism in pet birds. In the spleen, hemosiderin accumulates within sinusoidal macrophages. It is a golden brown granular cytoplasmic pigment that stains positive with Prussian blue.

Histiocytic lipid accumulation (splenic lipidosis)

Affected spleens are small and yellow (Fig. 8.44). This is due to the presence of histiocytes with a vacuolated cytoplasm in the spleen of pet birds that seems to be associated with chronic liver disease or reproductive disease in female birds. The majority of histiocytes throughout the splenic parenchyma and periarterial sheaths are expanded with a finely vacuolated cytoplasm to coalescing vacuoles (Fig. 8.45). Commonly, in the liver, both hepatocytes and Kupffer cells will also be enlarged, with cytoplasmic vacuolization. The lesion suggests altered fat metabolism.

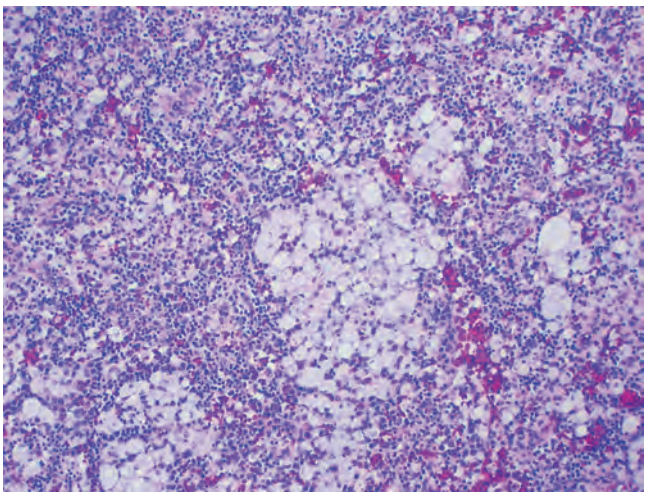

Figure 8.45 Infiltration of the spleen by macrophages containing lipid in their cytoplasm.

Neoplastic disease

Lymphoma

Multicentric lymphoma is the most common lymphoid neoplasia in psittacine and passerine birds. Diffuse or nodular involvement is characteristic of pet-bird lymphosarcoma (Fig. 8.46). Organs typically infiltrated include liver, spleen, kidneys, skin, bone marrow, gastrointestinal tract, thyroid gland, oviduct, lungs, sinus, thymus, testes, brain, mesentery, trachea, fat, periorbital muscles, and pancreas. The liver is most frequently involved, followed by the spleen and kidneys. These organs generally are enlarged and pale. Other diseases that grossly resemble visceral lymphosarcoma include amyloidosis, fatty liver syndrome, atoxoplasmosis (in mynahs and canaries), hepatitis, systemic mycobacteriosis, and other neoplasms. It is not uncommon for birds to also have secondary infections such as fungal pneumonia. Rarely hypercalcemia has been reported as a paraneoplastic syndrome in T-cell lymphoma in two Amazon parrots. A monoclonal hyperglobulinemia has also been recognized in a small number of cases.

Impression smears will contain large lymphoblastic cells that have replaced normal parenchyma (Fig. 8.47). Histologically a solid sheet of a uniform population of lymphoblasts and mature lymphocytes effaces the splenic architecture. The lymphoblastic cells have a large, round to indented vesicular nuclei, one or more prominent nucleoli, and a basophilic cytoplasm (Fig. 8.48). Mitotic figures are common.

Although lymphosarcoma in chickens commonly is associated with retrovirus (avian leukosis virus) or herpesvirus (Marek's) infection, there is no evidence to date of a viral link to the tumor formation in pet birds. Recent molecular investigations suggested a retroviral cause for multicentric lymphosarcoma in a starling. Retrovirus-induced lymphosarcoma has been suspected in other passerine birds, but this remains to be proven.

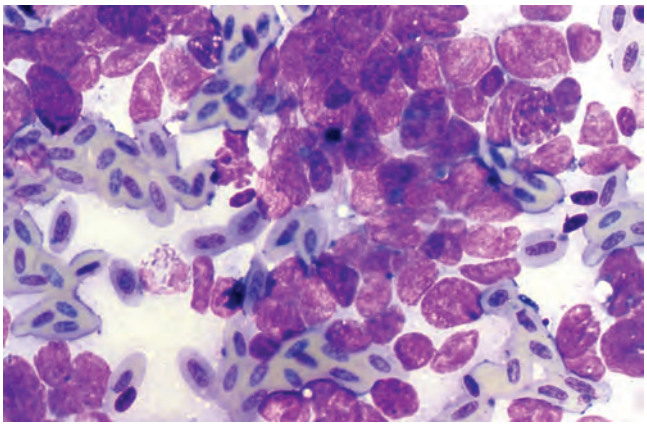

Figure 8.47 Splenic impression smear from a bird with malignant lymphoma. Numerous large, immature lymphoblasts are seen.

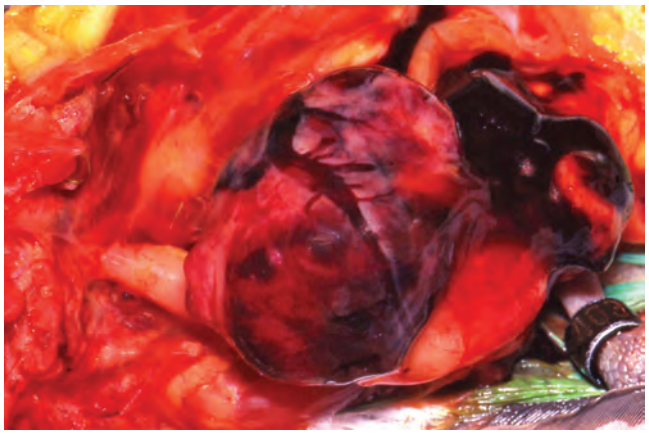

Figure 8.49 Markedly enlarged spleen in a bird with myeloproliferative disease.

Myeloproliferative disorders

Myeloproliferative disorders are neoplastic proliferations of nonlymphoid hematopoietic cells. These neoplastic cells generally infiltrate the spleen, liver, and bone marrow. The infiltration can result in massive enlargement of both the liver and the spleen (Fig. 8.49). In the spleen, the neoplastic proliferation can be difficult to differentiate from excessive granulocytic extramedullary hematopoiesis. The blast forms of the various cell lines are difficult to distinguish on hematoxylin–eosin stains, making it difficult to determine the neoplastic cell line. In poultry, this type of neoplasm is associated with infections by retroviruses of the leukosis/sarcoma group. A viral etiology has not been proven in psittacines.

Hemangioma and hemangiosarcoma

Hemangiomas are benign tumors of vascular endothelium. The malignant version is hemangiosarcoma, also known as malignant hemangioendothelioma or angiosarcoma. Hemangiomas are more commonly reported in budgerigars (*Melopsittacus undulatus*) than in other birds and usually occur in the skin or spleen. They are uncommonly described in larger psittacines. Hemangiosarcomas occur in the skin, liver, myocardium, and metacarpus. With the exception of the budgerigar, they are rarely described in the spleen. They are locally invasive, metastatic, and multicentric. Both tumors are characterized by the formation of vascular channels. The endothelial cells of hemangiosarcomas are less well differentiated than those lining the vascular spaces of hemangiomas (Fig. 8.50).

In chickens, hemangiomas and hemangiosarcomas are induced by a recently described strain of avian retrovirus, avian hemangioma virus (AHV). The typical type C retrovirus particle was demonstrated in the tumor by electron microscopy. Retroviruses or viral particles have not been found by electron microscopy in budgerigar hemangiomas.

Myelolipoma

Myelolipomas are uncommon tumors. They have been reported in the subcutis, spleen, and multifocally in the liver. Myelolipomas behave like lipomas, with slow progressive growth. They are

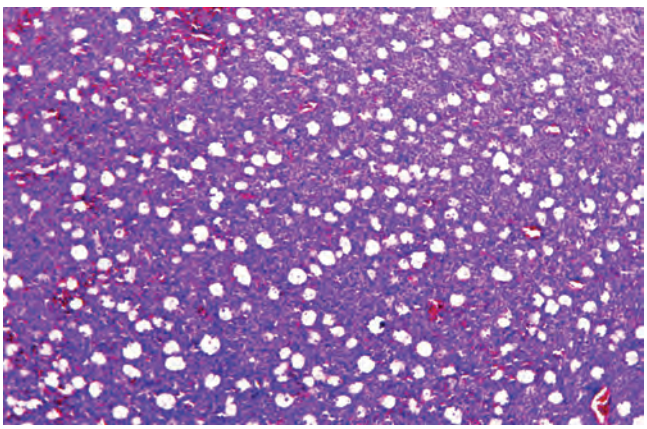

Figure 8.48 Effacement of splenic parenchyma by neoplastic lymphoid cells.

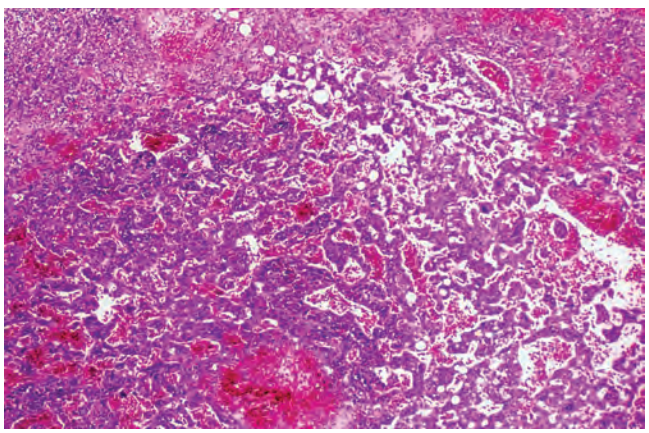

Figure 8.50 Splenic hemangiosarcoma. Irregular vascular channels are separated by proliferating, moderately undifferentiated endothelial cells.

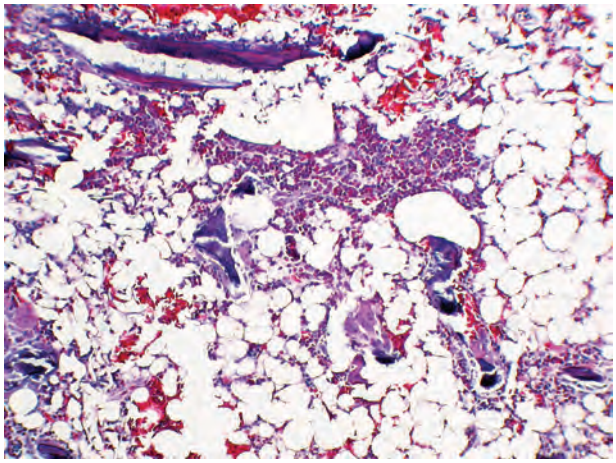

Figure 8.51 Splenic myelolipoma. Histologically these tumors comprise bone marrow elements.

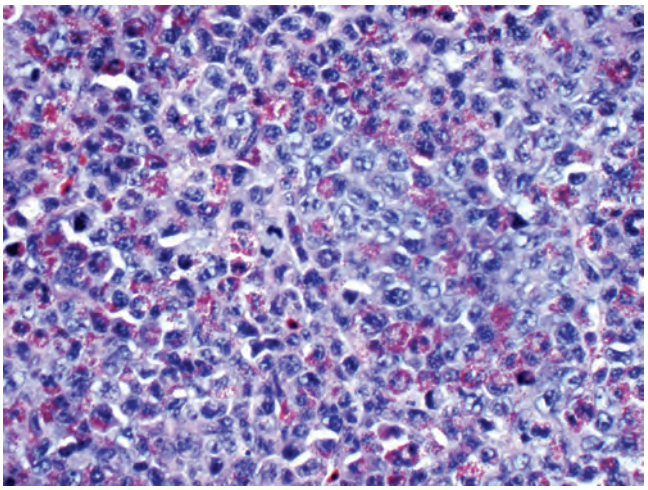

Figure 8.52 Myelocytoma which appears to have primarily heterophilic differentiation.

considered choristomatous (histologically normal tissue in an abnormal location) hematopoietic stem cell elements. Grossly they appear as masses of fat with hemorrhage and can resemble lipomas, xanthomas, and fibrosarcomas. They may contain focal areas of mineralization or bone formation.

Myelolipomas histologically are well-delineated, expansile, benign extra marrow neoplasms composed of varying proportions of fat and hematopoietic cells (Fig. 8.51). The differential diagnoses based on histologic examination of the tumor in the spleen include hemangiolipoma, osseous metaplasia, hematopoietic neoplasms, and extramedullary hematopoiesis. Hemangiolipomas are fatty neoplasms with endothelium-lined vascular channels. They occur as solitary tumors of the skin and ovary in fowl and as a solitary subcutaneous tumor in budgerigars. Osseous metaplasia, the formation of bone from soft tissue, comprises osteoid and spicules of mineralized bone associated with the hematopoietic cells.

Hematopoietic neoplasms (e.g., myelocytoma and myeloblastoma) result from proliferation of a single cell line, with a shift to immaturity (Fig. 8.52). These tumors are relatively common in domestic fowl but rare in exotic birds. Myelocytomas are neoplastic proliferations of nonlymphoid hematopoietic cells of bone marrow origin confined by a fine connective tissue capsule. Rarely this tumor appears as a mass in the skin of psittacines. In the few psittacine cases, one appeared to be arising from the Hardarian gland; however, other masses have not appeared to be associated with a specific organ.

Extramedullary hematopoiesis is a nonencapsulated, dense aggregate of hematopoietic cells that lack a fatty component. Extramedullary hematopoiesis is seen most frequently in the liver, spleen, kidney, yolk sac remnant, and bursa of Fabricius. It is common in birds with chronic bleeding disorders.

Fibrosarcoma

This tumor originates from fibrous connective tissue and is a common neoplasm in birds. Based on literature reports, fibrosarcomas (malignant) appear to be more common than fibromas (benign). The common sites of occurrence include the limbs, face, beak, syrinx, liver, small intestine, cloaca, spleen, air sacs, and lungs. Fibrosarcomas are white-to-gray, raised or rounded firm masses that have indistinct borders within the spleen. The spindle-shaped tumor cells are arranged in bundles forming interwoven fascicles. The cells are numerous and closely placed with indistinct cytoplasmic borders (Fig. 8.53). Fibrosarcomas are locally invasive and have a low to moderate metastatic potential.

Metastatic carcinomas

Metastatic carcinomas to the spleen are rare, with only metastatic gastric carcinoma reported. Gastric carcinomas may reach the spleen from local implants or through the vascular

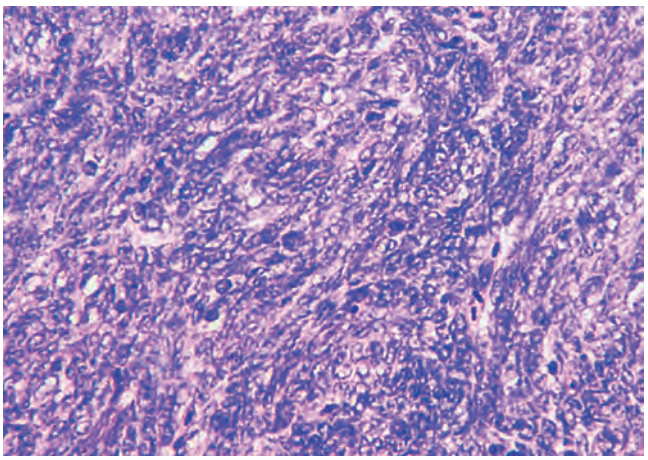

Figure 8.53 Primary splenic fibrosarcoma. Neoplastic cells are poorly differentiated and have indistinct cytoplasmic boundaries.

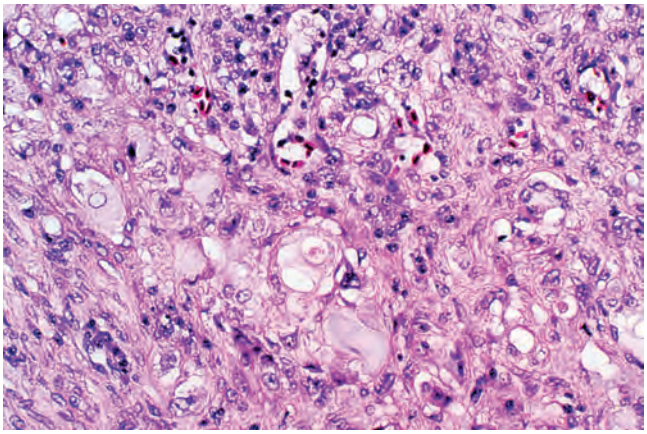

Figure 8.54 Proventricular carcinoma metastatic to the spleen. Tumor cells are individualized, and a few contain mucin in their cytoplasm.

system. In the spleen, gastric carcinomas form irregular tubular structures as well as individualized neoplastic cells. The cells are pleomorphic, with variably distinct cytoplasmic borders and variable amounts of either lacy basophilic pale cytoplasm or deeply granular basophilic cytoplasm. The cell nuclei are variably sized and hyperchromic, with indistinct nucleoli (Fig. 8.54).

Bone marrow

Lesions of the bone marrow are either hypocellular or hypercellular. Interpretation of erythrocytic versus granulocytic responses typically requires comparison with the peripheral blood counts and cytologic examination of the bone marrow cells.

Infectious disease

Inflammatory diseases caused by bacteria including *Chlamydia* and fungi can result in granulocytic hyperplasia (Fig. 8.55). Anemia induced by many disease processes will produce a similar appearance due to erythroid hypoplasia.

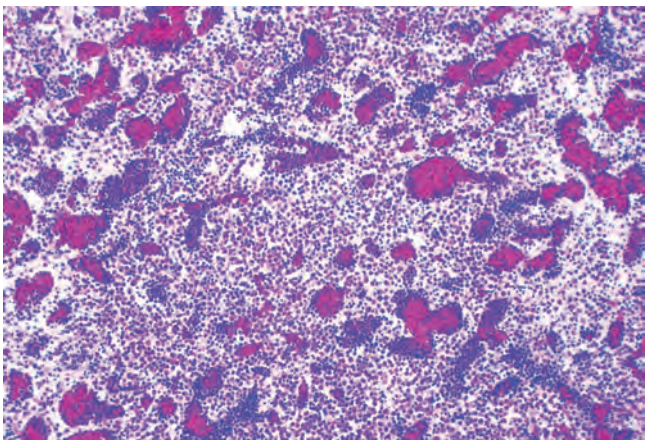

Figure 8.55 Diffuse nonspecific myeloid hyperplasia of the bone marrow.

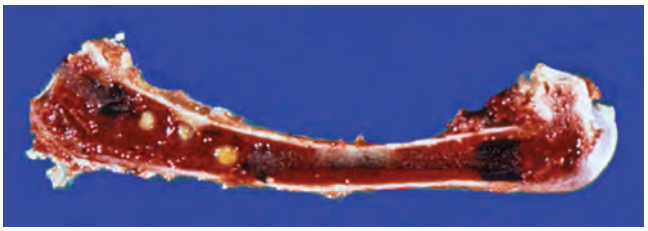

Figure 8.56 Multifocal granulomas in the bone marrow of a chicken with mycobacteriosis.

Mycobacterial infections can result in granuloma formation in the marrow (Fig. 8.56). Histologically severe myeloid hyperplasia and bone marrow infiltrations of macrophages are seen in early phases of the disease (Fig. 8.57). With chronicity focal collections of large macrophages containing cytoplasmic organisms may also be found (Fig. 8.58). The macrophages will eventually replace normal marrow (Fig. 8.59).

Bone marrow hypoplasia is described with several viral infections. Severe leukopenia and anemia from bone marrow hypoplasia is common in young African gray parrots and pigeons infected with circoviruses. Occasionally the typical cytoplasmic basophilic to amphophilic globular inclusions can be found in histiocytic-type cells. Other viruses have been isolated from bone marrow; however, specific lesions are not described. These viruses include herpesvirus, poxvirus, reovirus, and avian polyomavirus.

Toxins

A number of toxins can result in bone marrow hypocellularity. Ochratoxin A produced by *Aspergillus ochraceous* results in bone marrow depression, as does sulfaquinoxaline and cisplatin (*cis*-dichlorodiammineplatinum(II)) toxicity. The myelosuppression of cisplatin is suspected to be due to binding and cross-linking of DNA, with interference of DNA replication. At published dosages for birds, several benzimidazoles, such as fenbendazole,

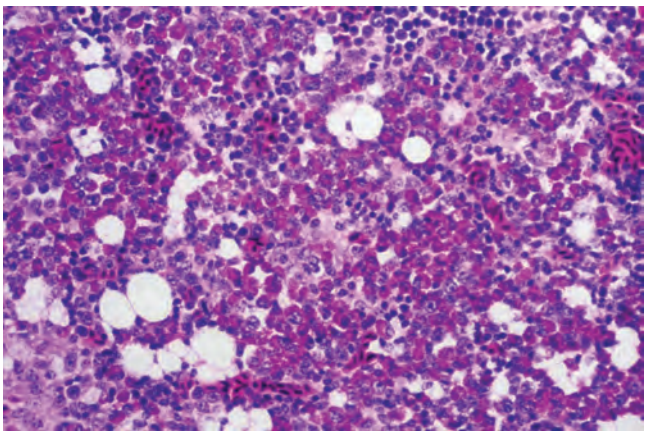

Figure 8.57 Severe myeloid hyperplasia and early macrophage infiltration of the marrow in a bird with avian mycobacteriosis.

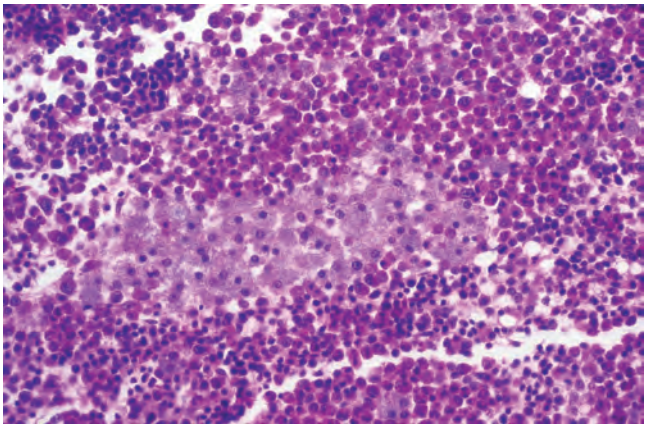

Figure 8.58 Avian mycobacteriosis with a focal collection of large macrophages containing mycobacteria in their cytoplasm.

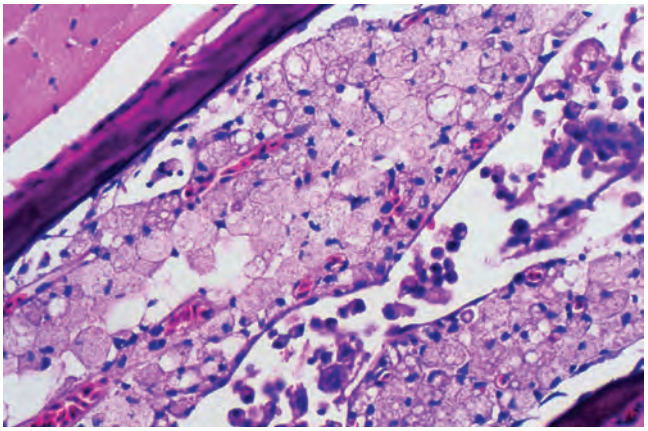

Figure 8.60 Xanthoma of the bone marrow. On routine sections, this must be differentiated from mycobacterial infection (Figure 8.59).

result in a marked heteropenia followed by a progressive anemia and bone marrow suppression. The inhibition of microtubule polymerization is suspected of interfering with mitosis in rapidly dividing cells of the bone marrow and the mucosa of the gastrointestinal tract.

Lead poisoning interferes with several stages of heme synthesis. It acts to inhibit delta-aminolevulinic acid dehydratase, heme synthetase, and the delivery of iron to the site of ferrochelatase action. The bone marrow will be hypocellular, with a marked decrease in mature erythrocytes and an increase in early and late polychromatic erythroblasts. Mitotic figures will be common. In birds, the nuclei of the erythrocytes may serve as lead-storage sites. Grossly the bone marrow can appear fatty or edematous. Other lesions of lead toxicity include hepatocyte necrosis and Kupffer cell hemosiderosis, nephrosis and sloughing of renal tubular epithelium with variable acid-fast intranuclear inclusion bodies in the cells of the proximal convoluted tubules, degeneration of the heart, pectoral skeletal muscles and muscular tunics of the ventriculus, neuronal degeneration of the brain and meningeal edema, and degenerative changes in peripheral nerves (vacuolated myelin sheath with rare swollen axonal segments).

Proliferative disease

Xanthoma

Xanthomas are not neoplasms but are locally invasive and appear as masses commonly in the skin. They rarely occur in internal organs and even more rarely have been identified within the bone marrow. The masses are of foamy macrophages, multinucleated giant cells, and cholesterol clefts (Fig. 8.60). Xanthomas have been reported most frequently in psittacine and gallinaceous birds. They are considered common in cockatiels and female budgerigars.

Neoplastic disease

Myeloproliferative disorders

Myeloproliferative disorders are neoplastic proliferations of nonlymphoid hematopoietic cells that originate in the bone

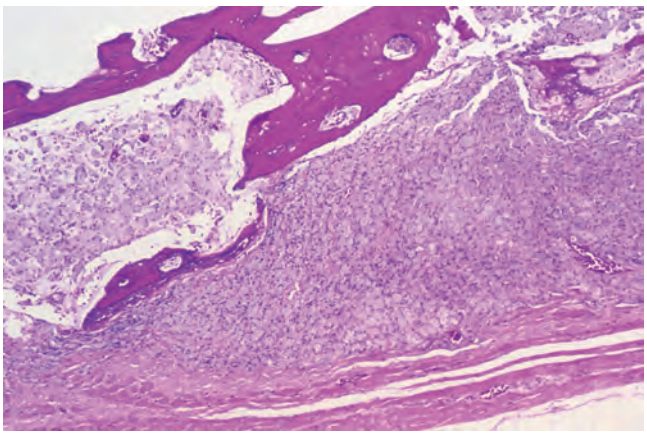

Figure 8.59 Severe avian mycobacteriosis. Diffuse replacement of bone marrow by large macrophages containing acid-fast bacteria.

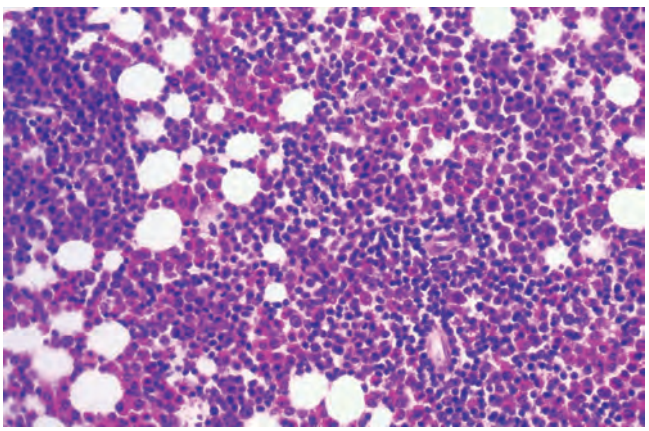

Figure 8.61 Myeloproliferative disease. Monomorphic immature myeloid cells replacing normal marrow elements.

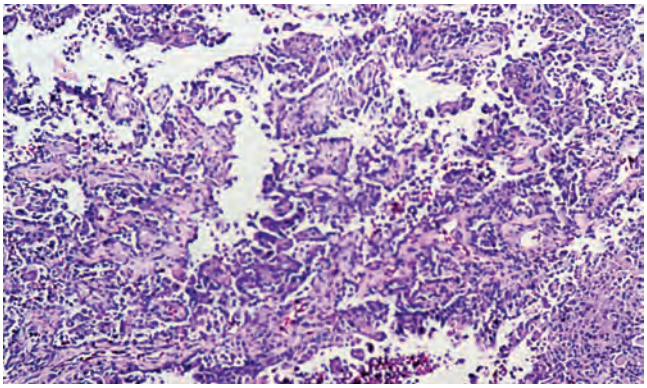

Figure 8.62 Hemangiosarcoma of the marrow. Primary bone involvement may be seen in some cases.

marrow. These neoplastic cells generally infiltrate the spleen, liver, and bone marrow. Hematopoiesis is suppressed by marked proliferation of tumor cells in the bone marrow (Fig. 8.61). Since blast forms of the various cell lines are difficult to distinguish on hematoxylin–eosin stains, other cytochemical stains are required to identify the neoplastic cell line. Although in poultry this neoplasm is associated with retrovirus infections, a viral etiology has not been proven in psittacine birds.

Hemangiosarcoma

Hemangiosarcomas, also known as malignant hemangioendotheliomas or angiosarcomas, are malignant tumors of vascular endothelium. In birds, they are locally invasive, metastatic, and multicentric. In the diaphysis of long bones, they have an aggressive osteolytic, radiographic appearance. Histologically they are typical of hemangiosarcoma in any location (Fig. 8.62).

Leukemia

Lymphocytic leukemia is characterized by effacement of the bone marrow with neoplastic lymphocytes. Chronic lymphocytic leukemia (CLL) is recognized in birds (macaw, Amazon parrot, and black swan) and typically they have a peripheral lymphocytosis, a large population of well-differentiated lymphocytes in the bone marrow, and few clinical signs. Of the birds examined using immunohistochemistry, the neoplastic cells were determined to be of T-cell origin. The immunohistochemistry was positive CD-3 antibody and negative for Bla.36 or CD79a. The neoplastic lymphocytes also infiltrated the liver, spleen, and kidney.

Metastatic tumors

Only one metastatic neoplasm to the bone marrow has been reported in pet birds. A leiomyosarcoma, which presented as a nodular growth attached to a rib cage, developed metastases to the bone marrow. This tumor also had metastases in the liver, spleen, and kidneys. The primary site was not determined.

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9 Musculoskeletal System

Skeletal muscle

Normal structure

Birds have both red and white muscle fibers, both of which are found in most muscles. Red and white fibers are differentiated by their myoglobin content. In the pectoral muscles of birds like the hummingbird, there may be only red fibers, which fatigue slowly. Two-joint muscles, which span two articulations between their origin and insertion, comprise most of the important strong muscles of birds. Histologically, avian skeletal muscle resembles mammalian skeletal muscle.

Near-hatch chicks and recently hatched chicks have a prominent pipping muscle extending from the top of the head down the back of the neck (Fig. 9.1). The myofibers in the other skeletal muscles in these chicks will be of similar number to the adult bird, but will be thin (Fig. 9.2).

Disease

Congenital disease

Muscular dystrophy is reported in chickens and turkeys but not in pet birds. The lesion is characterized by irregular atrophy, with myofibers lost and replaced by fat. The number of nuclei is increased, and fiber size is reduced.

Arthrogryposis is a term for congenital flexure or contracture of joints secondary to failure of proper skeletal muscle development (Fig. 9.3). There is atrophy of muscles that is secondary to congenital neurologic problems. Affected myofibers are lost and replaced by fibrous tissue. The condition can also be secondary to exposure to alkaloids from plants such as tree tobacco (*Nicotiana glauca*), lupines (*Lupinus* sp.), and poison hemlock (*Conium maculatum*) during development.

Noninflammatory disease

Atrophy

Muscle atrophy is a common reaction to many conditions, including disuse, denervation, generalized chronic disease, local compression, and aging. Grossly there is a diminution of muscle size (Figs. 9.4 and 9.5). In birds, particularly budgerigars, disuse atrophy may occur secondary to nerve compression caused by renal tumors.

Histologically a decrease in fiber size and cross-sectional area alterations of contractile elements is seen. There may be shrinkage of the plasma membrane, which pulls away from the external lamina, which in turn may become convoluted. The sarcoplasmic reticulum becomes more prominent, as do other organelles.

Hypertrophy

This is usually a compensatory change that results in an enlarged muscle mass. There may be increased numbers of fibrils, but histologic changes are often difficult to detect.

Steatosis

This is seen sporadically in birds, particularly obese Amazon parrots and other obese psittacine birds. An extensive increase in intramuscular fat, with replacement of myofibers, is noted. The cause is usually malnutrition, but metabolic disorders should be considered.

Trauma

Trauma results in hemorrhage, edema, and gross disruption of muscles. Extensive bruising of muscle is expected when birds strike windows, and wild birds that are hit by cars. Some degree of muscle injury is nearly always present in birds that have sustained bone fractures. Bite wounds from dogs or foxes in poultry will cause muscle damage and can result in extensive gangrenous changes if the birds survive. In general, traumatized muscle may become yellow-brown with chronicity (Fig. 9.6). The extent of the muscle reaction will depend on whether the injured area develops a secondary infection. Muscles surrounding a penetrating cat bite will be dry and have a cooked appearance if the wound becomes septic. Intramuscular injections usually lead to some necrosis (Fig. 9.7.) and mononuclear inflammatory infiltration, with macrophages, lymphocytes, plasma cells, and giant cells present in severe reactions. Free and phagocytosed amorphous material with variable tinctorial properties may be seen. The extent of the muscle necrosis varies with the nature and volume of the drug. Enrofloxacin is a commonly used antibiotic that is very irritating to muscle if given undiluted.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

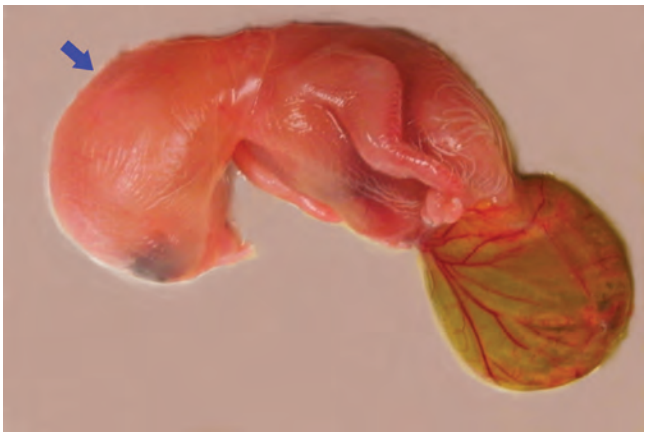

Figure 9.1 Normal pipping muscle (arrow).

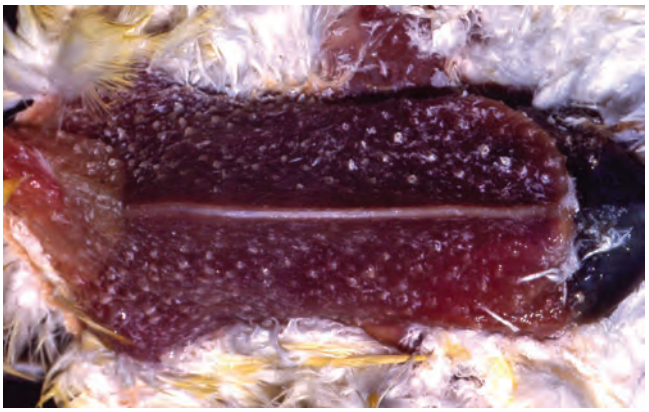

Figure 9.4 Marked atrophy of pectoral muscle (ventrodorsal view). Pectoral muscle atrophy can be associated with inadequate energy intake or chronic disease. Note that there is a slight serpentine deviation of the spine suggesting a mineral deficiency or imbalance in this bird as it was growing.

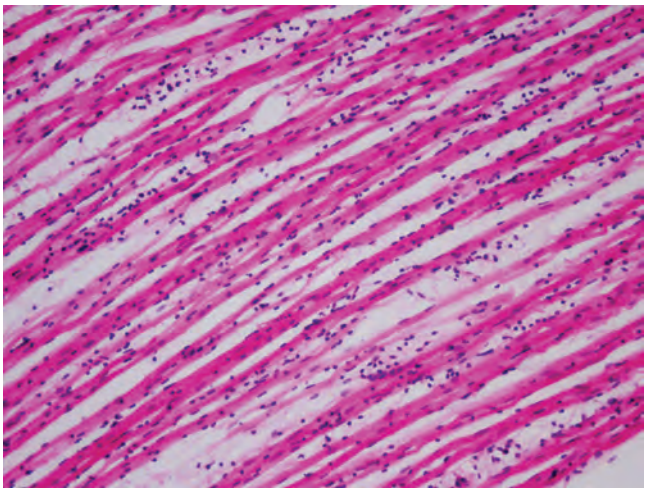

Figure 9.2 Normally thin myofibers in the pectoral muscle of a recently hatched chick. Note this chick was edematous and edema fluid separates the fibers.

Figure 9.5 Marked atrophy of the pectoral muscle (lateral view).

Figure 9.3 Multiple congenital joint flexures secondary to improper skeletal muscle development.

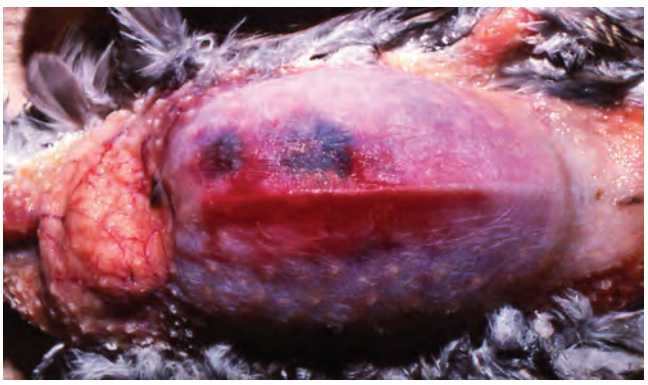

Figure 9.6 Focal area of traumatic hemorrhage and necrosis in the pectoral muscle.

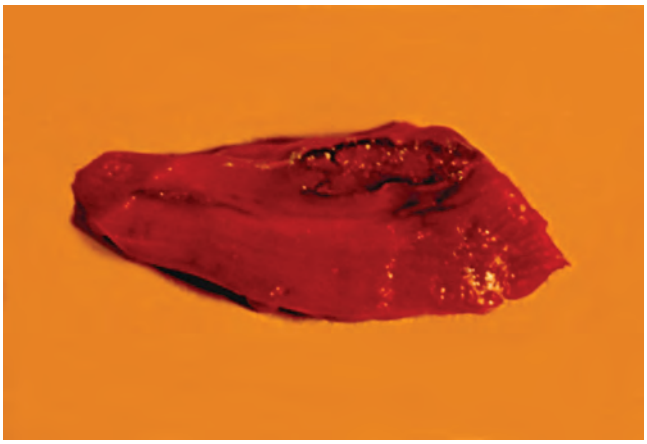

Figure 9.7 Muscle necrosis resulting from an intramuscular injection of an irritating drug.

Figure 9.8 Large area of pale pectoral muscle fibers in a bird with vitamin E deficiency.

Nutritional disease

Pectoral muscle mass is an important indicator of how long a bird had been in a catabolic state prior to death. Birds that die acutely will have substantial body fat, adequate heart fat, and a robust pectoral muscle mass. Subacute disease with decreased food consumption will result in a loss of heart fat, followed by muscle wasting. Birds with chronic disease often have severe loss of pectoral muscle mass. The rate of loss of pectoral muscle mass is at least, in part, proportional to the size of the bird. Smaller birds with higher metabolic rates lose fat and muscle mass faster than larger species. Typically, however, a robust, medium-sized parrot that is not eating or eating very little will lose most of its pectoral muscle in 5–7 days.

Vitamin E or selenium deficiencies are implicated in muscle disease in piscivorous birds that are fed a diet of improperly frozen and thawed fish. Any diet containing rancid polyunsaturated fat may cause similar lesions. A similar disease is seen in other species of birds, including companion birds.

Gross lesions of vitamin E and selenium deficiency are white streaks and patches in striated muscle (Fig. 9.8). Histologic changes include muscle fiber degeneration without inflammation. Individual fibers may be enlarged and hypercontracted, with loss of striations and with hypereosinophilia (Fig. 9.9). Fibers eventually become shrunken and fragmented, and there may be an infiltration of macrophages that phagocytose necrotic debris. Fibrosis and mineralization can be seen in chronic lesions (Figs. 9.10, 9.11, and 9.12). Myocardial, hepatic, and central nervous system lesions may also accompany the muscle lesions (Chapters 4 and 10).

The great-billed parrot is an uncommon avicultural species that has experienced a high mortality rate in captivity. A review of necropsies of these birds (D. Phalen 2001, unpublished data) shows that most have some degree of skeletal and cardiac muscle degeneration that resembles that seen in other species with vitamin E or selenium deficiency. An additional lesion that is also consistent with this etiology is a spongiform

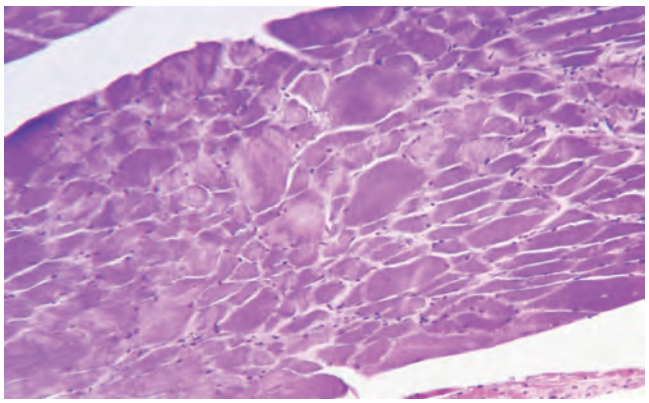

Figure 9.9 Early noninflammatory skeletal muscle degeneration in vitamin E deficiency. Fibers are swollen and fragmented.

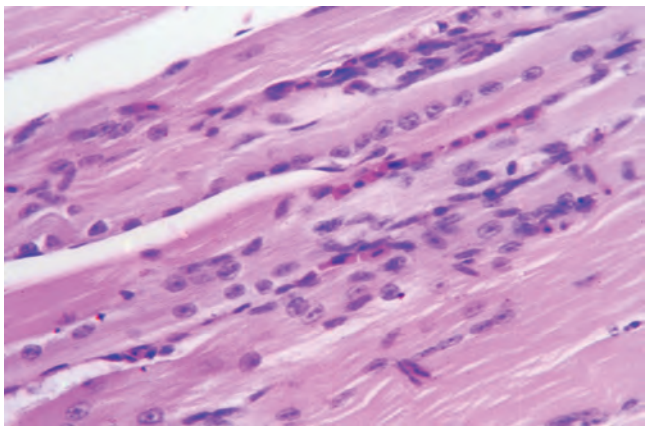

Figure 9.10 Shrinkage and fragmentation of myofibers in subacute to chronic vitamin E deficiency. There is some sarcolemmal nuclear proliferation and macrophage infiltration.

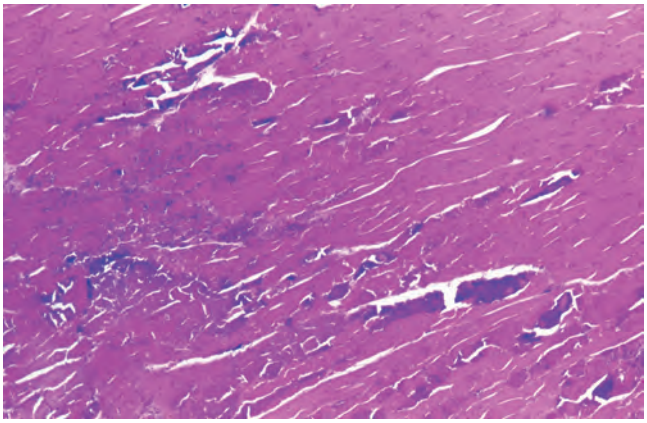

Figure 9.11 Chronic nutritional myodegeneration. In addition to degeneration and cell infiltration, there is early mineralization of myofibers (blue granules and clumps).

encephalopathy. Although the pathogenesis of this lesion is not proven, it is thought that a diet low in fat (the major source of vitamin E) may be the cause.

Exertional/capture myopathy

Stress-related or exertional rhabdomyolysis results in muscle necrosis with grossly noted yellow foci and hemorrhage in acute cases. With chronicity, firm white streaks are noted. At times, entire muscles or muscle groups will be affected and will be uniformly pale. Histologically necrosis and hemorrhage with variable fragmentation of myofibers are seen in acute cases. As the lesion ages, there is macrophage infiltration, fibroplasia, and mineralization. Exertional myopathy is most common in wild birds that are chased for long periods of time before capture or are allowed to struggle excessively once captured. In heavy-bodied chickens and turkeys and rarely in wild species of birds, exertion can cause muscle swelling resulting in compression of the arterial supply to the supracoracoideus muscle causing avascular necrosis.

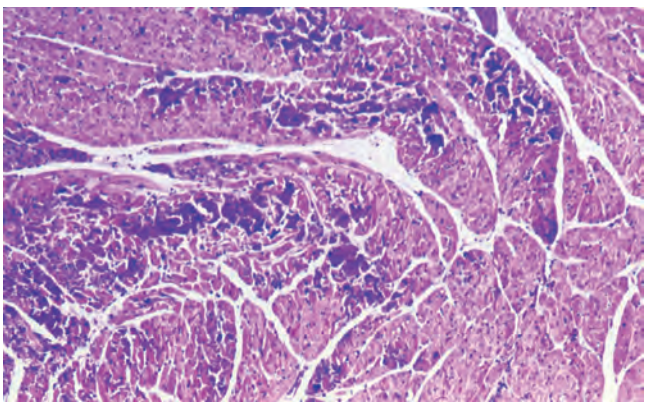

Figure 9.12 Severe mineralization in chronic nutritional myodegeneration.

Degenerative changes in the muscles of the cervical spine have been seen in recently hatched psittacine chicks. They are best observed when sections are stained for calcium. The cause of these lesions could be exertional or secondary to vitamin E or selenium deficiency.

Endocrinopathies

Hyperthyroidism and hyperadrenocorticism can lead to myofiber degeneration or atrophy. The morphologic changes are as described previously.

Toxic myopathy

Toxins such as ionophores used as coccidiostats and growth promoters, gossypol, and plants such as *Cassia* sp. have caused skeletal muscle lesions in birds, including ostriches, quail, and other African wild birds. Gross changes may not be noted, and histologic lesions can be minimal. Loss of striations, fragmentation, macrophage infiltration, and mineralization are reported. Although not specifically reported in common pet birds, the potential for exposure exists.

A disease of unknown etiology variously called lorikeet paralysis syndrome or clench-claw syndrome occurs across the eastern range of the rainbow lorikeet in Australia. It has been most commonly seen in wild rainbow lorikeets, but has also been recorded in captive animals. This syndrome may have more than one etiology and was originally thought to be the result of an encephalitis that may have been of viral origin. More recent studies have found encephalitis to be rare in these birds, but have found significant muscle lesions in affected birds. Lesions can be found in leg, wing, and laryngeal muscles. They are characterized by muscle degeneration and mineralization (Fig. 9.13). The cause of the lesions is not known, but metastatic mineralization of the kidney and ventriculus may also occur, so consumption of a toxic plant as the cause of these lesions is being investigated.

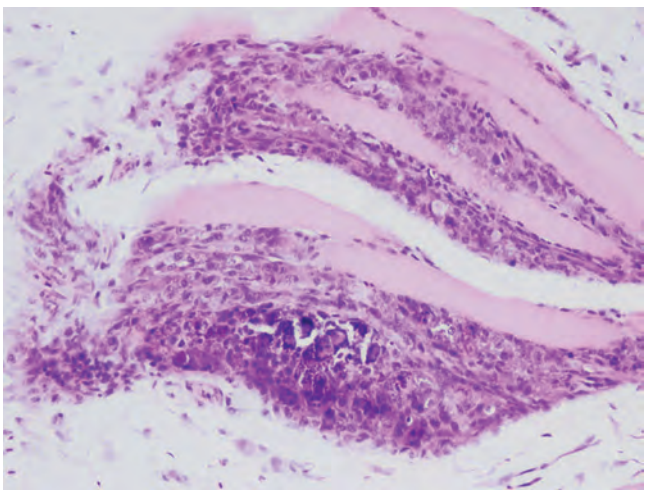

Figure 9.13 Skeletal muscle degeneration and mineralization in a rainbow lorikeet with the so-called clench claw syndrome.

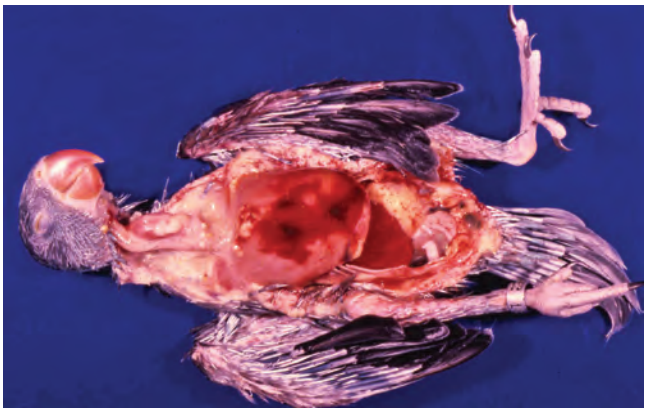

Figure 9.14 Marked skeletal muscle hemorrhage due to polyomavirus infection (budgerigar).

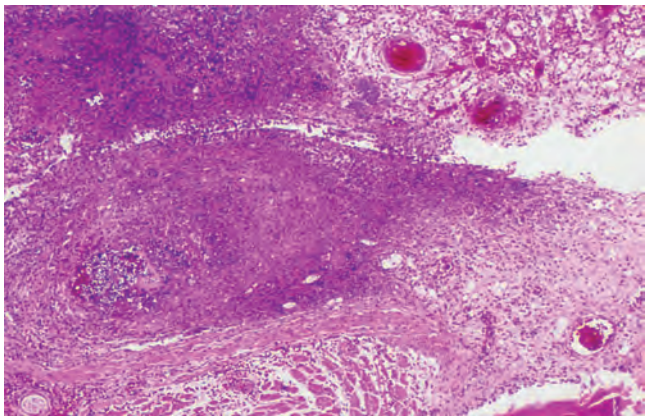

Figure 9.16 Myodegeneration and heterophil infiltration in acute bacterial myositis.

Other disease

Myasthenia gravis is an autoimmune disease of people and is seen in dogs and cats. Affected animals have clinical muscle weakness. The condition may be associated with thymic hyperplasia. Occasionally adult birds that die acutely are found to have thymic hyperplasia as an isolated lesion. Whether these birds have myasthenia gravis remains unproven. Consistent morphologic changes in skeletal muscle of these birds have not been demonstrated. Immune-mediated myositis has not been documented in birds.

Inflammatory disease: infectious disease

Although not common, a variety of infectious agents can cause myositis. The infections can be associated with trauma, extension from adjacent tissue, or hematogenous dissemination.

Viral myositis is uncommon. A proliferative, but nonneoplastic, fibromatosis of skeletal muscle has been produced experimentally by cloned recombinant avian leukosis virus. Polyomavirus infection in large psittacine birds may cause skeletal muscle lesions. Gross pallor and occasional hemorrhage are seen (Figs. 9.14 and 9.15). Myofiber necrosis, sarcolemmal karyomegaly, and inclusion body formation may be noted histologically. Poxvirus infections can be severe enough to result in a primarily lymphocytic infiltrate into underlying skeletal muscle.

Bacterial infections can be aerobic or anaerobic. They rarely are limited to skeletal muscle, usually also involving subcutis, fascia, or bone. Necrosis and accumulation of yellow caseous material is seen in severe lesions. Heterophils predominate in early lesions, with increasing numbers of macrophages and plasma cells with chronicity. Eventually granulation tissue may form. Organisms may or may not be seen (Figs. 9.16 and 9.17).

Mycotic infections are often due to local extension from air sacs or due to systemic disease. They are most common in immunosuppressed birds, although overwhelming infections are seen in otherwise normal birds. Grossly nonspecific areas of necrosis and, in some cases, abscess formation are present. Histologically the lesion is similar to that of bacterial infection, with specificity due to finding fungal organisms (Fig. 9.18). Infarction of an entire pectoral muscle was seen in a starling that

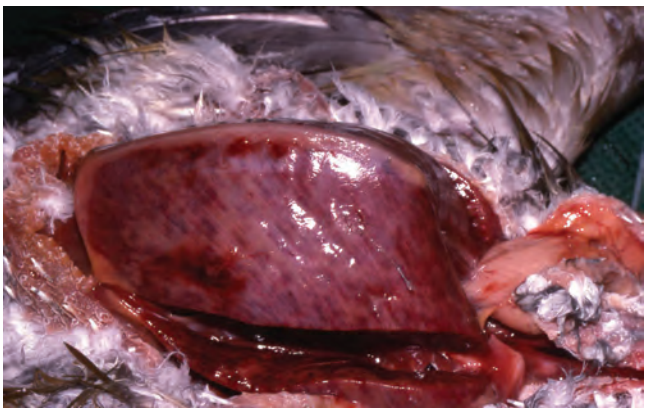

Figure 9.15 Severe intramuscular hemorrhage due to polyomavirus infection.

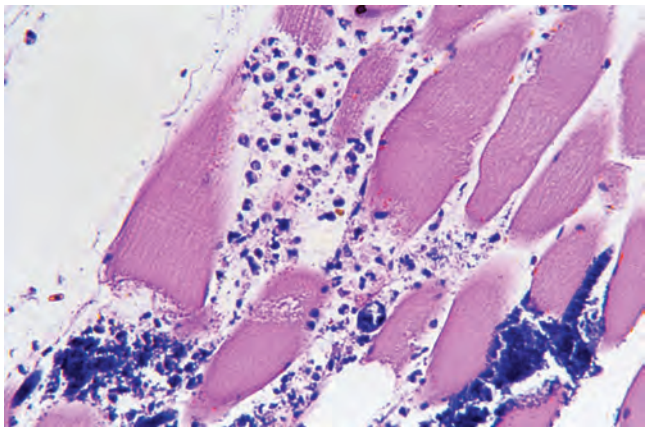

Figure 9.17 Bacterial myositis. Note the inflammation and large bacterial colonies.

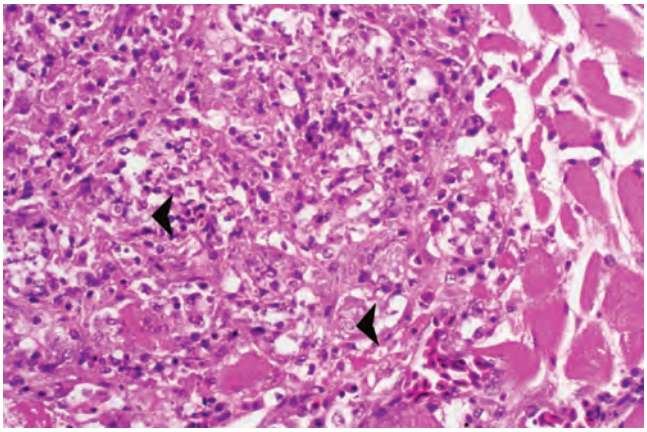

Figure 9.18 Mycotic myositis. Severe necrosis and an infiltrate of macrophages are seen. Fragments of fungal hyphae are difficult to see in many cases (arrowheads).

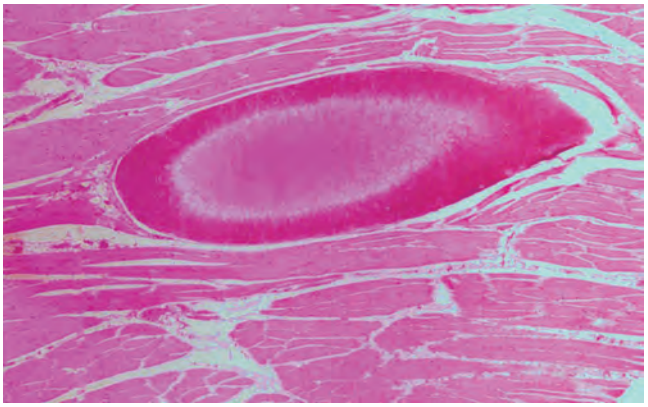

Figure 9.19 Cyst of Sarcocystis found incidentally in skeletal muscle of a New World psittacine bird.

had fungal-induced thromboembolism of the pectoral artery. A similar lesion was caused by thromboembolism in the brachiocephalic trunk of a Willie wagtail. Both birds presented with the inability to flap the wing on the affected side. The infarcted muscle mass maintained its normal volume while there was atrophy of the healthy pectoral muscle of the opposite wing as the result of starvation.

Parasitic infections of skeletal muscle associated with visceral larva migrans (*Baylisascaris procyonis*) are possible as incidental findings, with the parasite causing clinical signs when it invades the central nervous system (Chapter 10). Mites (*Laminosioptes cysticola*) can invade skeletal muscle in some cases. These mites have been found in chickens, turkeys, pheasant, geese, and pigeons. Gross changes vary from small white foci that may be mineralized to abscess formation and tracts that may lead to the skin. Finding the parasite or fragments is necessary for a definitive diagnosis.

Recent molecular studies demonstrate that there is a wide range of *Sarcocystis* spp. that infect birds and it is likely that many more species will be discovered in the near future. Most *Sarcocystis* spp. are adapted to their host and cause little disease. One species that commonly infects ducks in North America is *S. riyeli*. The definitive host for this parasite is the skunk. Large protozoal cysts (rice grains) are found in the pectoral muscles of these birds with apparently limited functional impact. Sarcocystosis is generally an incidental finding in most species of New World parrots. Mature sarcocysts filled with bradyzoites are seen within the muscle but do not elicit inflammation or muscle degeneration (Fig. 9.19). By contrast, sarcocystosis caused by *Sarcocystis falcatula* can cause severe myositis in Old World species of parrots, particularly the eclectus parrots. Gross changes may not be seen, but, if the infection is severe, small white foci or steaks may be present. Histologically necrosis, mononuclear inflammatory infiltrates, and myodegeneration can be found, with or without organisms (Fig. 9.20). The primary host for *S. falcatula* is the opossum. Birds become infected when they ingest an insect that has fed on opossum feces, or the insect itself acts to move the sporocysts onto the bird's food. Experimentally infection of budgerigars indicated that cysts are found in skeletal muscle by 8 days after inoculation. In breast muscle most cysts degenerated, but in other locations they matured in 44–77 days.

Sarcocystis calchasi is an emerging disease of domestic pigeons in Europe and North America. It is primarily associated with a severe encephalitis, but infection of muscle may also occur. This parasite is also shown to cause encephalitis accompanied by cysts in skeletal muscles in three species of Indo-pacific parrots in a bird collection in California.

Studies in Europe have documented large cysts (800 μm) in the muscles of parrots housed outdoors. Molecular characterization demonstrated that the cysts are caused by a species of *Hemoproteus* that also infects native birds.

Toxoplasma gondii and *Neospora caninum* have the potential to cause cysts in muscle and should be considered as a differential for parasitic muscle cysts. These organisms and others

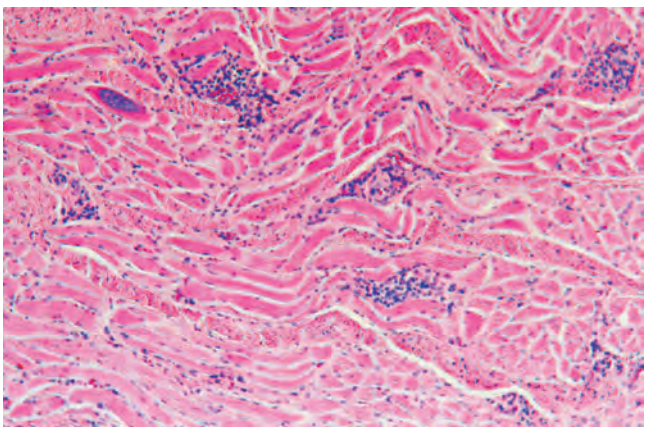

Figure 9.20 Multifocal myositis and cyst of Sarcocystis falcatula in skeletal muscle.

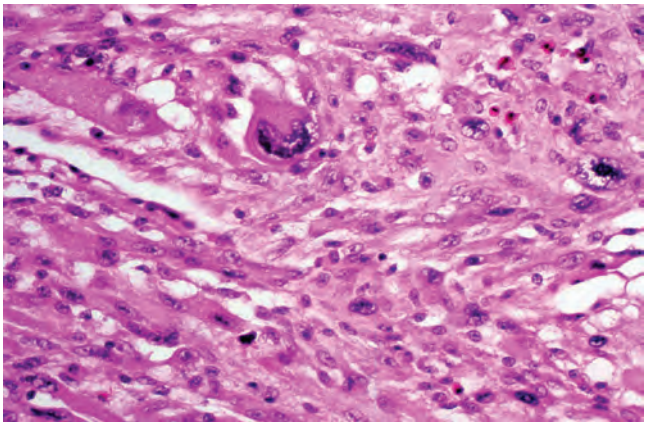

Figure 9.21 Rhabdomyosarcoma. Note the large, multinucleated cells and strap cells.

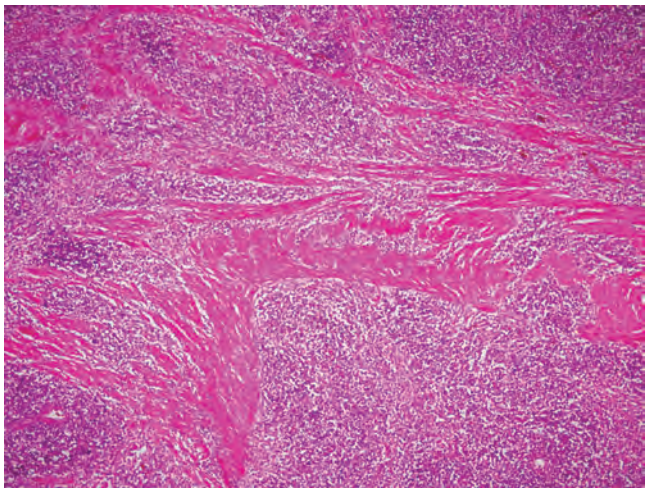

Figure 9.22 Lymphosarcoma caused by the Marek's disease virus infiltrating skeletal muscle in a chicken.

that might cause muscle cysts can be identified using immunohistochemistry or by PCR amplification of their DNA and sequencing.

Neoplastic disease

Rhabdomyoma and rhabdomyosarcoma

Primary tumors of skeletal muscle are infrequently reported in pet birds. A site predilection for these tumors is not observed. Grossly, benign tumors are tan-red and resemble normal skeletal muscle. They comprise striated myofibers, and cross striations are usually visible. Rhabdomyosarcomas have irregular borders and may be tan to gray. Histologically, strap cells and large multinucleated cells are present (Fig. 9.21). They are highly invasive into muscle and bone. In some instances, rhabdomyosarcoma can be difficult to distinguish from other poorly differentiated sarcomas. However, with special stains they are positive for actin, vimentin, and desmin. Fibromas, fibrosarcomas, rhabdomyomas, and rhabdomyosarcomas in chickens are caused by the avian leukosis virus group.

Metastasis of tumors to skeletal muscle is rare. Lymphosarcoma is one of the few tumors that will commonly invade skeletal muscle. Grossly there are gray-white masses that comprise diffuse sheets of immature lymphoid cells. In chickens, Marek's disease is the most common cause of lymphoid tumors of the muscle (Fig. 9.22). Local extension to adjacent muscle occurs with fibrosarcomas, myxosarcomas (Fig. 9.23), and air sac carcinomas and others. Malignant melanoma can invade skeletal muscle and is usually associated with skin and subcutaneous lesions. Tumor cells are usually pigmented but amelanotic types are seen. In penguins, malignant melanomas have been seen to develop in the muscles of the face.

Tendons and ligaments

Specific conditions of either tendons or ligaments are infrequently diagnosed but are likely to be common in traumatic injuries of the joints of the long bones. In addition to trauma, inflammation of tendon sheaths and neoplasia may also occur. Cranial luxation of the tibiotarsus is an uncommon but regular lesion seen in nestling parrots (Fig. 9.24). Ligaments supporting the knee in these birds are completely disrupted. Similar disruption of the ligaments is seen in traumatic elbow dislocations. The ligament of the extensor propatagialis muscle is often injured when wings are immobilized as part of the treatment for fracture of the bones of the wings. Bandages cause pressure necrosis of the overlying skin and the ligament. Resulting inflammation causes contracture and scarring of the ligament. Birds with this lesion are unable to extend their wing fully and fly. In systemic gout, urate tophi commonly form on the sheaths of the flexor tendons of the antebrachium and on the tendons of the feet.

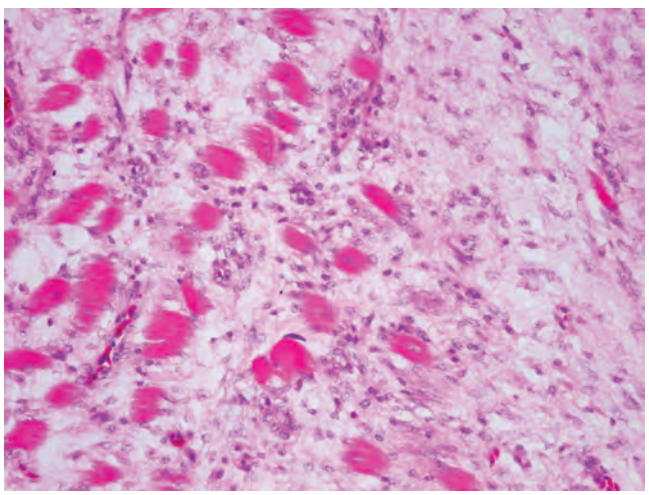

Figure 9.23 Myxosarcoma invading adjacent skeletal muscle.

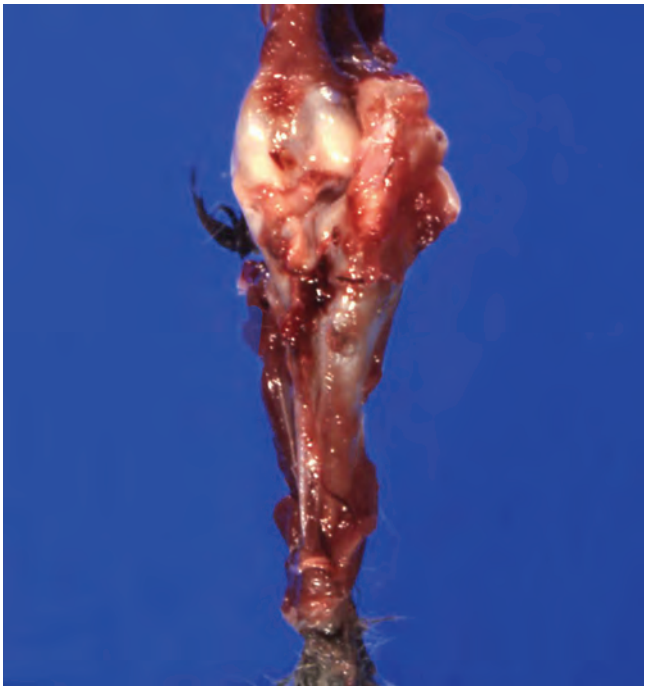

Figure 9.24 Congenital joint misalignment. There are a variety of causes for this condition.

Infectious agents that affect the tendons of poultry include *Mycoplasma synoviae*, other bacteria, and a reovirus. These diseases first start as an arthritis and spread locally to involve the tendons. A pleocellular inflammatory infiltrate is seen with all infections, and fibrin may be present. Organisms may or may not be seen. Although studies have found a few conures with antibodies to *M. synoviae*, and budgerigars have been experimentally infected with this organism, its role in clinical disease in pet birds is not documented.

Noninfectious inflammation associated with trauma or immune-mediated disease is usually mononuclear. Although lesions suggestive of immune-mediated disease are seen occasionally, the exact underlying cause is usually not determined.

Tendon sheath sarcomas are possible but rarely seen.

Bone and cartilage

Normal structure

There are several unique aspects to the avian skeleton. Birds have only a single ear ossicle (columella/stapes). They have an additional bone in the shoulder, the coracoid, that is not present in mammals. The coracoid articulates with the clavicle, humerus, and sternum. Birds also have articulated ribs, and their ribs have a prominent uncinate process, a feature shared with reptiles. The bird's sternum is a broad bone that covers most of the ventrum of the coelomic cavity. A prominent keel or carina that projects from the sternum acts as an attachment for the pectoral muscles. The keel is absent in ratites (ostriches, rheas, emus, and kiwis). There are eight thoracic vertebrae. Thoracic vertebrae 1 through 6 are fused to form the notarium. Thoracic vertebrae 7 and 8 are fused together with the combined lumbar vertebrae, ilium, pubis, and ischium to form the synsacrum.

The bird's wing also has a reduced number of bones. In the manus, they have a large major digit and a small, nearly vestigial minor digit. The three metacarpal bones are fused. A third short digit, the alula, articulates with the leading edge of the fused metacarpal bones just distal to the articulation with the carpal bones. There are only two carpal bones: the radial and the ulnar. In contrast to mammals, the ulna is a larger bone than the radius.

The hind limb also has several fused bones. The tibia is fused with the proximal tarsal bones and is referred to as the tibiotarsus. The distal tarsal bones fuse with a single tarsal bone to become the tarsometatarsus. The number of toes present and their orientation will vary with the species. Most birds have four toes, but several species have only three, and the ostrich has only two.

Air sacs extend into many bones, replacing the marrow. The degree of pneumatization is somewhat species specific. In most birds, the femur, humerus, sternum, skull, and at least some of the vertebrae are pneumatized.

Avian bone matrix varies with the skeletal site, reflecting the differing functions of bone. The avian physis has four zones from epiphysis to medulla: the zones of proliferation, prehypertrophy, hypertrophy, and ossification.

Relationship of bone to eggshell formation

Female birds, in order to lay an egg, must transport a considerable amount of calcium to the shell gland and subsequently the eggshell itself within a short period. There is insufficient calcium in the average bird's diet to support this demand; therefore birds have evolved a type of medullary bone that can serve as a storage site for calcium mobilization. Medullary bone develops in long bones. As a hen prepares to lay, spicules and then trabeculae develop from the endosteum of the surrounding compact bone. The medullary bone is strongly basophilic and clearly distinguishable from the cortical bone (Fig. 9.25). During the cycle of ovulation/ovipositioning, periods of medullary bone formation alternate with periods of depletion. If dietary calcium is insufficient to replace the calcium lost to egg laying, the medullary bone is lost completely and the cortical bone is reabsorbed.

Disease/lesions of bone

General reactions to injury

Direct physical injury leads to osteoblastic proliferation (from the osteogenic layer of the periosteum) and new bone formation. Bone necrosis is seen secondary to neoplasia, vascular lesions, trauma, or osteomyelitis.

Fracture repair is similar to that in mammals. There is initial hematoma formation followed by mesenchymal cell proliferation, which matures into osteoblasts that form the woven bone

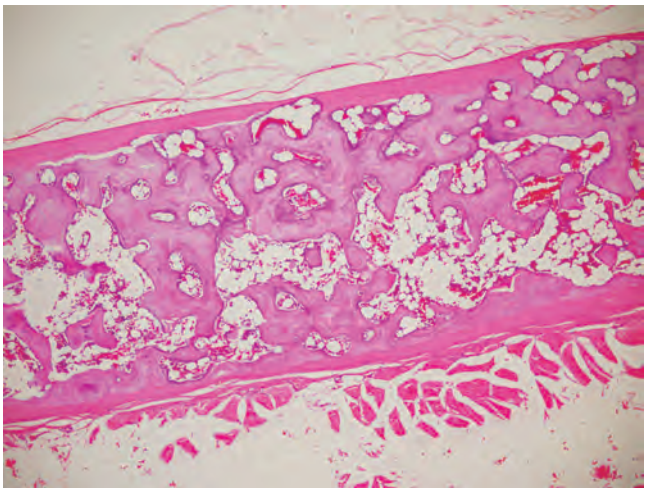

Figure 9.25 Intramedullary bone. Basophilic intramedullary bone is deposited in long bones prior to the onset of egg laying.

Figure 9.26 Congenital polydactylia. These lesions are sporadic and have not been related to any specific cause.

of the callus. Eventually, the woven bone is replaced by lamellar bone. Birds are unique in that if the fracture site is stabilized, they will form an endosteal callus instead of a periosteal callus. However, if movement continues to occur at the fracture site, a periosteal callous will also form.

If a limb is not used, bone resorption will increase and bone formation will diminish.

Abnormalities of development

Developmental anomalies can be genetic, adaptational, or due to teratogens. Congenital long-bone deformities are the most commonly recognized bone malformations. Unilateral micromelial is described in a penguin species. The cause of this lesion is not known, but multiple toxins including organophosphates, diazinon, cadmium, and selenium can cause these lesions. Limb deformities in owls including missing or deformed bones in wings and legs and dislocation of radius and carpometacarpus have been blamed on exposure to polychlorinated biphenyls, polychlorinated dibenzo-p-dioxins, and polychlorinated dibenzofurans. Micromelia has also been associated with inappropriate incubation temperatures. An inherited chondrodystrophy is described in the California condor, chicken, turkey, and Japanese quail. Other miscellaneous anomalies include brachygnatha, polydactylia, syndactyly, scoliosis, and spina bifida (Figs. 9.26, 9.27, and 9.28). These conditions are primary structural defects associated with localized problems during embryogenesis and occur sporadically in pet birds. Other congenital anomalies resulting in deformities may arise late in fetal life and are alterations in a previously normal structure. Their cause is often not apparent but may include the position of the embryo in the egg and the turning frequency of the egg.

Chondrodystrophies

Tibial dyschondroplasia is seen in turkeys, chickens, and ducks but is not reported in pet birds. Copper deficiency, specific toxins, excessive dietary cysteine, and acidosis are all implicated in its pathogenesis. Grossly an unmineralized core of cartilage extends from the articular cartilage of the tibia distally into the diaphysis. Histologically the cartilage core comprises hypertrophic chondrocytes. This lesion is believed to be the result of a defect in vascularization of the cartilage, resulting in an insufficient supply of mineral ions and nutrients to cartilage. As a result, matrix vesicle formation and subsequent mineralization are not properly supported, and some chondrocytes in the growth plate do not reach normal size and thus undergo premature necrosis.

Nutritional/metabolic disease

Nutritional chondrodystrophy

Deficiencies of manganese, choline, biotin, nicotinic acid, zinc, or pyridoxine cause a generalized disorder of growth of long bones in poultry, and similar lesions are seen in companion birds. Linear growth is primarily impaired, but mineralization

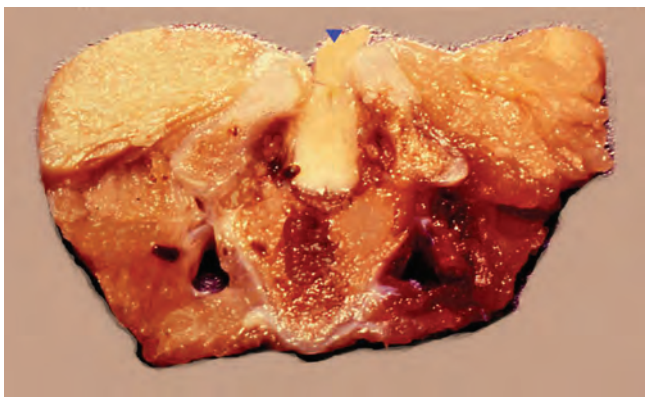

Figure 9.27 Cross section of the vertebral column through an area of spina bifida. The dorsal portions of the vertebra were missing, and there was a space that communicated with the surface (arrowhead).

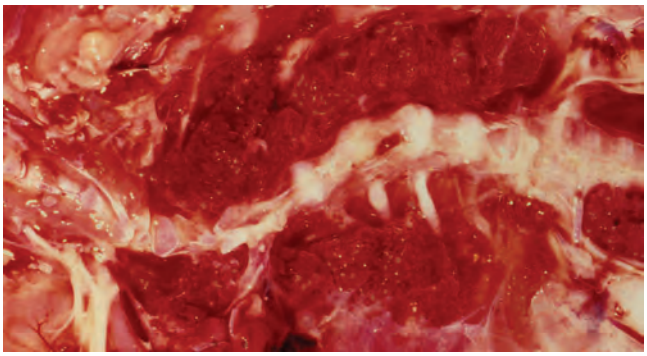

Figure 9.28 Marked spinal column scoliosis.

and appositional growth are not affected. Bones become short, and joints enlarge. Varus or valgus leg deformities with gastrocnemius tendon displacement are other manifestations of this disorder. Histologically the zone of proliferation is hypoplastic and disorganized.

Osteoporosis (osteopenia)

Osteopenia is characterized by a reduction in bone mass, with the remaining bone normally mineralized. It is a failure of bone matrix formation. It is not a simple loss of apatite and collagen; there are changes in the collagen molecule biochemistry and therefore the physical properties of the collagen fiber. Increased lysine hydroxylation and change in the intermolecular cross-link profile lead to increased turnover of collagen and increased bone fragility. Causes of osteopenia/osteoporosis include starvation; calcium, copper, phosphorus, or vitamin D_3 deficiencies; and reduced physical activity. Grossly the cortical bone has reduced thickness and is more porous. The bone is easily fractured and may bend when pressure is applied (Fig. 9.29). The trabecular bone becomes thinner and is eventually lost (Figs. 9.30 and 9.31).

Figure 9.29 Severe osteopenia leading to bone deformation with pressure. This female bird had produced numerous eggs and was egg bound at the time of death.

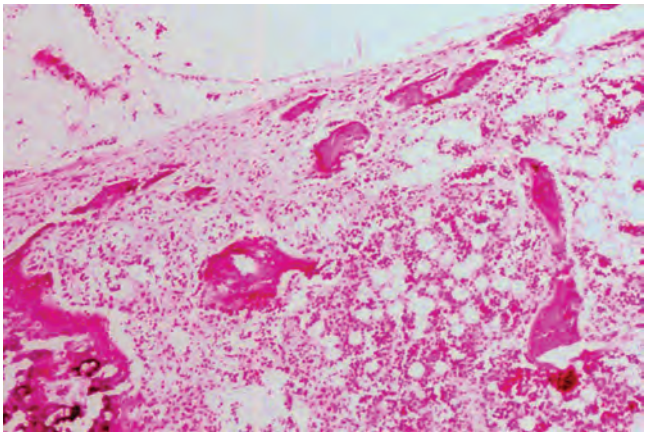

Figure 9.30 Severe osteopenia illustrating marked loss of continuity of the cortical bone.

Rickets and osteomalacia

The name applied to this condition depends on the age of the bird. Rickets is seen in birds in which the skeleton is still growing. Osteomalacia occurs in birds that are fully grown. These problems are due to a failure of mineralization of matrix leading to bone deformities and fractures.

Rickets is the result of the failure of mineralization of newly deposited osteoid. Insufficient dietary calcium, vitamin D_3, or phosphorus and excess phosphorus or calcium will all cause rickets. Grossly the joints of birds with rickets may be swollen. Bones are soft and the metaphyses flared (Fig. 9.32). Curving deformities of long bones and folding fractures are common. The histologic lesion will depend on the cause of the rickets and the duration of the dietary imbalance. The following descriptions are based on work done in chickens and on cases we have seen in other avian species.

The bone lesions of calcium-deficient rickets are characterized by disorganization and thickening of the zone of proliferation with poor physeal vascularization. Thick seams of unmineralized osteoid surround trabeculae, and metaphyseal

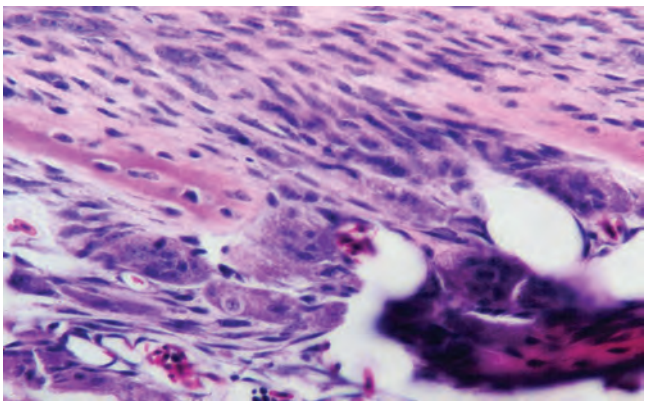

Figure 9.31 Detail of cortical bone remnant in a case of osteopenia.

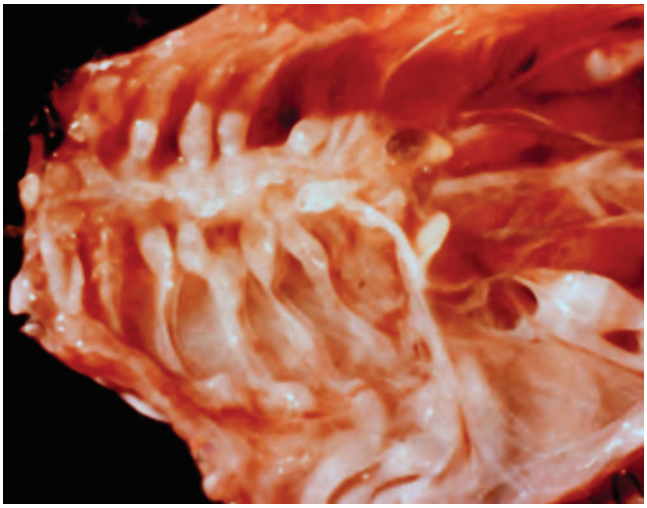

Figure 9.32 Multiple nodules on the ribs of a chicken with rickets.

fibroplasia may occur. The zone of proliferation is unchanged in hypophosphatemic and excessive calcium rickets, but the hypertrophic zone is elongated, and there is defective mineralization of the hypertrophic cartilage cells resulting in long columns of cartilage, surrounded by wide unmineralized osteoid seams extending into the primary spongiosa (Fig. 9.33). Vitamin D_3-deficiency rickets results in a lengthening and disorganization of the proliferating zone and variable lengthening and dysplasia of the mineralizing zone. The primary spongiosa is initially lengthened with unmineralized cartilage and subsequently becomes short with short, thick cartilage columns.

Angular limb deformities of the legs. These are a common problem in hand-raised chicks and, to a lesser extent, in parent-raised chicks. Underlying nutritional deficiencies are often present in these birds. Other birds, however, will have an adequate diet but improper bedding. As a result, their feet slide out from under them, and bending of the bones occurs. These are complex lesions and rotation and bending of the bones can occur in the tibiotarsus, femur, tarsometatarsus, or in all of these bones. The resulting bone lesions will then significantly affect the soft tissue structures and can result a luxation of the gastrocnemius tendon and malformation of articular surfaces.

A very common nutritionally related disease seen in captive ducks is commonly referred to as airplane or angle wing. These ducks have dorsal rotations of their wings as the result of skeletal and joint changes of the carpus. It is most often seen in ducks fed poultry starter rations. Growing ducks should be fed less than 15% protein and chicken starter diets contain more than this.

Osteodystrophy fibrosa

Increased osteoclastic resorption of bone and replacement of the bone with fibrous tissue characterize this condition. It is the result of persistently elevated parathyroid hormone that can be a physiologic response to persistently low blood calcium or the result of unregulated release of parathyroid hormone from a neoplasia of the parathyroid.

Nutritional secondary hyperparathyroidism, which is a disease of birds that are no longer growing, is caused by a diet that is either deficient in calcium, or contains excessive phosphorus, or both. All seed diets fall into this last category. Excessive phosphorus interferes with intestinal absorption of calcium, resulting in hypocalcemia.

Renal secondary hyperparathyroidism occurs when the kidney is so severely damaged that it is unable to excrete excess phosphorus and unable to produce sufficient 1,25-dihydroxycholecalciferol. Phosphate retention leads to hyperphosphatemia, hypocalcemia, and increased parathormone (parathyroid hormone or PTH) excretion. This condition has not been documented in pet birds.

Birds with secondary hyperparathyroidism have soft bones that may bend, fracture, or become deformed due to increased osteoclastic resorption of cancellous bone and fibroplasia (Fig. 9.34).

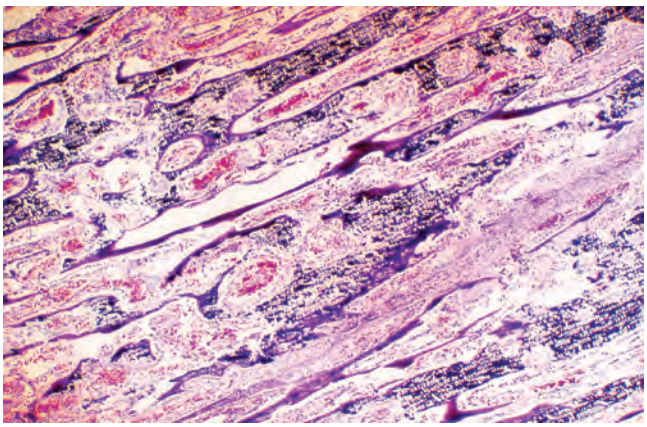

Figure 9.33 Marked lengthening of the zone of hypertrophy in rickets.

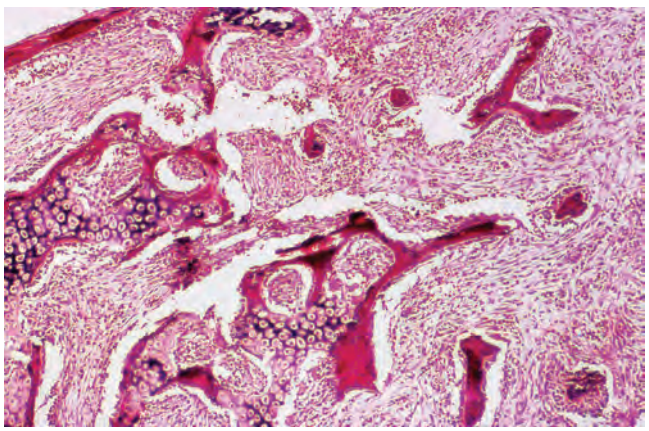

Figure 9.34 Loss of normal bone and proliferation of fibrous connective tissue in osteodystrophy fibrosa.

Bone disorders secondary to improper diet are extremely common in all captive species of birds. While most commercial hand-rearing diets are balanced for calcium and phosphorus and contain sufficient vitamin D_3, it is not uncommon for bird breeders to add supplements to these formulas diluting the mineral concentrations or altering their ratio. Some bird breeders still make their own hand-feeding diets, and these often do not contain a proper mineral content and balance. It has also been common for wildlife carers to feed carnivorous birds meat-based diets that have little calcium or are supplemented with calcium but the ratio of calcium to phosphorus is inappropriate. The practice of feeding ground beef to carnivorous birds such as kookaburras, magpies, butcher birds, and the roadrunner can also result in the development of rickets in the young of these birds.

Many pet bird owners and some aviculturalists will feed a seed-based diet that is not supplemented with calcium. Chicks fed these diets from their parents will develop rickets. In other instances, birds will be fed a varied diet that if eaten in the ratio provided would have the proper mineral balance for bone growth and maintenance. Birds, however, do not always eat everything that is provided to them and thus may feed themselves and their chicks' foods containing little calcium. An example of this is the African gray parrot, who when supplied with fresh corn will often feed this to their chicks in exclusion of other foods supplied. Adult birds fed low-calcium diets for many years will eventually develop osteoporosis and will sustain pathological fractures. Persistent egg laying is very common in pet cockatiels, budgerigars, and lovebirds. If the egg laying is not stopped with medical therapy or if sufficient calcium is not provided then bones will weaken and fractures are common.

Vitamin C deficiency

Dietary requirements for vitamin C in birds are species dependent. No requirement has been demonstrated for common pet birds. For those that cannot synthesize the vitamin, a clinical deficiency is possible. A deficiency leads to arrested osteoblastic activity. Since spicules of calcified cartilage remain as the only support for the metaphysis, fractures and hemorrhage may result and can be seen grossly and histologically.

Vitamin A deficiency

Vitamin A is needed for osteoclast function. With a deficiency, osteoclast production is reduced, resulting in an imbalance between modeling and remodeling of bone. The failure of bone remodeling causes bone thickening and irregularity, with compression of adjacent soft tissue. The condition is infrequent but seems to involve the vertebrae rather than long bones. Histologically, excessive amounts of dense, mature bone are seen (Fig. 9.35). Birds deficient in vitamin A may also have squamous metaplasia in other organ systems.

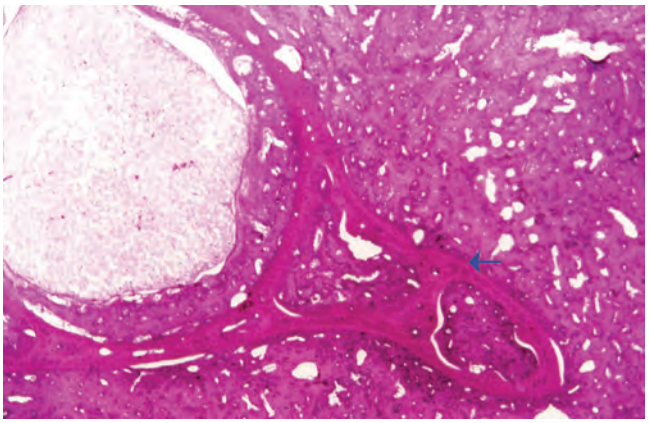

Figure 9.35 Marked osteosclerosis/bone proliferation associated with chronic vitamin A deficiency. Older cortex is indicated by the arrow.

Polyostotic hyperostosis

This is the development of medullary bone in bones such as the femur, ulna, and radius, bones of the pectoral girdle, and vertebrae that would not normally develop medullary bone. This condition is thought to be associated with reproductive disorders such as ovarian tumors and ovarian cysts that cause prolonged estrogen secretion. However, these diseases are not always present in birds with polyostotic hyperostosis. This disease has been seen in chickens and ducks that are fed laying diets but no longer lay eggs. Radiographically, increased medullary bone will be visible. The extent of bone involvement will depend on the duration of the underlying disease process. Affected bones are hard and difficult to break. Histologically, medullary bone is present and it is indistinguishable from normal medullary bone with the possible exception of the degree that it fills the medullary cavity and the bones that are affected.

Degenerative bone disease/trauma

Osteochondrosis

This is a focal area of disordered endochondral ossification in an area of growth that was previously normal. It can occur in the epiphysis (articular or nonarticular) and the growth plate. Nonarticular sites include areas of tendon and ligament attachment. Articular cartilage sites are associated with chondrocyte necrosis and cartilage dissection.

Osteochondrosis may be a dyschondroplasia that leads to degenerative changes, or it may be secondary to biomechanical forces and associated with ischemia, trauma, or improper nutrition. Three forms are recognized: osteochondritis dissecans, physitis, and subchondral bone cysts. Although these lesions are seen primarily in poultry, bone cysts have also been reported in an ostrich, cockatiel, cockatoo, and African collared dove.

Osteochondritis dissecans develops when fractures of the epiphyseal cartilage extend to the articular surface. Ossified cartilage and free cartilage fragments may be present in the joint.

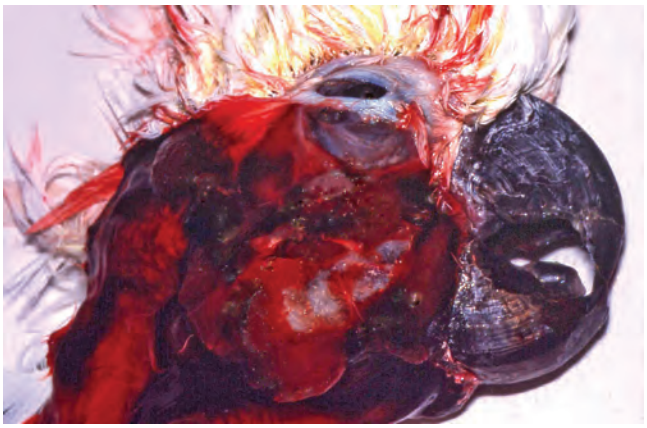

Figure 9.36 Severe hemorrhage associated with a fracture of the zygomatic process.

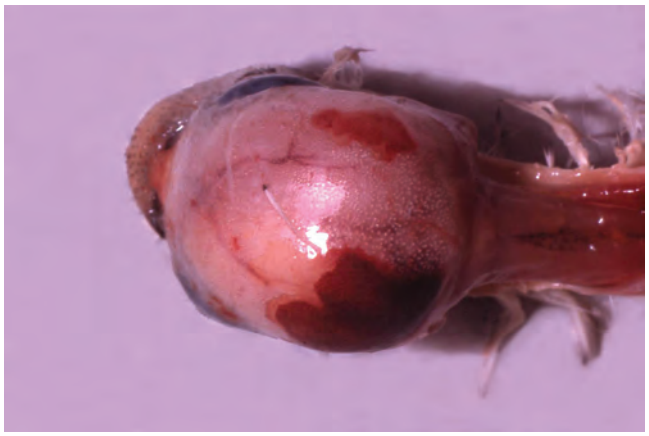

Figure 9.38 Hemorrhage involving the bones of the skull. This must be differentiated from postmortem congestion.

Physitis usually results in widening of the physis associated with resorption of damaged bone. Subchondral bone cysts may be a sequel to linear defects in weight-bearing cartilage, possibly due to the accumulation of synovial fluid in the lesion and impairment of the cartilage vasculature.

Fractures occur commonly in pet birds, pigeons, poultry, and wildlife (see the previous section) and can result in severe hemorrhage in the surrounding tissue (Fig. 9.36). Fractures of the calvarium occur most commonly in wild birds, but overall they are relatively infrequent. Fractures of the calvarium can result in hemorrhage that can be within the bone or on either surface of the bone (Figs. 9.37 and 9.38). It is very common for blood to pool within the woven bone of the skull in any bird dying from any cause. This change can be readily mistaken for hemorrhage and misinterpreted as an indicator of a skull injury. Humeral fractures are often midshaft to distal and oblique. The sharp end of the bone often penetrates through the skin resulting in a contaminated wound and associated muscle damage. Healing is similar to that in mammals, and poor fracture healing leads to fibrous and chondroid callus formation (Fig. 9.39). Underlying causes include malnutrition, loss of blood supply, excessive movement, and infection. When ulna and radius fractures occur adjacent to each other, healing may result in a synostosis that can prevent flight.

Young clumsy birds such as African gray parrots and Amazon parrots trying to learn to fly in the confines of a home or small aviary will often land hard on their sternum. This can result in a tear in the skin ulceration and damage to the margins of the keel and subsequently osteomyelitis. This then may be aggravated by the bird chewing at the site.

Ischemic necrosis of bone may be caused by neoplastic interruption of vascular supply, primary vascular disease, infection, or trauma with or without fracture. Bone that has undergone aseptic necrosis has a dry chalky appearance grossly. Histologically there is necrosis and loss of osteocytes, the marrow cells stain poorly, and vascular fibrous tissue invades the area.

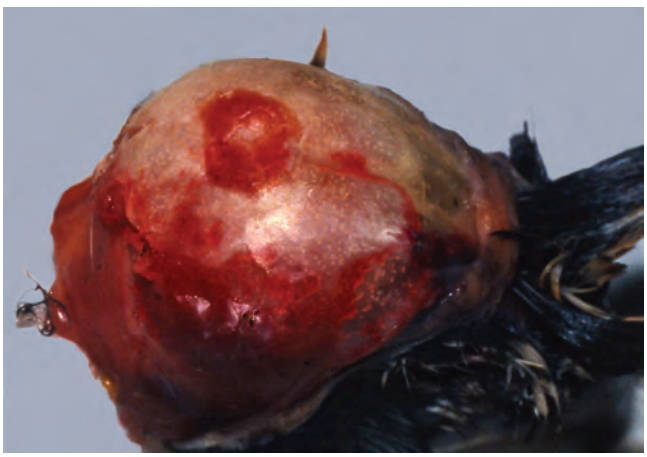

Figure 9.37 Traumatic skull fracture and hemorrhage. Without the fracture, true bone hemorrhage must be differentiated from postmortem congestion.

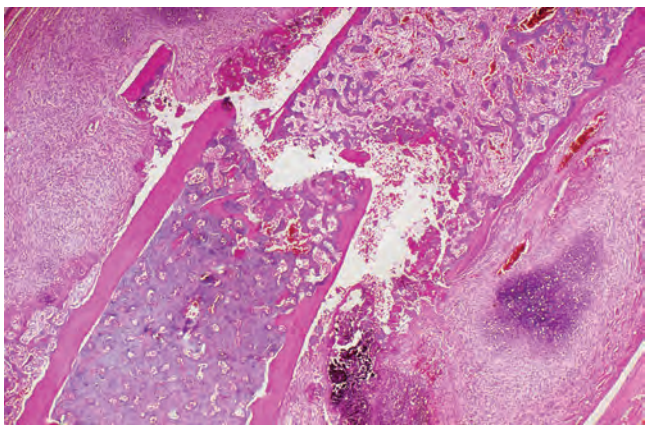

Figure 9.39 Nonunited fracture with marked fibrous and cartilaginous callus associated with movement.

Bone cysts apparently secondary to trauma are reported in a cockatoo and in cockatiels, and bone cysts of unknown origin are reported in an African collared dove and an ostrich. Grossly, the lesion contained hemorrhagic fluid covered by an osseous shell without an associated endothelium. Histologically there were areas of new bone formation and connective tissue stromal proliferation as well as bone remodeling. The locations of the bone cysts include the alula, radius, metacarpus, and skull.

Toxic bone disease

Although an excessive intake of vitamin D_3 leading to soft tissue damage has been documented in pet birds, effects on the bone, as seen in mammals, with prolonged uptake of small amounts of vitamin D_3, have not been reported in birds.

We have seen histologic bone changes suggestive of toxicity in a few cases. The lesion results from persistent hypercalcemia that depresses PTH production and stimulates calcitonin secretion by C cells. Calcitonin lowers serum calcium levels by encouraging redeposition of calcium salts in the linings of the canalicular–lacunar system within the bone and by depressing bone resorption by osteoclasts. Elevated calcitonin levels also stimulate osteoblasts to deposit woven bone having a basophilic matrix on preexisting bone surfaces. In our cases, there has been a minimal amount of osteosclerosis, rather than osteopenia.

Lead is bound to the mineral phase of bone leading to a "lead line," which is a growth retardation lattice secondary to lead-induced malformation of osteoclasts. The osteoclasts may contain acid-fast inclusion bodies in some species, but this is not documented in pet birds.

Vitamin A excess leads to lesions in the cartilaginous growth plates, thinning of the osteogenic layer of the periosteum, and osteoporosis. These changes have not been reported in pet birds.

Chronic fluorine toxicity results in osteopetrosis. The cortexes of the bones become thicker, obliterating the marrow cavity. Bone trabeculae are dense, and the periosteum is thickened at lower doses, whereas, there may be osteoporosis at higher doses. Although not documented in pet birds, the microscopic appearance is similar to vitamin A deficiency and vitamin D toxicity and should be considered as a possible differential diagnosis.

Polychlorinated biphenyls, polychlorinated dibenzo-p-dioxins, and polychlorinated dibenzofurans can cause limb abnormalities in wild birds (angular limb deformities above).

Inflammatory bone disease: osteomyelitis

The condition is usually infectious and may be caused by a variety of aerobic and anaerobic bacteria, *Mycobacteria*, fungi including *Aspergillus* spp., and *Candida* spp. The infection can be localized or be part of a generalized disease. Osteomyelitis may also be secondary to trauma or neoplastic disease. Grossly osteomyelitis is characterized as a swelling of soft tissue and irregularity of the affected bone. There may be an associated fracture that may be difficult to differentiate from a primary fracture. Caseous material is present in the lesion. Histologically, early lesions will have large numbers of heterophils with increasing numbers of plasma cells, macrophages, and giant cells seen with time (Fig. 9.40). Organisms are usually, but not always, found. Abscesses may form, and the lesion may become encapsulated (Fig. 9.41). If secondary to a fracture, there is interference with healing. Bacterial toxins and ischemia can lead to bone necrosis, and sequestra may form.

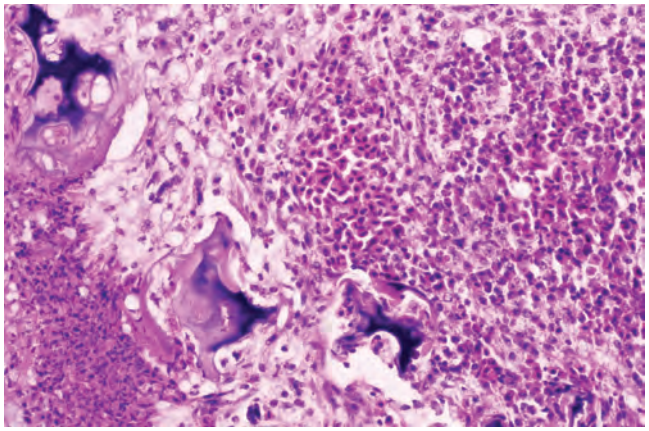

Figure 9.40 Early bacterial osteomyelitis with necrosis and a pleocellular inflammatory infiltrate.

Ornithobacterium rhinotracheale is observed to infect a range of species including chickens, ducks, geese, pheasants, red-legged partridge, quail, guinea fowl, ostrich, pigeon, gull, and rook. This organism predominately causes upper respiratory disease and can cause a severe peritonitis. Uncommonly it causes an osteomyelitis of the skull with an extension to the inner ear resulting in vestibular signs. It may also infect joints and vertebrae.

Mycobacterial infections in birds commonly involve the bone. Lesions predominate in the bone marrow, but can extend into the surrounding bone stimulating bone proliferation and lysis.

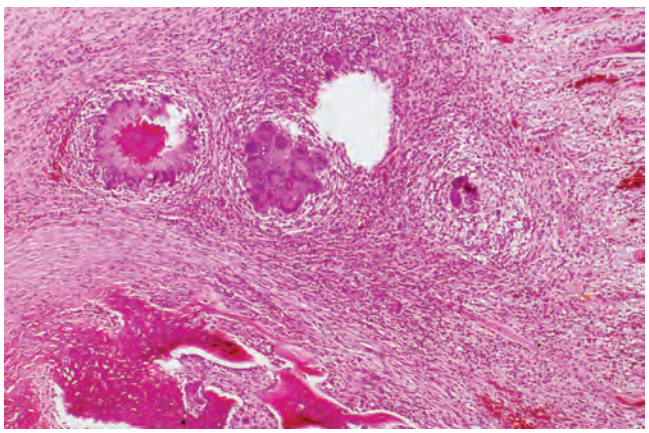

Figure 9.41 Chronic bacterial osteomyelitis. Note the multiple microabscess formation and severe connective tissue proliferation.

Granulomas often containing multinucleated giant cells will be present in the lesion. The number of acid-fast organisms in the lesion will vary from abundant to rare.

Cryptococcus gattii has been reported to cause lytic and proliferative lesions of the humerus and ulna, and in Australian species, osteomyelitis of the bones of the face. *Histoplasma capsulatum* is reported to cause osteomyelitis in a female juvenile eclectus parrot causing cortical lysis of the tibia, ulna, and radius and pathological fractures as part of a systemic disease.

Proliferative bone disease

Exostosis/enostosis/osteophytes

Deposition of woven bone can occur on periosteal or medullary surfaces of cortical compacta as well as on the surfaces of cancellous bone. A variety of causes have been identified, including infection, trauma, and metastatic neoplasia. These lesions are single or multiple hard masses affecting any bone. They comprise trabeculae of mature woven bone. There may be associated soft tissue damage due to pressure from the proliferative bone.

Osteopetrosis

In chickens, osteopetrosis can be caused by retroviruses that lead to increased osteoblastic proliferation or decreased osteoclastic resorption. There is a marked diaphyseal swelling of long bones due to massive growth of subperiosteal bone. Although the histologic appearance and numbers of osteoclasts are unremarkable, there is what appears to be a neoplastic proliferation of osteoblasts. This condition has not been reported in pet birds.

Neoplastic disease

Neoplasia can be of bone, cartilage, or marrow origin, as well as metastatic.

Osteomas are benign neoplasms of bone. They are seen sporadically in pet birds. They present as large, hard swelling in any location but are most common in the skull or vertebrae (Fig. 9.42). Histologically they comprise normal-appearing cancellous bone with marrow spaces (Fig. 9.43).

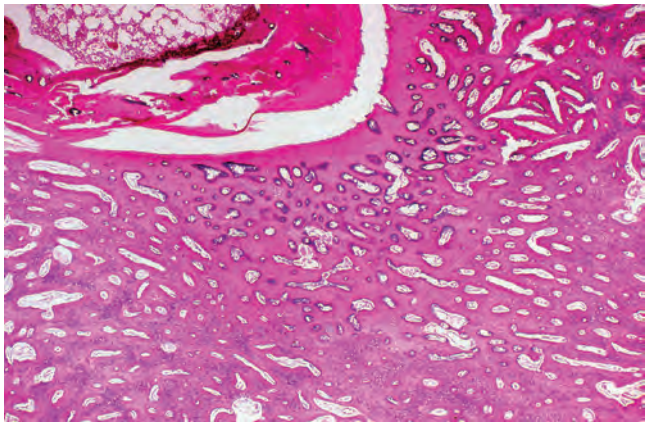

Figure 9.43 Typical histologic appearance of avian osteoma.

Osteosarcomas, which are the most common primary tumor of bone, usually appear as a firm mass that replaces normal bone (Fig. 9.44). Histologically osteosarcomas comprise fusiform or stellate-shaped cells forming bundles and sheets. There is variable osteoid and/or bone production (Figs. 9.45, 9.46, and 9.47). Considerable superficial reactive bone often surrounds the osteosarcoma. Therefore a deep biopsy is necessary in order to reach the actual tumor (Fig. 9.48). Osteosarcomas are predominately found on the wings and legs and less commonly on the axial skeleton. A tumor has also been identified in the skull and another originating in the eye. Osterosarcomas rarely metastasize.

Parosteal osteosarcomas arise from the surface periosteum of bone, with no marrow involvement. In mammals, they may contain osseous, fibrous, and cartilaginous elements. These rare avian tumors are histologically difficult to differentiate from osteosarcoma (Fig. 9.49).

Chondromas are firm masses comprising well-differentiated cartilage. They are infrequently seen and have no particular site

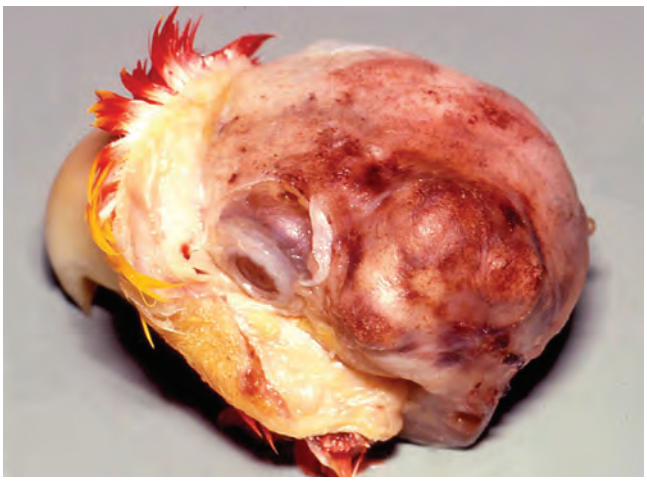

Figure 9.42 Severe skull deformation due to osteoma formation.

Figure 9.44 Bone destruction associated with osteosarcoma of the femur.

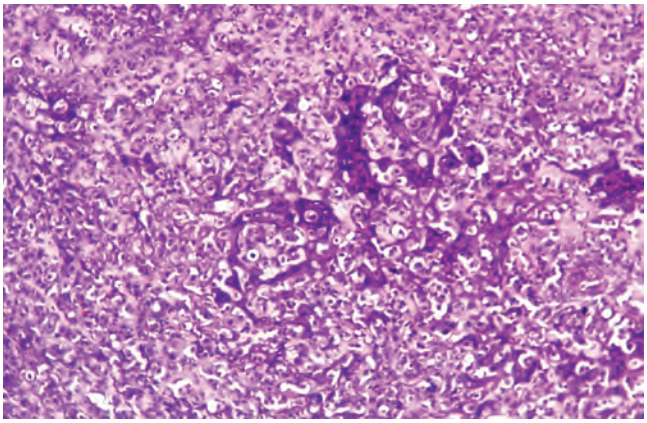

Figure 9.45 Osteosarcoma with formation of osteoid and immature bone.

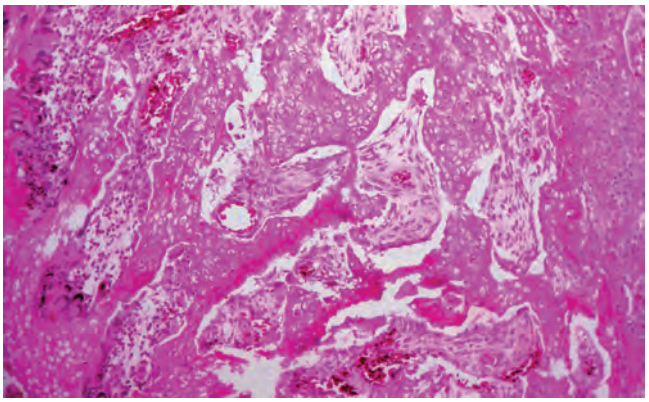

Figure 9.48 Marked reactive new bone formation on the surface of an osteosarcoma. If the biopsy is not deep enough, this may be the only material sampled.

predilection. Chondrosarcomas comprise poorly differentiated cartilage and have a high mitotic index. They are more cellular than chondromas, and there may be minimal matrix formation (Fig. 9.50). In our experience, they are more common than chondromas.

Osteochondroma is infrequently reported in pet birds; however, we have seen one tumor that was composed of bone trabeculae covered by a cartilage cap in a cockatiel (Fig. 9.51). It was a solitary nodule. An osteochondroma was also reported in the tracheal wall of a bird.

Giant cell tumors of bone are unusual and have no specific gross features. Histologically, they are characterized by numerous neoplastic multinucleated giant cells and a reactive fibroplasis and mononuclear cell infiltration (Fig. 9.52).

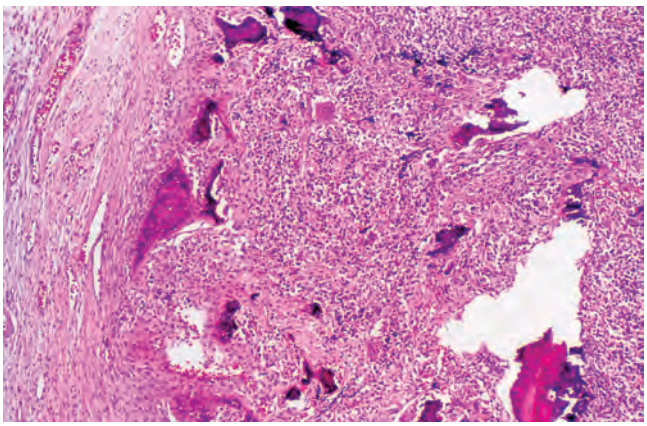

Figure 9.46 Cellular and productive osteosarcoma with large amounts of mineralized bone.

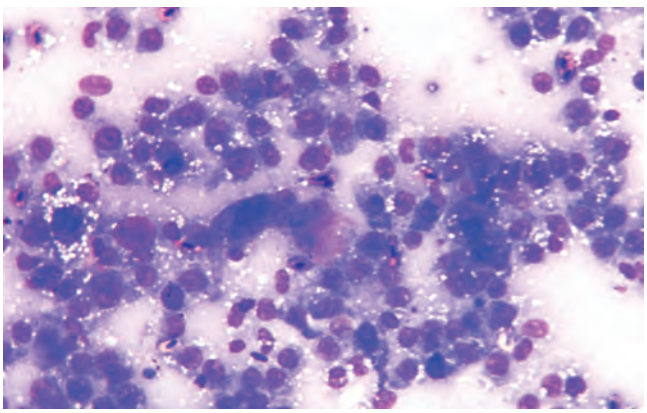

Figure 9.47 Impression smear of an osteosarcoma. Note cellular pleomorphism, pink material that may be osteoid, tumor cells with cytoplasmic vacuolation, and multinucleated cells representing osteoclasts.

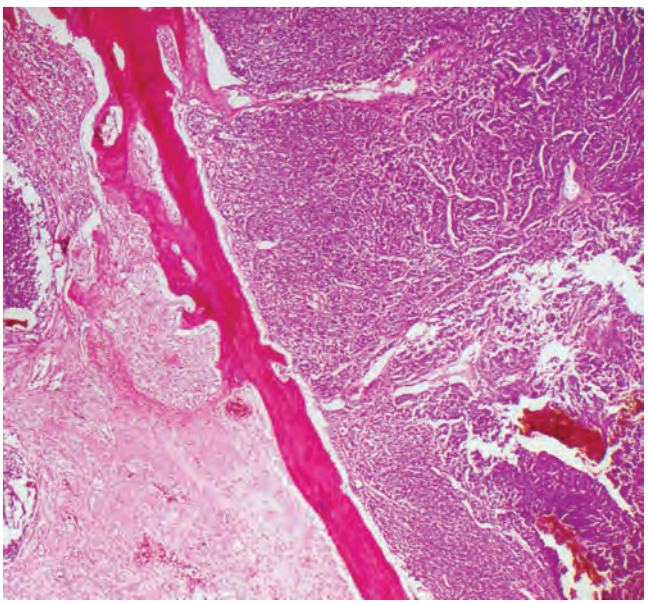

Figure 9.49 Parosteal osteosarcoma. Note the poorly differentiated tumor cells arising from the bone surface.

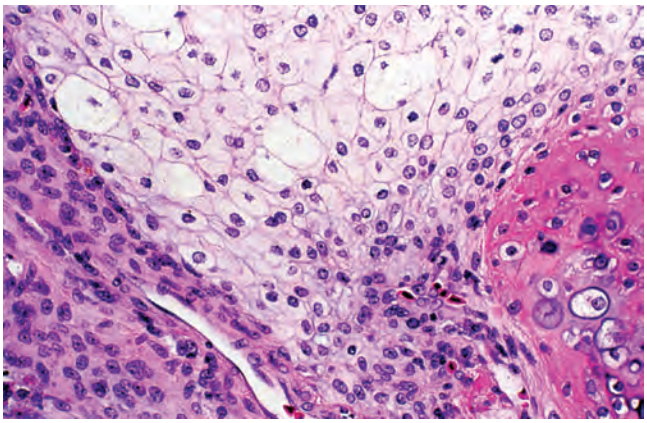

Figure 9.50 Cellular chondrosarcoma. Some attempt at lacunar formation is noted.

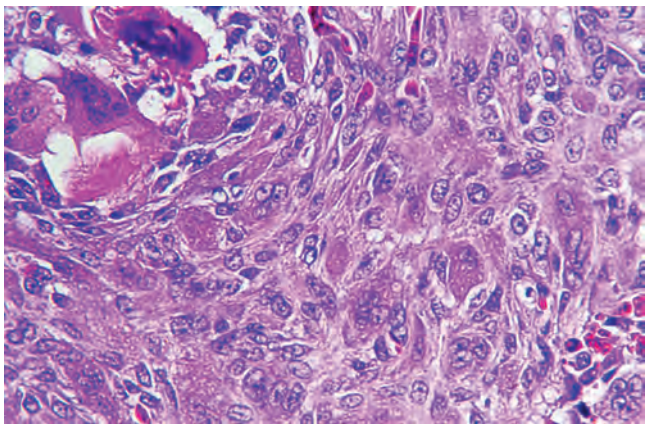

Figure 9.52 Large multinucleated cells seen in giant cell tumor of bone.

Fibrosarcoma can arise in the medullary space and may be difficult to differentiate from nonproductive osteosarcoma histologically in some cases. They may also be more typical, containing interlacing bundles of fusiform cells with vesicular nuclei.

Hemangiosarcoma may also be seen in the medullary cavity. There may be associated fractures. The tumors are usually reddish brown, and there may be excessive associated hemorrhage. Their histologic appearance is described in Chapter 1.

The bone may also be occasionally involved in systemic malignant lymphoma.

Metastases/secondary tumors

Air-sac carcinomas may involve pneumatized bones by extension. Grossly they are firm masses often involving the shoulder or upper wing (Fig. 9.53). These are highly aggressive masses and often cause pathological fractures. They typically occur in older birds (20 years old or older). Histologically, moderately undifferentiated to poorly differentiated mesothelial cells form tubules, trabeculae, and papillary structures. There is variable stromal proliferation, and bone spicules may be present interspersed with neoplastic tissue (Fig. 9.54). When located near joints, these tumors may be confused with synovial sarcomas, and immunohistochemistry may be necessary for differentiation.

Other carcinomas may metastasize to bones. Grossly there is usually proliferative new bone formation and associated soft tissue swelling. The neoplastic tissue is usually infiltrative within trabecular bone, and there may be associated bone necrosis and fibroplasia (Fig. 9.55).

Local extension into bone can also occur with muscle and connective tissue tumors (Fig. 9.56).

Disease of the joints

Congenital disease

Congenital dysplasia, luxation, or subluxation is seen in many avian species. The causes are often multifactorial, including genetics, nutrition, and trauma.

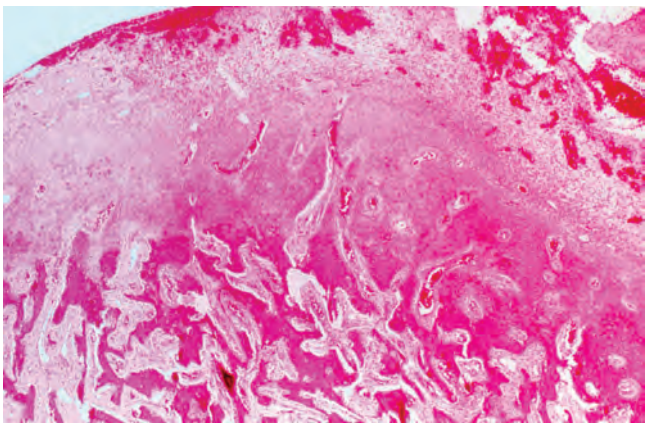

Figure 9.51 Lesion consistent with osteochondroma. The cartilaginous cap overlies an area of trabecular bone formation.

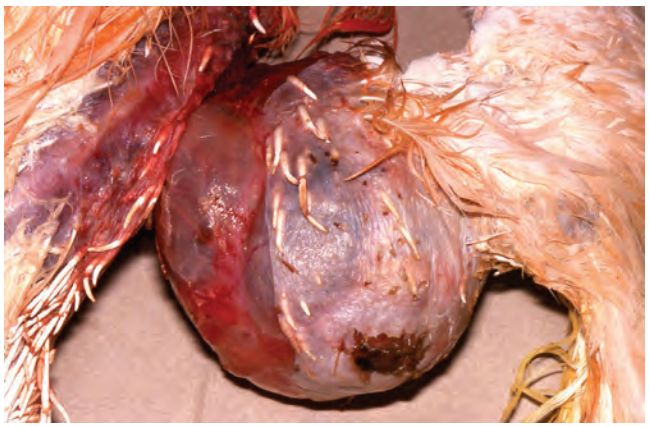

Figure 9.53 Air-sac carcinoma involving the humerus. This tumor can form in any pneumatized bone, but is most common in the humerus.

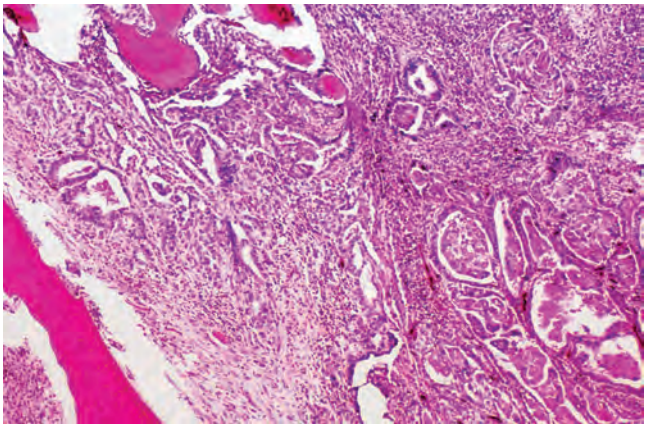

Figure 9.54 Air-sac carcinoma. Tubular structures and cords are seen infiltrating bone.

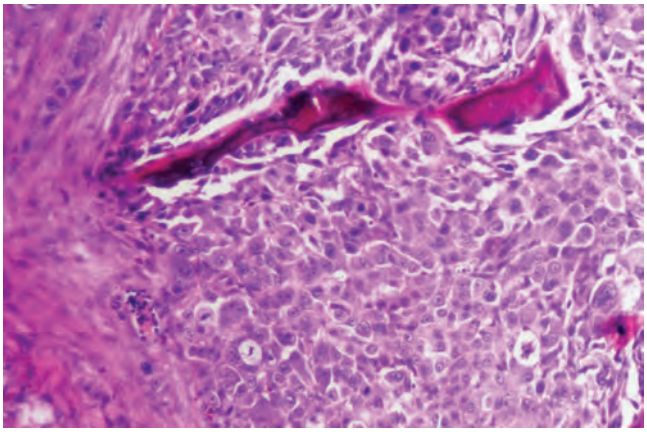

Figure 9.55 Proventricular carcinoma metastatic to bone. Poorly formed nests of large anaplastic tumor cells are seen.

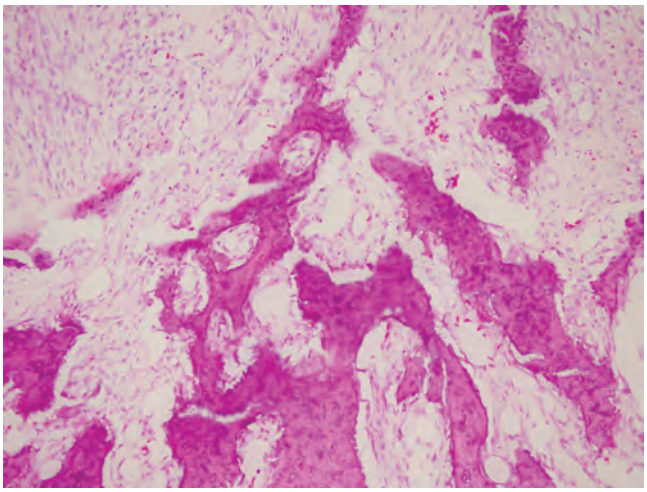

Figure 9.56 Myxosarcoma invading bone and causing lysis.

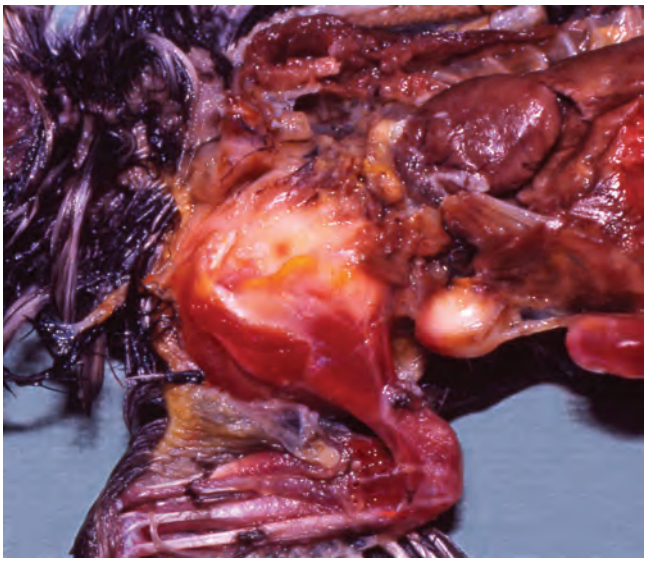

Figure 9.57 Severe bacterial arthritis. The reaction has spread to the surrounding soft tissue.

Inflammatory disease

Infectious arthritis in birds may be due to bacteria, including *Streptococcus* spp., *Staphylococcus* spp., *Escherichia coli*, *Salmonella* species, *Chlamydia psittaci*, *Mycoplasma* sp., and Reoviruses. Infectious arthritis of the elbow and hock joints is a common manifestation of salmonellosis in pigeons. In other species, any synovial membrane may be involved (Fig. 9.57). Grossly, in acute cases, there is exudate and fibrin in the joint. Histologically an infiltration of heterophils and a few macrophages is common whether the condition is bacterial, viral, or due to mycoplasma (Fig. 9.58). Inflammatory cells variably infiltrate the synovium. The synovial membrane of the chronically inflamed joint is lined by hypertrophic synoviocytes and forms villi while the joint capsule becomes fibrotic due to organization of edema by fibrous tissue that limits the normal

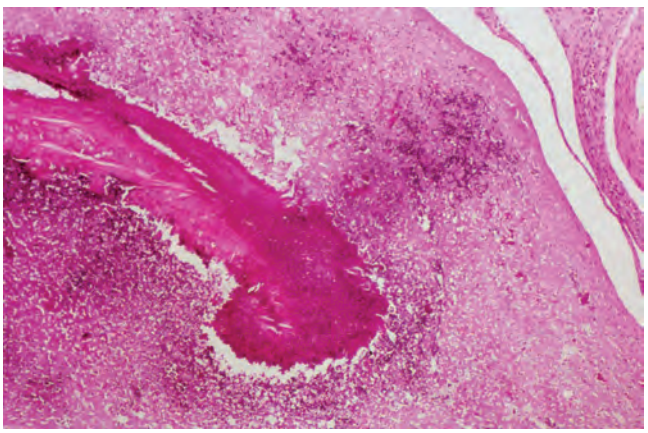

Figure 9.58 Bacteria-caused arthritis. Severe necrosis, cellular proliferation, and exudate formation are noted.

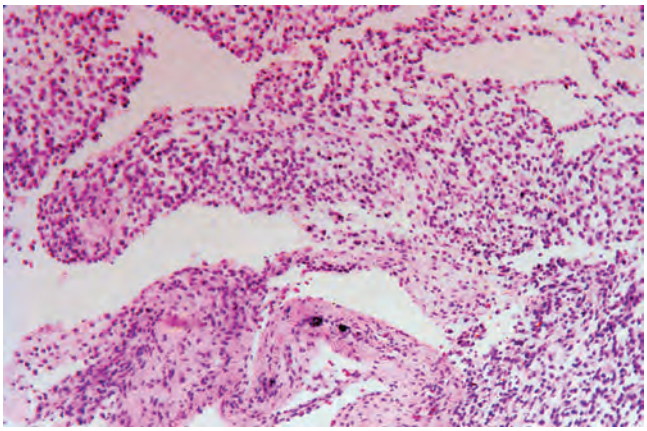

Figure 9.59 Chronic arthritis/synovitis with marked villar formation.

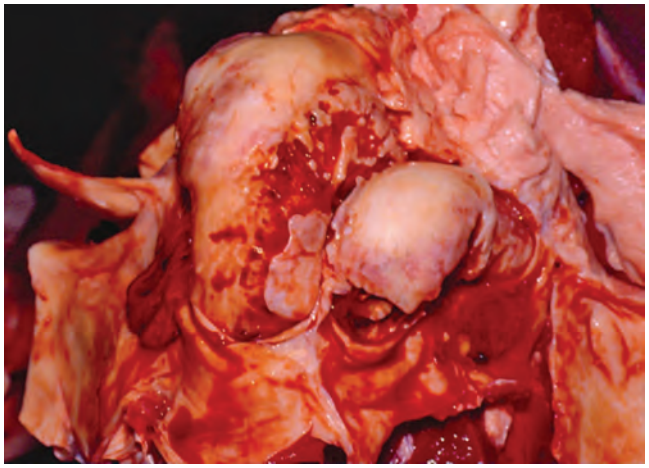

Figure 9.61 Chronic arthritis of unknown cause in an ostrich. Note the severe erosion of the cartilage, joint capsule thickening, and bone proliferation on the margins of the cartilage.

range of joint motion (Figs. 9.59 and 9.60). Lymphocytes and plasma cells predominate in the reaction. Eventually there is granulation tissue formation. Chronic arthritis of any cause can result erosion of the cartilage and bony proliferations surrounding the joint (Fig. 9.61).

A common disease of raptors (Fig. 9.62.) and waterfowl is pododermatitis also known as bumble foot. This disease is caused by physical damage to the bottom of the foot, resulting in bacterial penetration of the skin. Infection spreads to adjacent tendons, joints, and ultimately, bone. The disease in raptors is usually due to the use of improper perches and other management problems and improper substrate in waterfowl. Infections of the tibiotarsal–tarsal metatarsal joints are very common in backyard ducks. The origin of these infections is not known, but may come from injuries to the bottom of the foot.

Microfilaria have been found in inflamed joints, particularly in cockatoos, but their role in the pathogenesis of the lesion is difficult to determine. This is a rare disease of wild cockatoos and is not seen in hand-raised birds in North America and Europe.

Noninfectious arthritis is most often secondary to articular urate deposition (gout). Affected joints are swollen, and when incised there is chalky- or caseous-appearing material within the joint and adjacent soft tissue (Fig. 9.63). Histologically the urates are usually amorphous, although crystalline urates may be seen. A pleocellular inflammatory infiltrate, including giant cells, is present. There is variable tissue necrosis (Fig. 9.64).

Trauma, with or without foreign body penetration, may also lead to arthritis. If the joint does not become septic, the reaction is usually mononuclear, with giant cells seen in more chronic cases. There may be variable hemorrhage.

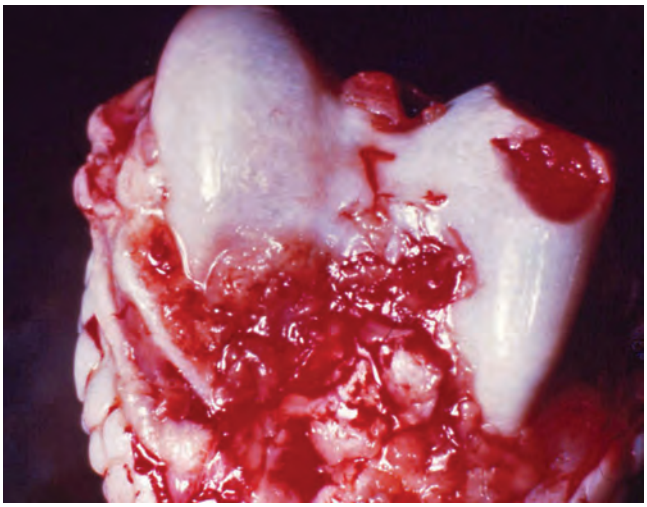

Figure 9.60 Synovial thickening and reddening and some cartilage erosion in a chicken with Mycoplasma synovitis.

Figure 9.62 Pododermatitis (aka bumblefoot) in a peregrine falcon. With chronicity these lesions can extend into the underlying tendons and bone.

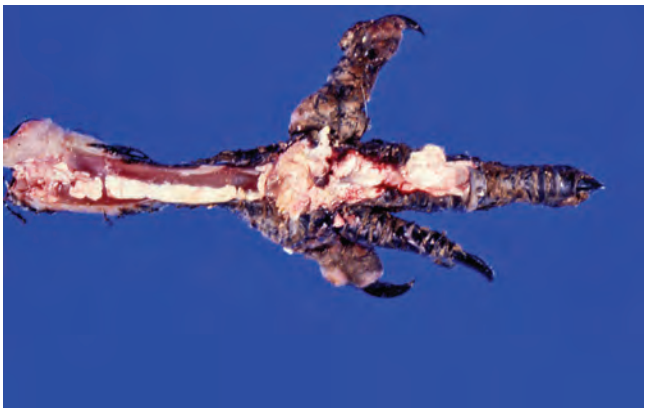

Figure 9.63 Severe articular urate deposition (gout) with extension into tendon sheaths and surrounding soft tissue.

Joint hemorrhage without any inflammatory component is usually from trauma; in conures, however, the possibility of "conure bleeding syndrome" is a differential diagnosis.

Degenerative joint disease

In pet species, degenerative lesions of the joints are usually found in older psittacine birds. Causes include previous trauma or infection, or metabolic conditions such as gout. The most common cause, however, is likely to be a degenerative osteoarthritis as is seen in aged individuals of other species. Grossly affected joints are enlarged, and there may be cartilaginous erosions. Also noted are cartilaginous flaps and free cartilage in the joint cavity. Eventually there is formation of osteophytes and fibrosis in the joint capsule and periarticular soft tissue.

Neoplastic disease

Synovial sarcoma is occasionally reported in birds. The tumor is similar to that seen in mammals and is characterized by gross destruction of the joint and bone associated with a proliferative mass. Histologically there are mucin-containing and fusiform cells. Spaces or clefts may be seen. The tumor can be difficult to distinguish from air-sac carcinoma of bone, since synovial sarcomas of birds may have two populations of cells, one of which is an epithelial type that will have some of the same immunohistochemical staining properties as carcinomas. This tumor can metastasize widely.

Multiple foci of cartilaginous proliferation (chondromatosis) involving the synovium and perisynovial soft tissue have been reported in raptors. The lesion may be an example of metaplasia of unknown cause rather than neoplasia.

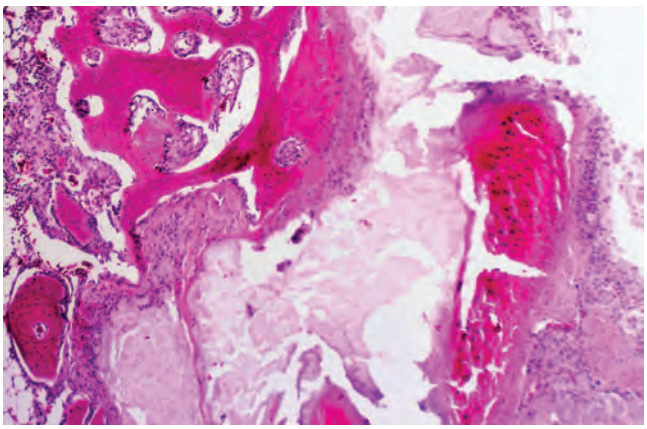

Figure 9.64 Amorphous urates typical of articular gout.

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10 Nervous System

Normal structure

The avian brain is covered by the semiopaque and relatively tough meninges. The cerebral hemispheres are lissencephalic (there are no sulci or gyri), tapered to a point rostrally, and rounded caudally. The telencephalon and diencephalon developed in a divergent path than those of mammals and have few homologous structures. The mesencephalon and rhombencephalon are derived from reptile brain as they are in mammals and contain structures homologous with the mammalian brain. The prominent features of the mesencephalon are the paired optic lobes, which project laterally under the ventral surface of the cerebral hemispheres. The optic nerves are short and thick and cross on the ventral surface of the brain just cranial to the optic lobes. The cerebellum is relatively large and has the characteristic folia seen in other animals. However, it only has a middle lobe; the lateral lobes found in mammals are absent. Birds have four ventricles in their brain. The villous choroid plexus projects into the lateral ventricles along their walls and from the roof of the third and fourth ventricles. Pathologists who are used to the microscopic anatomy of mammalian brains will find the avian cerebral hemispheres to be far more cellular. Many more glial cells are found in close proximity to the bodies of neurons in birds. The cerebellum, however, contains the molecular, Purkinje, and granular cell layer as seen in other animals.

Unlike in mammals, the spinal cord is the same length as the spinal canal and extends to the last caudal vertebra. Therefore, birds do not have a cauda equina, and spinal nerves pass laterally to the adjacent intervertebral foramina. There are cranial and caudal enlargements in the area of the brachial and lumbosacral plexi. In the dorsal midline of the lumbosacral enlargement is the rhomboidal sinus, which is unique to birds. The rhomboidal sinus separates the left and right dorsal columns, leaving a cleft occupied by the gelatinous (or glycogen) body. This structure comprises glial cells rich in glycogen and innervated by unmyelinated fibers. The ventral part of the gelatinous body encloses the spinal canal. The function of the gelatinous body is unknown. The structure of the peripheral nervous system is similar to that of mammals.

Central nervous system

Congenital anomalies

A variety of sporadic defects have been reported in several species of birds, including poultry. Abnormalities of the brain have been seen associated with avian encephalomyelitis virus infection. An autosomal recessive gene in northern goshawks led to problems with feather melanocytes and mild degeneration of cerebellar white matter. Documented anomalies in pet birds are less frequent. A meningomyelocele has been reported in association with a spinal column defect in a scarlet macaw. The bird presented with a tract that extended from the skin over the thoracic spine to the spinal cord. Portions of the cord and meninges were herniated into the area of the spinal defect. Histologic changes were confined to distortion of normal architecture and mild degeneration. This lesion occurs sporadically in other psittacine birds (Fig. 10.1).

Hydrocephalus is seen in a variety of psittacine birds. It seems to be more prevalent in older birds, indicating a possible acquired, rather than congenital, lesion. It usually involves the lateral ventricles, which are grossly distended, and leads to compression of the overlying cortex. If ruptured, the cortical tissue collapses and becomes flaccid, and excessive fluid will drain from the area of rupture. At necropsy there is variable distortion and thinning of the cerebral cortex, and if severe, removal of the cortical remnant allows structures at the base of the brain to be visualized (Fig. 10.2). There is often herniation of the cerebellum into the foramen magnum. Histologically there is distortion and degeneration of nerve tissue in what was the cerebral cortex. Cerebellar hypoplasia has been reported in fig parrots.

Lafora body neuropathy has been reported in psittacine birds, probably as a result of a congenital defect in intracellular metabolism. There is no gross lesion, and histologically glycoprotein-containing cytoplasmic inclusion bodies are seen in neurons.

A genetic defect leading to lysosomal storage disease is described in emus but is not seen in companion birds. It is a GM_1 and GM_3 gangliosidosis. Birds are typically 6–10 months old at the onset of the disease and have a history of slowed growth, poor weight gain, and upper motor neuron signs. Gross lesions are not

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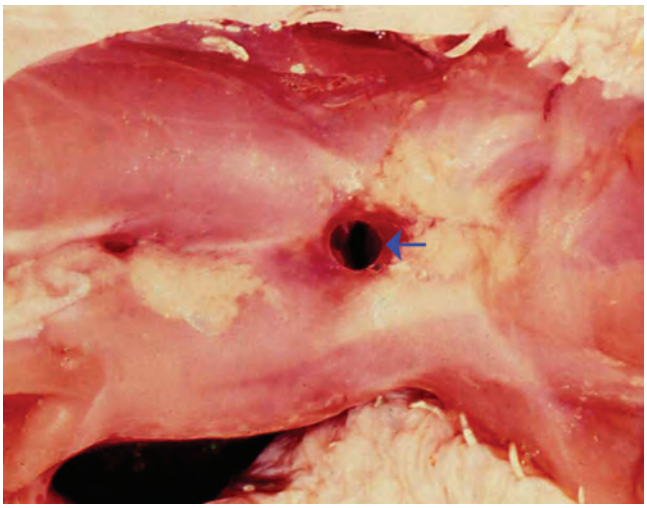

Figure 10.1 Congenital meningomyelocele that extends from the spinal cord to the skin (arrow).

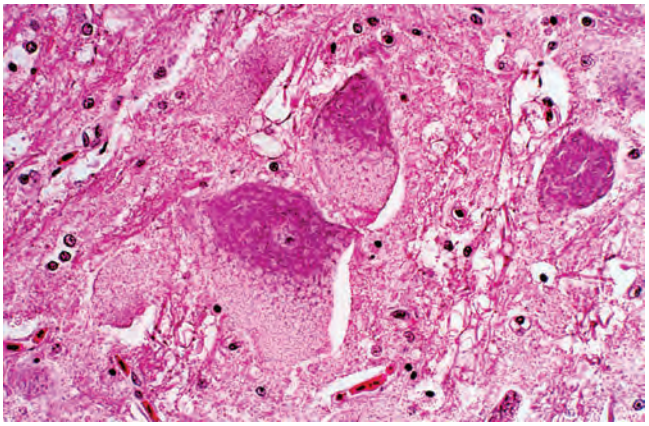

Figure 10.3 Enlarged neurons with vacuolated cytoplasm typical of lysosomal storage disease in emus.

seen, but histologically there is neuronal distension and enlargement with vacuolation of the cytoplasm. Neurons of the brain, spinal ganglia, and autonomic ganglia may be affected. Neuronal cytoplasm has a foamy appearance and may have a slight tan color, but no other staining is seen in hematoxylin–eosin sections (Fig. 10.3). Ultrastructurally there are numerous membranous cytoplasmic bodies.

Lesions similar to what has been called "congenital lipoma" have been seen in the brain and spinal cord of birds. These are considered to be proliferative congenital growths that arise from embryonic mesenchymal covering of the central nervous system (CNS). Grossly they are similar to lipomas in any location, being gray-white and slightly translucent (Fig. 10.4). Histologically, they are primarily composed of normal-appearing adipose and fibrous connective tissues (Fig. 10.5). Although benign, the location of these lesions usually results in a poor prognosis.

Toxins can cause problems in the developing brain. Methylmercury fed to female ducks accumulated in eggs and was believed to cause demyelination, neuronal shrinkage, and necrosis in the brains of hatchlings. Exposure to dioxin and dioxin-like compounds can lead to asymmetric brain formation in birds. The forebrain and tectum are most commonly affected. This problem is seen primarily in wildlife.

Inflammatory disease

Inflammatory disease of the CNS can be noninfectious or infectious. Noninfectious diseases that can cause inflammatory lesions include some toxins, autoimmune disease, and immune-mediated conditions, none of which have been well documented in pet birds. Viruses, bacteria, fungi, protozoa, and metazoan parasites all can cause inflammatory disease of the CNS.

Viral disease

A variety of viruses cause nervous system disease. In general, perivascular cuffing, gliosis, and neuronal degeneration characterize lesions. Inclusion bodies may or may not be present.

Figure 10.2 Severe hydrocephalus leading to loss/collapse of remaining cortical tissue at necropsy. Basal ganglia and other structures are visible.

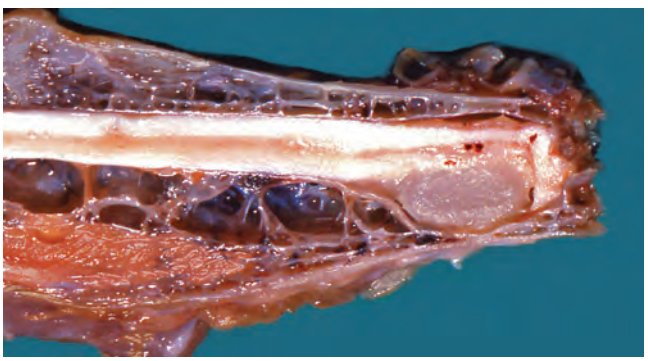

Figure 10.4 Congenital "lipoma" involving the spinal cord.

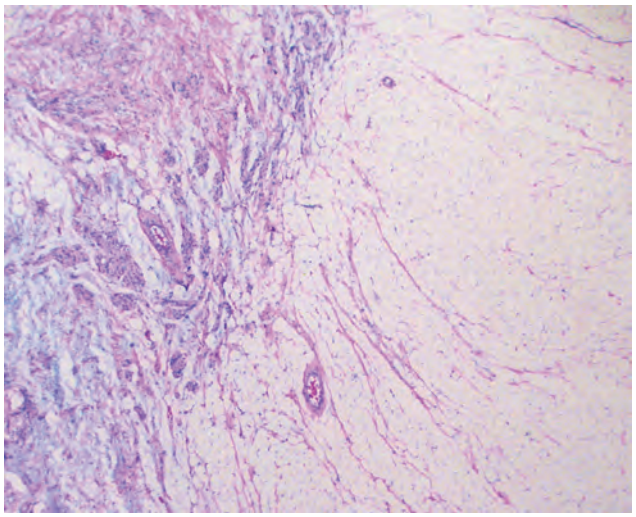

Figure 10.5 Histologic appearance of congenital lipoma from the brain of a duck.

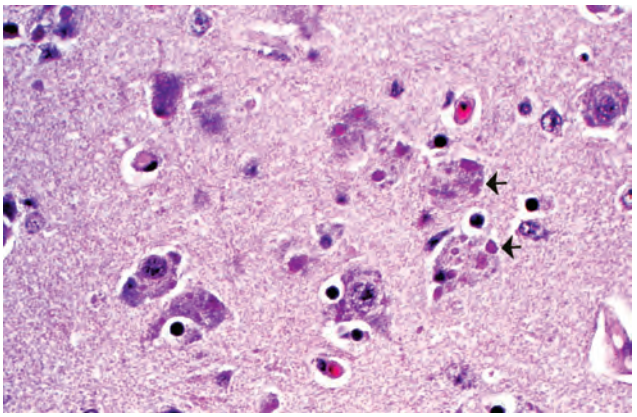

Figure 10.7 Shrunken neurons with cytoplasmic inclusion bodies (arrows) in avian PMV-3 infection.

Paramyxovirus

A number of paramyxoviruses (PMVs) cause neurologic disease in birds, and PMV-1, 2, 3, and 5 have been documented in pet birds. PMV-1 is the cause of Newcastle disease in domestic poultry. Exotic Newcastle disease has been extirpated from the United States, but in the past has entered this country through smuggled nestling double-yellow head and yellow-naped Amazon parrots and through fighting cocks. A closely related PMV-1 is a common cause of encephalitis in racing pigeons. This virus has a worldwide distribution. PMV-3 is the most common cause of encephalitis in psittacine and small passerine birds. PMV infections rarely cause gross lesions, and histologically the disease process is variable. Some birds have no inflammatory changes, whereas, others have perivascular cuffing by lymphocytes and plasma cells, minimal necrosis, gliosis, and endothelial hypertrophy (Fig. 10.6). Hemorrhage is occasionally seen, and syncytial cells may be found in some cases. Intracytoplasmic inclusion bodies are usually not seen but may be present (Fig. 10.7). Australian grass parakeets (*Neophema* sp.) and cockatiels are the birds that are most frequently affected by PMV-3. Chronic pancreatitis is a manifestation of this disease in *Neophema* (Chapter 3).

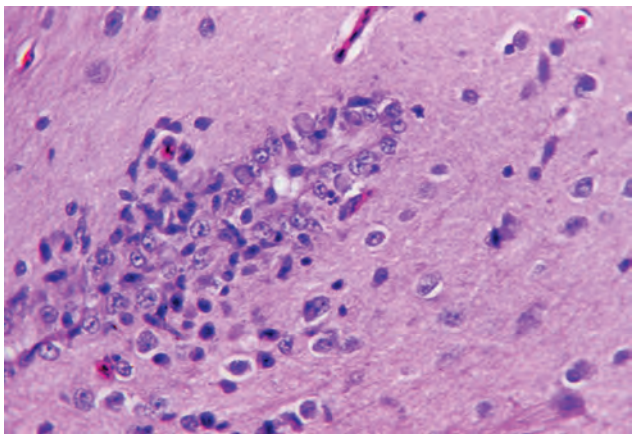

Figure 10.6 Perivascular cuffing and mild hypercellularity in the brain of a bird with PMV-3 infection.

Togavirus

Eastern equine encephalitis (EEE) and western equine encephalitis (WEE) are seen in emus, and EEE is considered to be the cause of avian viral serositis in psittacine birds. Gross CNS lesions, other than variable hemorrhage, are not seen with EEE or WEE. Histologic changes include nonsuppurative encephalitis, neuronal degeneration, and meningitis. Gross lesions of viral serositis are limited to parenchymal organs and will be discussed with the appropriate system. Histologic changes in the brain of birds with avian viral serositis include nonsuppurative meningitis and encephalitis. Lymphocytes are the primary cell type seen in the reaction.

Avian bornavirus (proventricular dilatation disease). For years, proventricular dilatation disease (PDD) affected both the autonomic nerves, particularly those of the digestive system (Chapter 3), and the CNS. Recently this disease was determined to be caused by avian bornavirus (ABVD). Most commonly, signs of this disease relate to the digestive system. However, CNS disease often accompanies the disease of the nerves of the digestive tract, and CNS lesions may be the predominant feature of some infections. PDD does not cause gross lesions in the CNS. Histologic changes are of a typical nonsuppurative inflammatory process most severe in the brain stem and spinal cord (Fig. 10.8). Gliosis and neuronophagia are occasionally seen. Between 60% and 100% of the birds in various case surveys have microscopic brain lesions. Spinal cord lesions are also common, but most pathologists rarely evaluate the spinal cord.

Picornavirus

This virus has been occasionally implicated as a cause of encephalitis in pet birds, but there is minimal documentation.

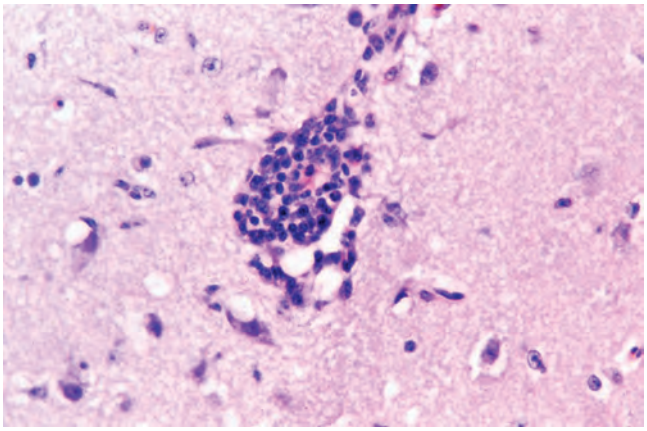

Figure 10.8 Perivascular inflammation in the brain of a bird with PDD.

Figure 10.10 West Nile virus infection causing meningeal and brain congestion and hemorrhage.

Histologic lesions are typical of nonsuppurative encephalitis. The causative agent of avian encephalomyelitis of chickens is a picornavirus. Natural disease has also been reported in turkeys, quail, and pheasants. The disease in chickens is seen in chicks of 1–2 weeks of age. No gross lesion is seen in the CNS, but small white foci have been reported in the ventricular musculature in some cases. Histologically CNS lesions are nonsuppurative and similar to those of other viral encephalitis, including perivascular cuffing by lymphocytes and gliosis. Neuronal degeneration may also be seen, with central chromatolysis of neurons considered characteristic of the disease in chickens (Fig. 10.9). For a definitive diagnosis, the virus must be isolated or antibodies demonstrated by ELISA tests.

Influenza A

This has occasionally been isolated from psittacine birds including African gray parrots, cockatoos and budgerigars, mynahs, and passeriformes. There are occasional reports of influenza virus-induced neuronal disease. The virus is reported to cause gross hemorrhage and histologic changes in wild birds, which include gliosis, neuronal degeneration, perivascular cuffing, and occasional meningitis.

West Nile virus

This virus, which causes systemic disease as well as CNS lesions, has infected a variety of pet and wild birds. Grossly, meningeal and brain congestion and hemorrhage are found (Fig. 10.10). Histologically the hemorrhage is most severe in the cerebellar folia (Fig. 10.11). There is lymphoplasmacytic meningitis and variable encephalitis. In mild cases, lesions are more common in the cerebellum and brain stem but may be generalized in the more severe disease. Cuffing of vessels by lymphocytes and plasma cells, gliosis or glial nodule formation, and neuronal necrosis are seen. Purkinje cells may be completely lost, and degenerative changes are common in the molecular layer of the cerebellum. In psittacine birds perivascular cuffing by

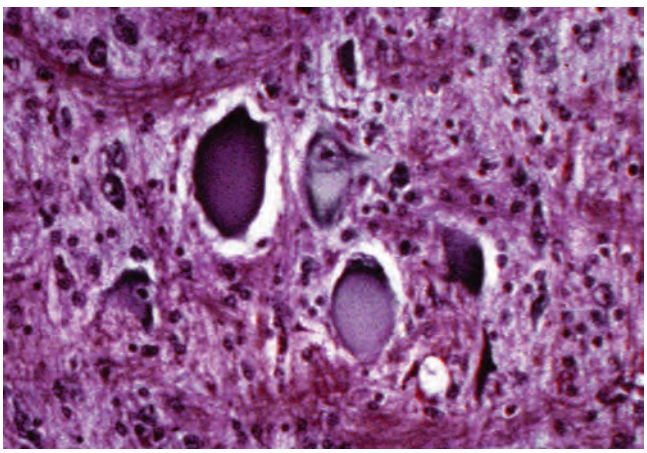

Figure 10.9 Marked neuronal central chromatolysis in the brain of a chicken with avian encephalomyelitis.

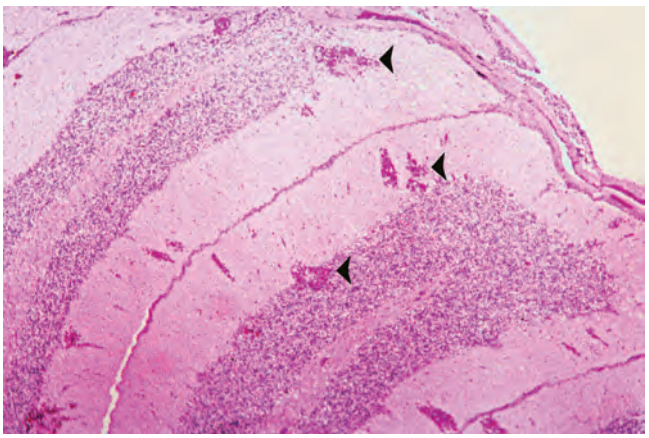

Figure 10.11 Multiple foci of hemorrhage and necrosis in a bird with West Nile virus infection (arrowheads).

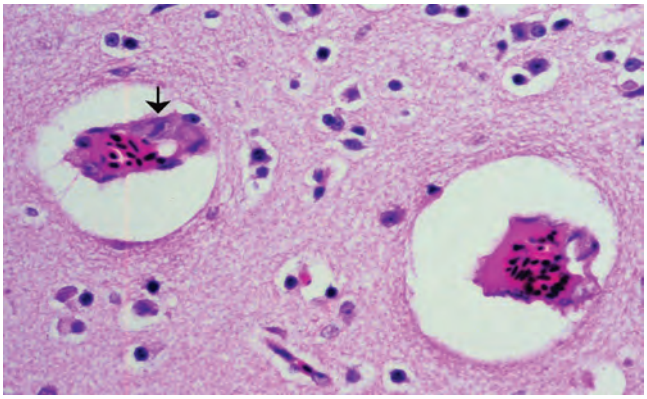

Figure 10.12 A degenerating endothelial cell with an intranuclear inclusion body consistent with adenovirus infection (arrow). There is usually no associated inflammation.

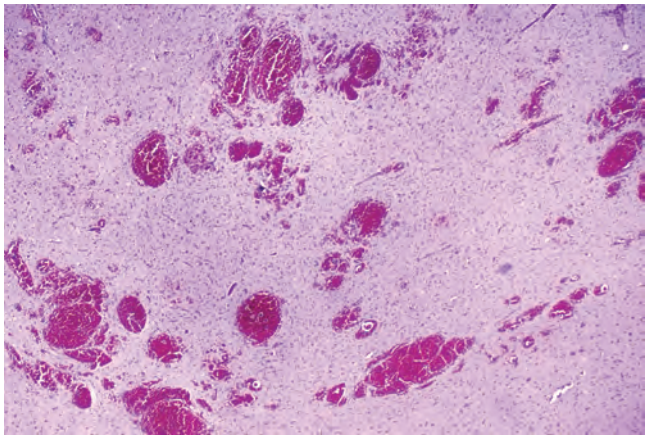

Figure 10.13 Multifocal brain hemorrhage in a bird with polyomavirus infection.

lymphocytes and histiocytes was noted occasionally, primarily in the cerebrum and brain stem.

Lesions are also seen in the heart, intestine, spleen, pancreas, lung, and kidney. Grossly there may be pale foci or streaks. Splenic and renal enlargement and hemorrhage in all affected organs are seen. Histologically a lymphoplasmacytic and histiocytic inflammatory infiltrate, necrosis, and hemorrhage characterize the lesions. Adenitis of the adrenal gland can also occur. Differential diagnosis includes other viral diseases and other causes of hemorrhagic brain lesions.

Adenovirus

Neurologic signs associated with adenovirus infection are most common in cockatiels and budgerigars. No gross lesion is present, and histologic changes include degeneration of small blood vessels, endothelial necrosis, and intranuclear inclusion bodies in endothelial cells (Fig. 10.12). Inflammation is usually minimal or absent, but a nonsuppurative encephalitis is reported in budgerigars. Adenovirus inclusions have also been reported in the brain of a Moluccan cockatoo with a progressive CNS disease.

Avian polyomavirus

In some outbreaks in budgerigars, significant cerebellar lesions may be seen. Affected chicks will have prominent intention tremors. Characteristic intranuclear inclusion bodies with karyomegaly are abundant in the molecular layer of the cerebellum. Two cases of a progressive fatal neurologic disease caused by avian polyomavirus have been reported in cockatoos.

Lesions in these birds were confined to the gray matter. They included hemorrhage and degeneration of astrocytes and neurons, with characteristic intranuclear inclusions found in some of these cells (Figs. 10.13 and 10.14). Inflammation was not seen in these birds. The second case was concurrently infected with the psittacine beak and feather disease virus, suggesting that immunosuppression may play a role in this disease.

Bacterial infection

Numerous bacteria, including *Staphylococci* sp., *Salmonella* sp., *Escherichia coli*, *Pseudomonas* sp., and *Klebsiella* sp., are possible causes of meningitis, encephalitis, and myelitis. Inflammation of the brain and meninges can be from direct extension of an infection from the sinuses, nasal cavity, or inner ear, or may be the result of a bacteremia or septicemia. Gross lesions are absent in many cases, but exudate can occasionally be seen in the meninges, and in chronic cases, abscesses can be found in the brain.

Infiltrating inflammatory cells and fibrin deposition thicken the leptomeninges (Fig. 10.15). Malacia and a pyogranulomatous inflammatory lesion with the presence of intralesional bacteria characterize bacterial induced lesions. In some cases, septic thrombi are present in blood vessels (Fig. 10.16).

Chlamydia psittaci will affect serous membranes throughout the body and can induce a nonsuppurative meningitis.

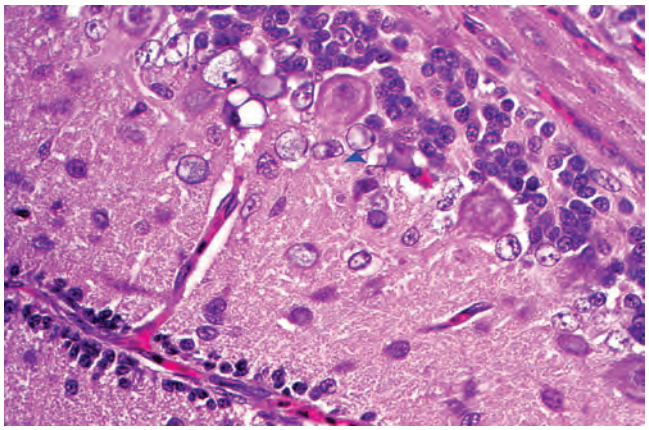

Figure 10.14 Chromatin margination and clear intranuclear inclusion body (arrowhead) occasionally seen in the brain of birds with polyomavirus infection.

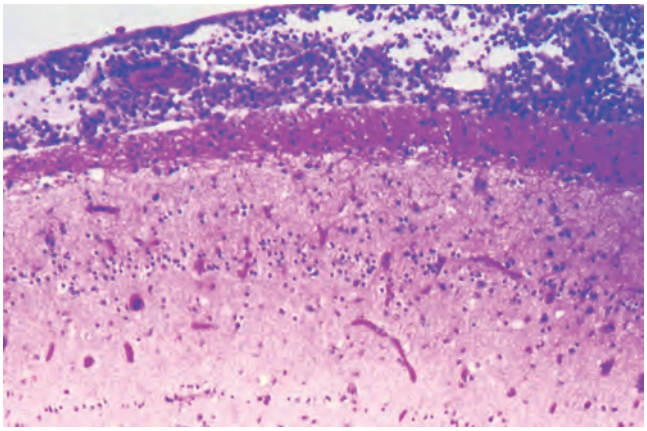

Figure 10.15 Severe leptomeningitis due to bacteria. Heterophils and macrophages are present, and there is minimal edema and fibrin deposition.

Mycobacterial infection of the CNS is usually part of a systemic process. Gross lesions are proliferative and gray-white or yellow. Early microscopic changes are similar to those seen in mycobacteriosis in other organs and contain heterophils, lymphocytes, and small macrophages. As the lesion progresses, large macrophages containing organisms are seen. There may be variable necrosis (Figs. 10.17 and 10.18). In psittacine birds infected by *M genavense*, gross lesions were not seen in the brain or spinal cord, and histologically there was gliosis and mild vacuolation of white matter, as well as perivascular cuffs of macrophages and lymphocytes.

Fungal infection

As with bacterial disease, fungal infections can be bloodborne or may occur secondary to extension from the nasal cavity or sinuses. The brain, spinal cord, and meninges all may be affected. Gross changes depend on the chronicity of the lesion and vary from none to the presence of granulomas. Microscopically, pyogranulomatous inflammation and fungal hyphae are noted in the lesion and in the blood vessel walls (Figs. 10.19 and 10.20).

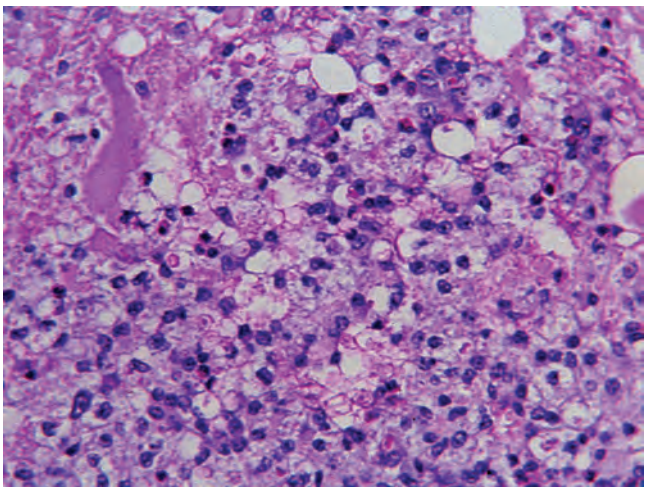

Figure 10.16 Bacteria-caused encephalitis. Note the necrosis and infiltrate of heterophils and a few macrophages. Inflammatory cells plug several blood vessels.

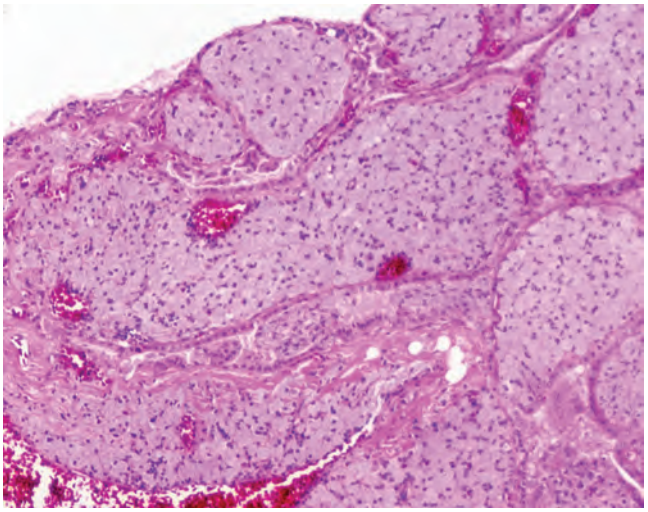

Figure 10.17 Mycobacterial encephalitis. The primary infiltrate comprises large macrophages with slightly granular cytoplasm.

Parasitic infection

Several protozoa, including *Sarcocystis*, *Toxoplasma gondii*, and *Leukocytozoon* sp., may cause brain lesions. The most common in pet species has been presumed to be *S. falcatula*; however, recent reports of the identification of *S. calchasi* for a cause of encephalitis in columbiformes and psittacine birds indicate the possibility that, in the absence of polymerase chain reaction (PCR) sequencing, the presumption that *S. falcatula* was the cause of the encephalitis seen was in error. Encephalitis usually occurs as a part of systemic disease and seems to be more prevalent in birds that have had prolonged natural disease or

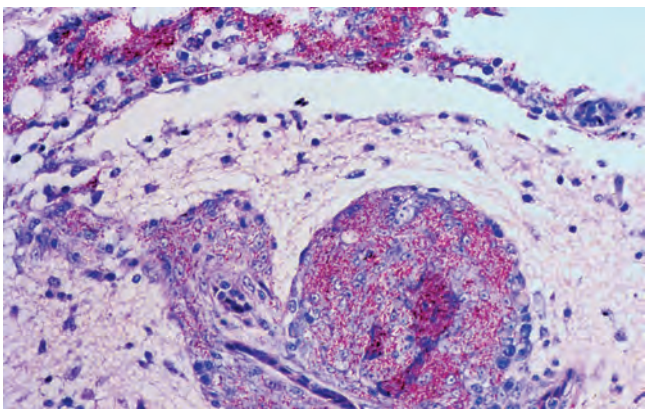

Figure 10.18 Acid-fast stain to illustrate intracytoplasmic organisms in mycobacterial encephalitis.

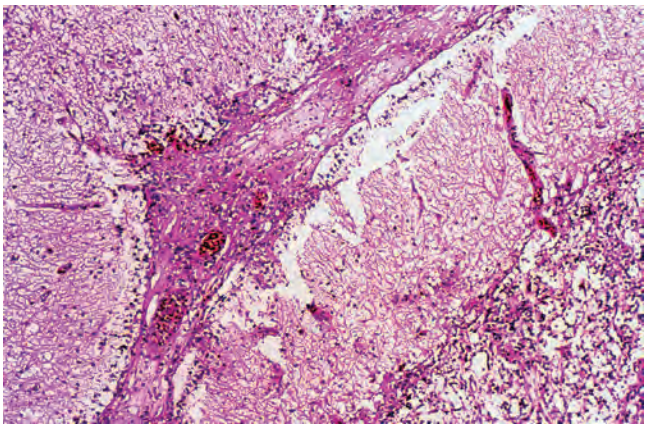

Figure 10.19 Meningoencephalitis due to fungal infection. At a lower magnification, the lesion is morphologically similar to a bacterial infection.

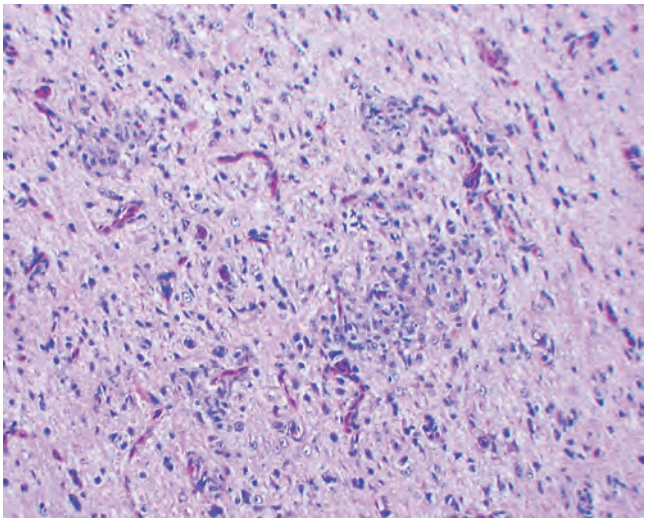

Figure 10.21 Focus of gliosis in the brain of a bird with systemic sarcosporidiosis.

survived for sometime due to aggressive therapeutic regimens. Gross lesions are usually absent in the CNS, but some birds may have skeletal muscle lesions.

Histologic changes include a necrotizing encephalitis and a pleocellular reaction that may include giant cells. Schizonts and merozoites are present in the lesion but can be few and difficult to find in some cases. Associated blood vessels have variable endothelial swelling and are cuffed by plasma cells, lymphocytes, and macrophages (Figs. 10.21 and 10.22).

Toxoplasmosis causes similar histologic lesions. Immunochemistry or electron microscopy may be needed to differentiate the lesions. Toxoplasmosis is infrequently seen in pet birds in North America.

Leukocytozoon infection may lead to the formation of megaloschizonts in the brain. On careful gross examination, these may present as small white foci, but they are difficult to see. Histologically they are similar to megaloschizonts in other organs, and there is minimal cellular reaction unless they rupture. These lesions are found in pigeons and some species of wild birds.

Wandering nematode parasites (cerebrospinal nematodiasis) can cause severe lesions in the avian brain. It has been reported in at least 90 avian species. *Baylisascaris procyonis* is the most common and is the result of ingestion of food contaminated with raccoon feces. The condition is more prevalent in zoos and outdoor aviaries. In severe cases, there is grossly noticeable malacia and hemorrhage. Microscopic malacic tracts are seen, and fragments of parasites may be found. A nonsuppurative inflammatory reaction is present, and there can be gitter cell accumulation, gliosis, axonal swelling, and minimal hemorrhage. Cuffing of associated blood vessels by lymphocytes and plasma cells is common (Figs. 10.23 and 10.24).

Chandlerella quiscali is a filarial parasite of grackles. The adult worm lives in the ventricles of the brain, and microfilaria are

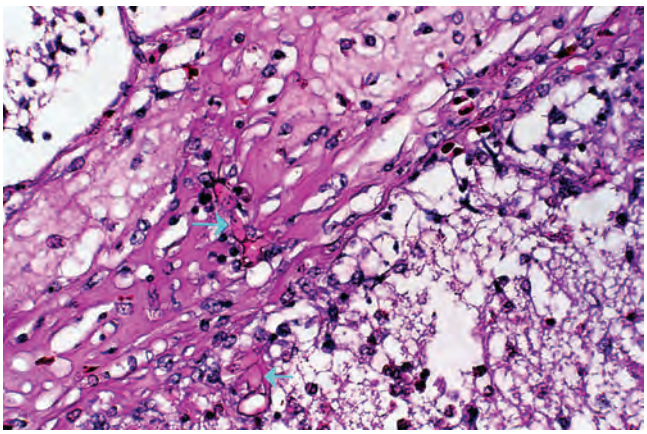

Figure 10.20 Fragment of a fungal hypha (arrows) within the lesion illustrated in Figure 10.12. The exact organism cannot usually be determined based on its microscopic appearance.

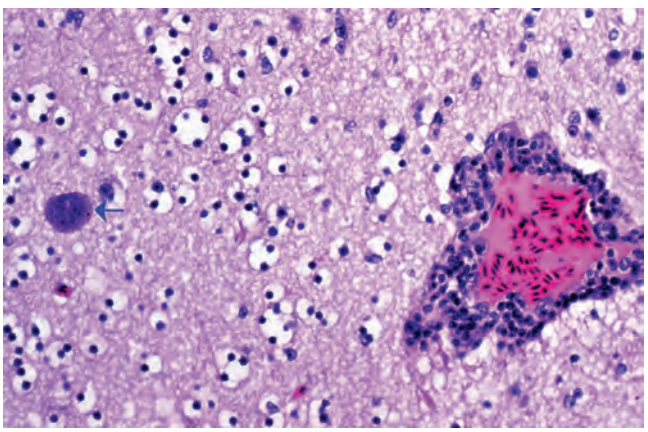

Figure 10.22 Sarcosporidial encephalitis. Note the perivascular cuffing and one protozoal cyst (arrow).

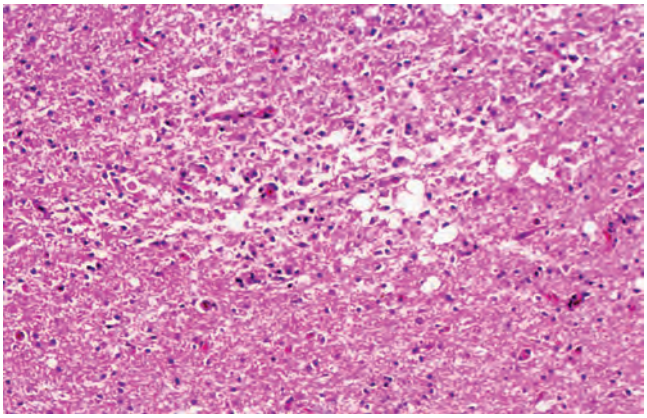

Figure 10.23 Encephalomalacia following nematode migration in the brain.

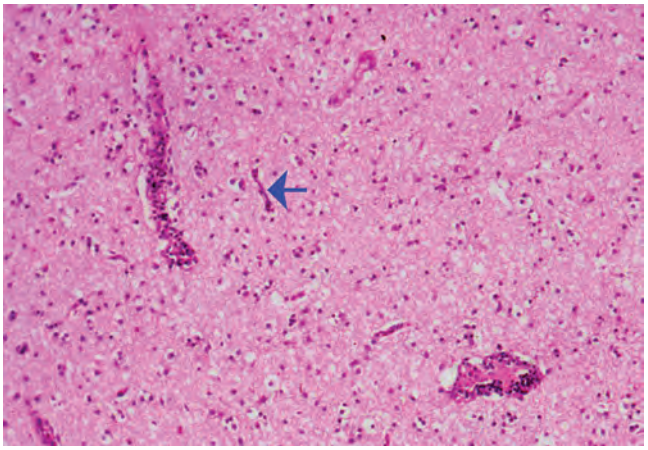

Figure 10.25 Minimal perivascular inflammation associated with microfilariasis involving capillaries in the brain. Although difficult to see, a microfilaria is present in one small capillary (arrow).

readily demonstrated in the blood. Emus, 2–6months old, can be devastated by this parasite. Birds have a history of ataxia and torticollis. Many larval forms of the parasite are found in the spinal cord and brain. They elicit a lesion similar to that caused by *B. procyonis*.

Microfilariasis with plugging of the small vessels in the brain, ischemia, and clinical disease is a condition that is most prevalent in wild or wild-caught cockatoos but could be found in any bird with subcutaneous or peritoneal cavity filariasis. Microscopically, in addition to the microfilaria, there may be small areas of malacia and variable congestion. There is usually no inflammatory response (Fig. 10.25).

Noninflammatory disease

Infectious disease

Spongiform encephalopathy results from an abnormal conformational change in brain glycoprotein that creates infectious proteins called prions. A condition resembling bovine spongiform encephalopathy is reported to occur in psittacine birds. Gross lesions are not seen. Histologically there is vacuolar degeneration of neurons in specific nuclei of the cerebellar peduncles and brain stem (Fig. 10.26). There may be single or multiple discrete cytoplasmic vacuoles in affected neurons. Mild spongiosis of white matter and gliosis are also seen. A prion has yet to be isolated from these birds.

Physical/traumatic head injuries

One of the most common causes of traumatic brain damage is aggression from cage mates or attack by wild predatory birds on unprotected captive birds. There is often, but not always, associated bruising and hemorrhage of the skin and subcutis over the skull, and, in severe cases, there may be damage to the external portion of the skull.

When there has been trauma, the meninges and brain will be hemorrhagic, and the hemorrhage will extend into the brain

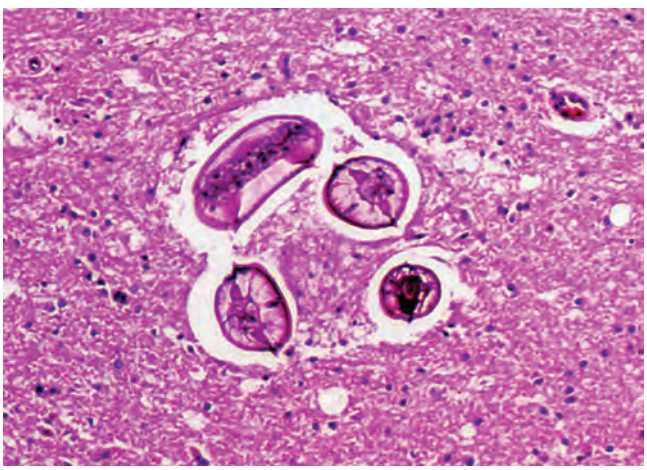

Figure 10.24 Nematodes, probably *Baylisascaris* sp., in the brain due to aberrant migration.

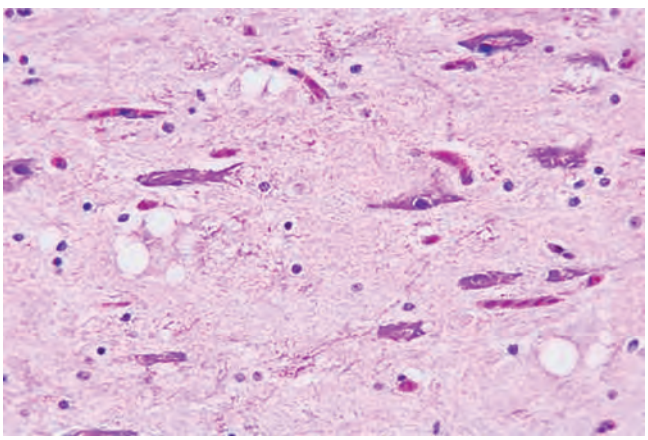

Figure 10.26 Multiple neuronal vacuolation typical of spongiform encephalopathy due to possible infection.

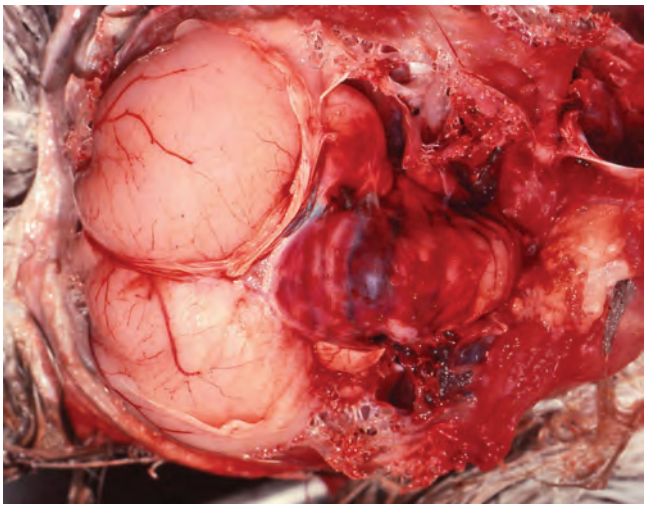

Figure 10.27 Trauma-induced hemorrhage of the brain and meninges.

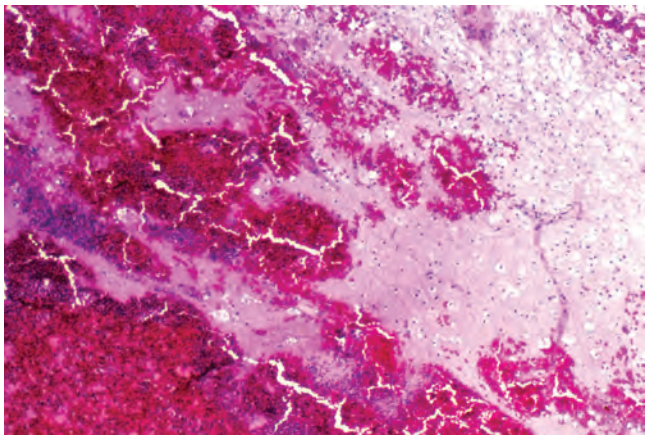

Figure 10.29 Severe malacia and hemorrhage within the brain parenchyma.

parenchyma (Figs. 10.27 and 10.28). If there is only severe congestion, either antemortem or postmortem, no hemorrhage will be noted when the brain is incised. Histologically the hemorrhage is accompanied by variable malacia (Fig. 10.29).

Head injuries must be differentiated from postmortem pooling of blood in venous sinuses of the calvarium (Fig. 10.30). This postmortem artifact is very common and will not be associated with damage to the skin or brain or with meningeal hemorrhage.

Thrombosis can lead to acute ischemia and hemorrhage. A common cause of thrombosis in female birds is yolk emboli. Parenchymal changes are similar to those just described, but yolk emboli are found in affected arteries (Fig. 10.31). In more chronic lesions, there may be an accumulation of gitter cells and amorphous yellow-brown material (Fig. 10.32).

Cases of brain hemorrhage and malacia without any identifiable cause are sporadically seen. Morphologically they resemble the traumatic lesion described (Fig. 10.33). Hemorrhage in the brain and spinal cord may also occur in cases of conure bleeding syndrome, a problem of conures whose etiology and pathogenesis are not well understood.

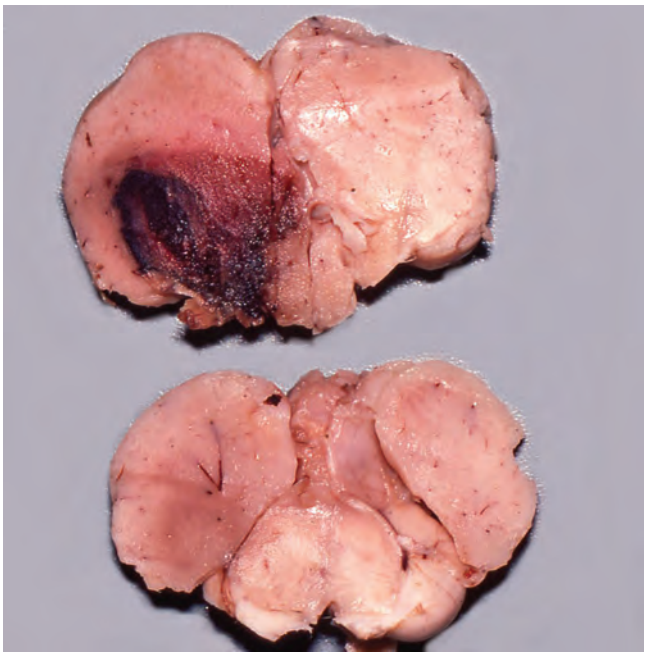

Figure 10.28 Hemorrhage deep within the brain following severe trauma.

Toxic neuropathy

Toxins known to cause problems in the avian brain include lead, zinc, sodium, poisonous plants, mycotoxins, and insecticides. Gross changes are not usually seen. Neuronal degeneration and variable edema are noted in cases of lead poisoning. Edema and

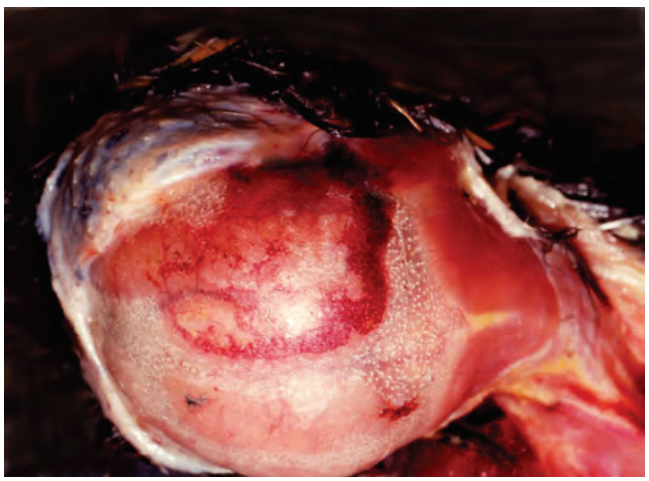

Figure 10.30 Postmortem pooling of blood in the calvarium. This must be differentiated from trauma. Trauma will cause hemorrhage in the brain which will not be seen with this type of postmortem change.

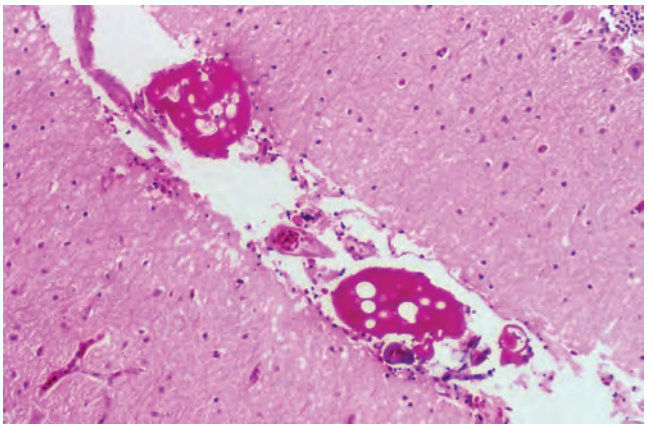

Figure 10.31 Embolus of yolk material in a cerebral vessel. Some of the separation of brain parenchyma is artifactual.

hemorrhage are seen with sodium intoxication, and neuronal degeneration may be found in zinc toxicity. The latter can be histologically similar to infectious spongiform encephalopathy as previously described, and electron microscopy will be necessary to make a definitive diagnosis.

Mycotoxins cause encephalomalacia, which may be grossly visible if severe. Organic phosphate and carbamate insecticides can lead to demyelination in the spinal cord and peripheral nerves.

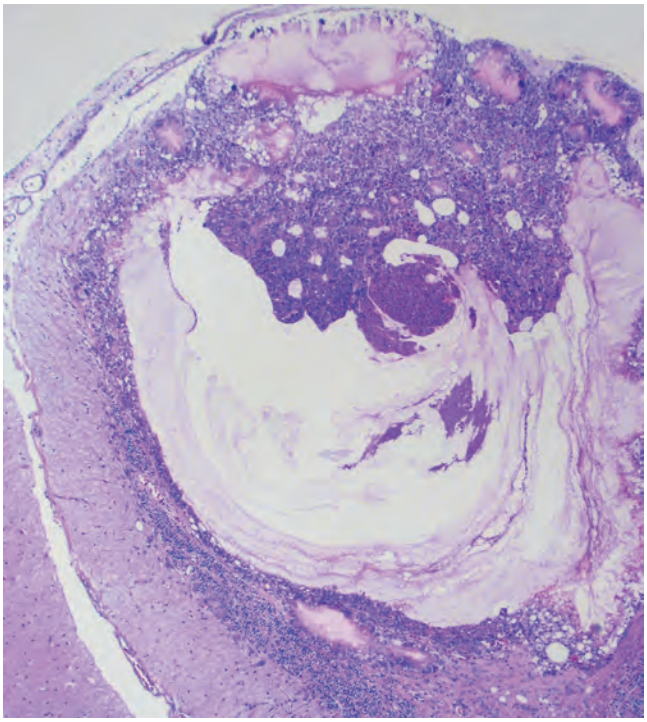

Figure 10.32 Malacia, gitter cells, and amorphous material within the brain following yolk embolization.

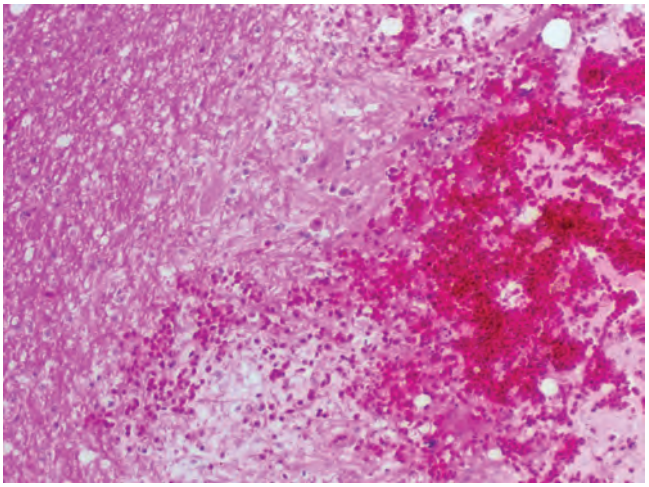

Figure 10.33 Infarct of the brain. This type of lesion can be seen in vascular disease, but often no specific cause is determined.

Nutritional deficiencies

Vitamin E deficiency affects several organ systems including cardiac, ventricular, and skeletal muscle and skin. It may cause encephalomalacia in poultry, emus, and, occasionally, psittacine birds. Grossly there may be hemorrhage and edema of the brain, particularly involving the cerebellum (Fig. 10.34), but often no lesion is seen. Histologic changes include malacia, gliosis, and neuronal necrosis primarily involving the cerebellum.

Brain lesions believed to be associated with vitamin E deficiency occur in great-billed parrots. There is degeneration and loss of Purkinje cells and a spongiform degeneration of the white matter of the cerebellum and, in severe cases, of the cerebrum. Prominent myocardial and skeletal muscle lesions are also present in these birds.

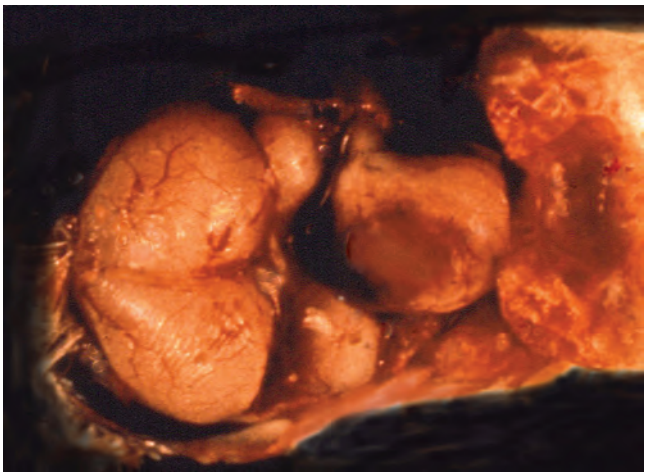

Figure 10.34 Irregular, swollen cerebellum in a chicken with vitamin E deficiency.

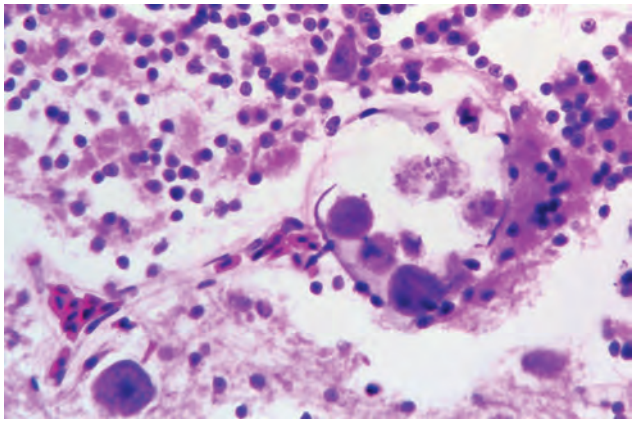

Figure 10.35 Foci of cerebellar mineralization. This is an occasional incidental finding. The tissue separation is artifact.

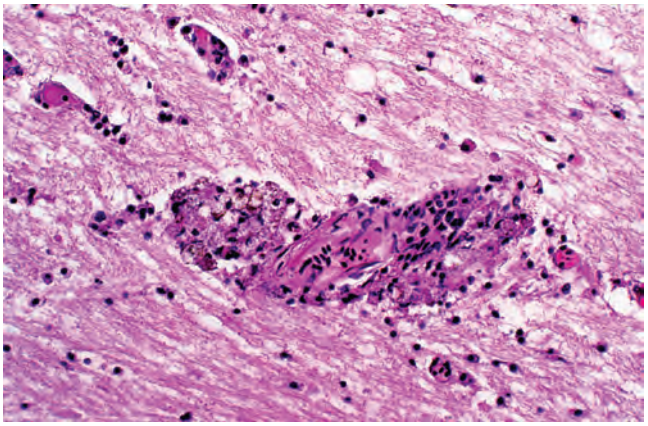

Figure 10.37 Perivascular accumulation of iron pigment-containing macrophages in a toucan with a generalized iron storage.

Degenerative lesions

Cerebellar degeneration of unknown cause was seen in a turquoise parrot (*Neophema pulchella*). No gross change was noted, but histologically the granular layer was small and there was neuronophagia and necrosis.

Mineralization is an occasional incidental finding in the brain, as is lipofuscin deposition in neurons (Figs. 10.35 and 10.36). Lipofuscin is a common finding in the neural cell bodies of older parrots. Generally the lesion is mild, but in some birds, the lesion is prominent. It is suspected that in most cases this pigment accumulation does not have a functional significance.

Hemosiderin-containing macrophages may accumulate in the brain of birds (particularly toucans and mynahs) with severe iron metabolic problems (Fig. 10.37).

Proliferative lesions

A variety of primary and metastatic tumors are reported in the avian brain and spinal cord. Although much of the literature concerns domestic poultry, most tumors described are found in pet birds.

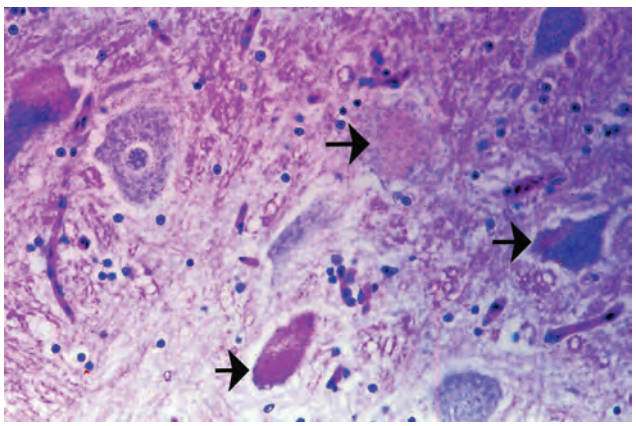

Figure 10.36 Scattered neuronal lipofuscin accumulation (arrows). Although considered an incidental finding in most birds affected, lipofuscin accumulation may indicate inadequate dietary antioxidants.

Meningioma

These tumors are usually solitary within the meninges and are of variable shape. They are firm and gray-white to yellow. If there has been any hemorrhage, they may be slightly reddened. Microscopically, tumor cells usually have abundant cytoplasm and are fusiform. Whorls and bundles of neoplastic cells are the most common pattern. These tumors grow by expansion, and some compression of adjacent brain may be seen.

Avian meningeal tumors not morphologically typical are also occasionally seen. They appear to be undifferentiated sarcomas with pleomorphic cells arranged in sheets (Fig. 10.38). There may also be minimal invasion of the brain (Fig. 10.39).

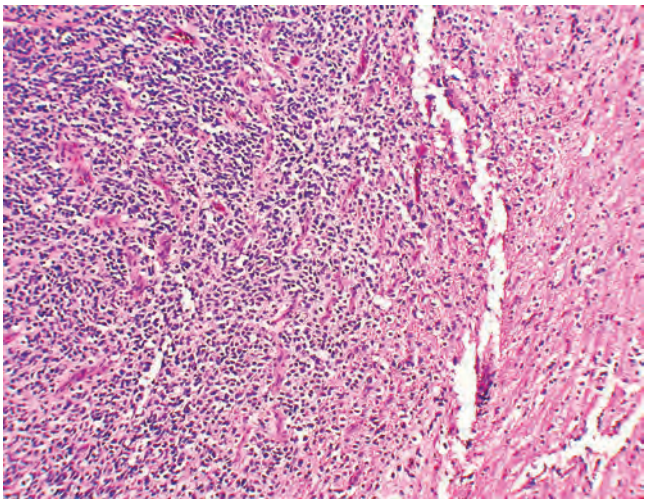

Figure 10.38 Meningeal tumor consistent with possible sarcoma. The exact cell of origin may not be apparent morphologically.

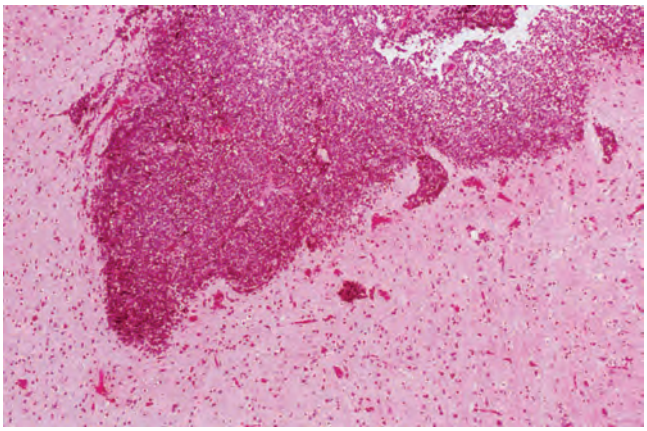

Figure 10.39 Undifferentiated tumor arising in the leptomeninges with extension into the brain.

Choroid plexus papilloma

These tumors present as well-defined papillary structures within ventricles. They are gray-white to red. Histologically the tumors have a vascular connective tissue stroma covered by epithelial cells that are cuboidal or columnar and resemble normal choroid plexus.

Primary tumors of glial cells

Glioblastoma multiforme, astrocytoma, and oligodendroglioma are all seen in birds. Grossly these tumors may be difficult to detect, particularly in early stages. There may be some enlargement and distortion or dislocation of normal structures. Asymmetry can be noted on coronal sections of brain (Fig. 10.40). If there is necrosis or hemorrhage, the area of tumor may resemble an abscess or infarct.

Glioblastoma multiforme is cellular and has a pleomorphic histologic appearance. Some cells resemble differentiated astrocytes, whereas, others are elongated and fusiform with numerous mitotic figures (Fig. 10.41).

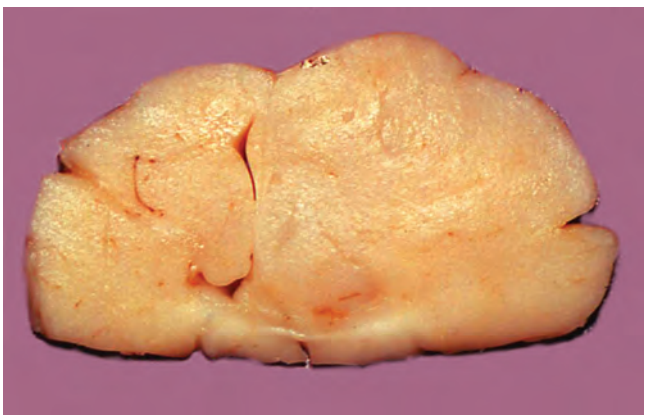

Figure 10.40 Glioma of the avian brain. There is unilateral distortion of the brain with loss of normal ventricular architecture.

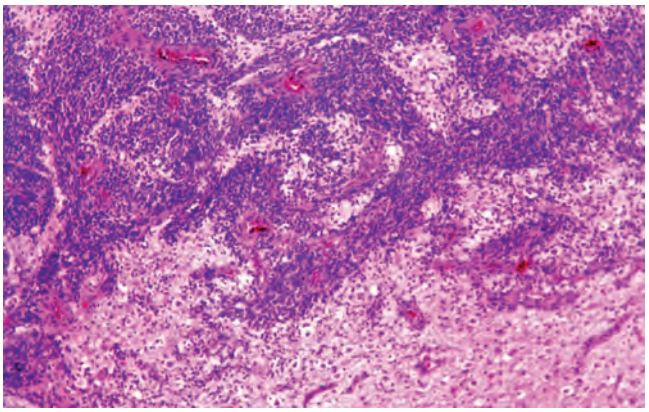

Figure 10.41 Glioblastoma multiforme replacing brain parenchyma.

Astrocytomas are usually fairly uniform, with hyperchromatic nuclei and abundant cytoplasm. Cell process can be seen with silver stains. Few mitotic figures are present. Oligodendrogliomas are cellular and composed of sheets of small cells with hyperchromatic nuclei and poorly staining cytoplasm. Mitoses are infrequent.

Medulloblastoma and neuroblastoma

These primary tumors of neuronal cells have infrequently been documented in companion bird species. Medulloblastoma is considered an embryonic neoplasm (primitive neuroectodermal tumor or PNET) that may arise from the external granular layer of the cerebellum. Grossly it is usually well defined and histologically comprises anaplastic cells that may form rosettes. Definitive differentiation of neuroblastoma from glial tumors requires immunohistochemistry.

Metastatic tumors of the brain

Metastatic carcinomas, various sarcomas including lymphosarcoma and hemangiosarcoma, and malignant melanoma have been seen in the avian brain. These will be described with their primary system (Figs. 10.42, 10.43, and 10.44). In chickens, Marek's disease may cause initial minimal perivascular cuffing, but with chronicity a lymphoproliferative lesion develops (Fig. 10.45).

Peripheral nervous system

Inflammatory disease

Peripheral nerves can be involved in a variety of infectious and noninfectious diseases. In many conditions, the histologic changes are similar due to the limited responses of peripheral nerves.

Viral disease

PDD was mentioned previously as a primary disease of the nervous system, and its lesions are more prevalent in the peripheral

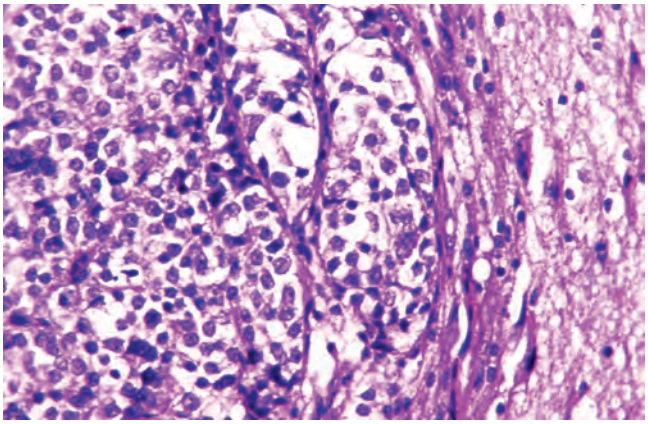

Figure 10.42 Adrenal carcinoma (interrenal cell origin) metastatic to the spinal cord.

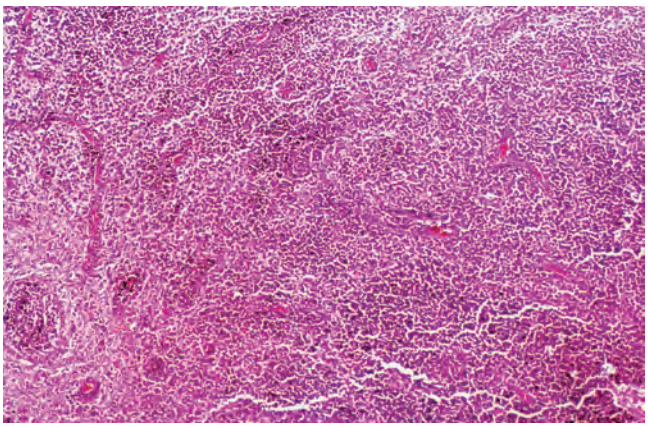

Figure 10.43 Lymphosarcoma in the brain. Brain parenchyma is almost completely effaced.

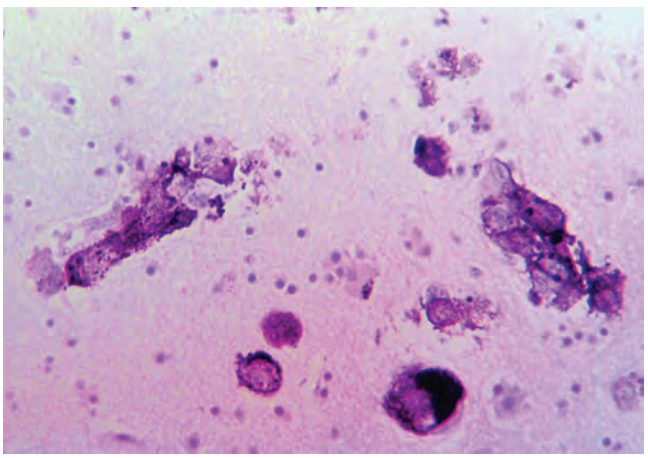

Figure 10.44 Malignant melanoma. Multiple small accumulations of neoplastic melanophores are present in the brain parenchyma.

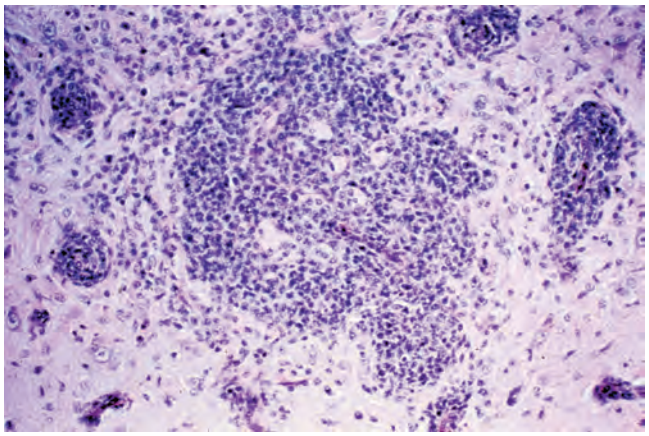

Figure 10.45 Lymphoproliferative reaction in the brain of a chicken with Marek's disease.

nervous system. Gross changes are usually referable to the heart (Chapter 1) or to the gastrointestinal tract (Chapter 3). Histologic lesions are seen in peripheral nerves and nerve ganglia. The most prevalent change is a lymphoplasmacytic inflammatory infiltrate around and within nerves and ganglia (Fig. 10.46). In some early cases, there may also be a heterophilic component.

West Nile virus also can cause a peripheral neuritis that is morphologically similar to PDD (Fig. 10.47). The species of bird and the characteristics of other lesions must be evaluated in making a distinction between the two diseases. A similar infiltration of peripheral nerve is seen in chickens with Marek's disease. In some cases this appears to be a lymphoplasmacytic inflammatory reaction (Fig. 10.48), and in others it is more consistent with a lymphoid neoplastic infiltration.

Other infections

Bacterial, mycobacterial, and fungal infections can involve adjacent peripheral nerves, with lesions typical of the primary problem.

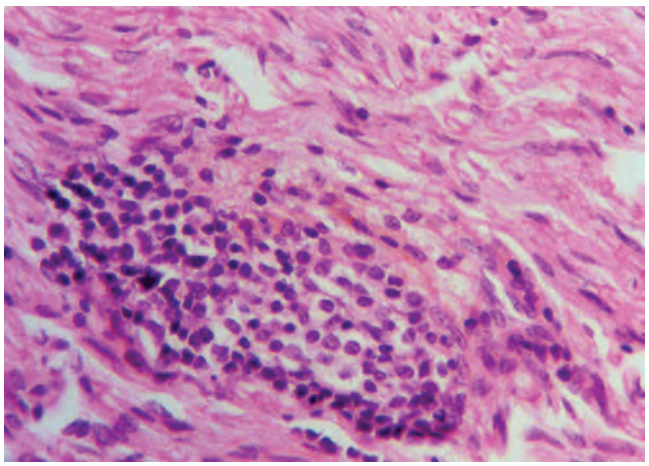

Figure 10.46 Peripheral neuritis typical of PDD. Note the localized accumulation of lymphocytes and a few plasma cells.

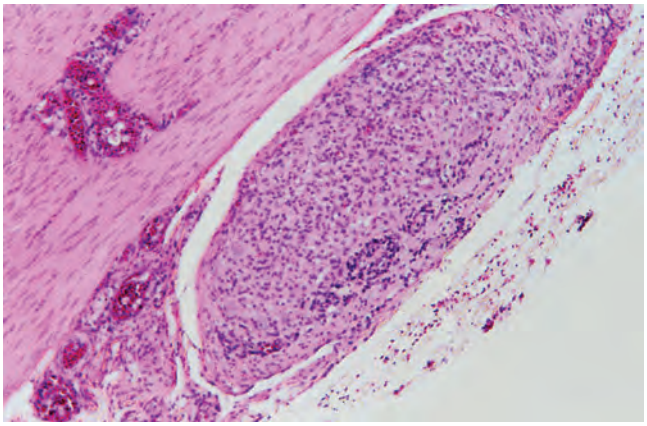

Figure 10.47 Mild lymphoplasmacytic inflammatory infiltrate into the peripheral nerve of a bird with West Nile virus infection. Note the morphologic similarity to PDD infection (Fig. 10.35).

Noninfectious disease

Inflammation of nerves is also seen in some cases of trauma. Nerves are involved in the reaction, as are other tissues in the affected area.

Noninflammatory disease

Toxins

Arsenic toxicity can lead to a peripheral neuropathy. Gross lesions are not seen. Histologic changes include axonal fragmentation, demyelination, and Schwann cell proliferation.

Trauma

Many cases of trauma lead to noninflammatory nerve degeneration, associated with direct nerve involvement or secondary to compression. There is no gross change, and microscopically demyelination and axonal loss are noted (Fig. 10.49).

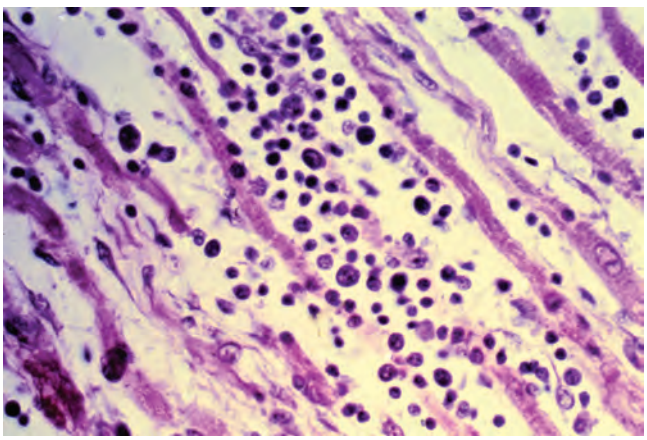

Figure 10.48 Marek's disease. Peripheral nerve infiltrated by pleomorphic lymphoid cells and plasma cells.

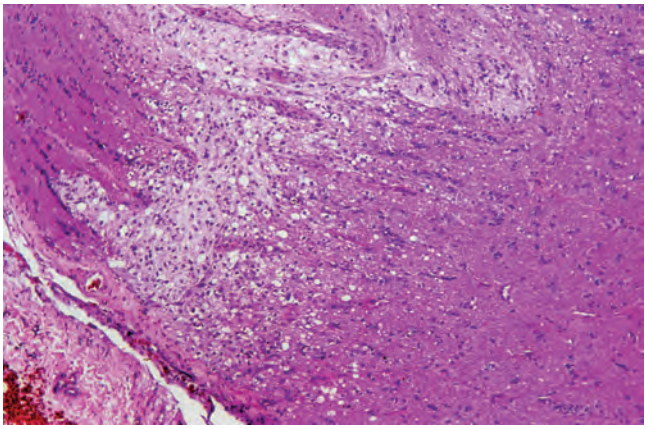

Figure 10.49 Peripheral nerve demyelination and degeneration secondary to trauma.

Nutritional deficiencies

Riboflavin (Vitamin B_2) deficiency leads to classic "curled toe paralysis" in chickens and can cause polyneuritis and degeneration in a variety of birds. Grossly there may be slight swelling and discoloration of large nerves such as the sciatic. Histologic changes consist of Schwann cell proliferation, demyelination, and axonal degeneration. Similar changes are occasionally reported in birds with thiamine deficiency.

Neoplastic disease

Schwannomas are sporadically seen in pet birds. They can be single or multiple white, firm nodules. Storiform patterns, whorls and bundles of cells with fibrillar cytoplasm, and spindle-shaped nuclei are seen (Fig. 10.50). Mitotic figures are rare, and there is variable stroma. Basic myelin protein can be demonstrated with immunohistochemistry. In more malignant tumors, the cells are less well differentiated, and there is an increase in the mitotic index.

Ganglioneuromas are also seen in pet birds, particularly involving the adrenal gland and associated ganglia. These

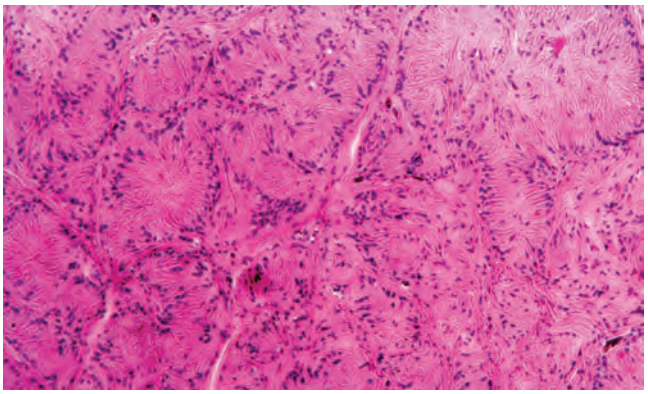

Figure 10.50 Numerous storiform patterns with palisading cells separated by minimal stroma.

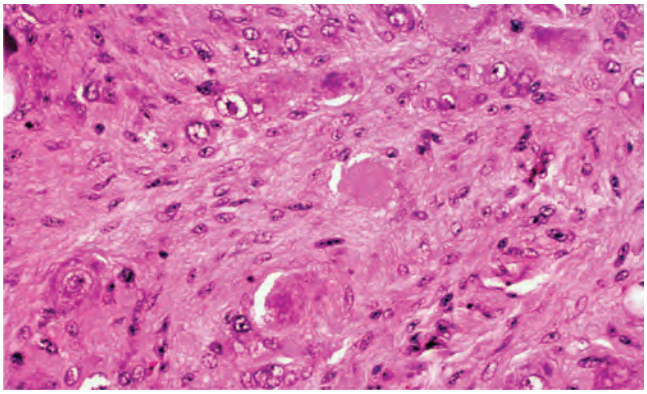

Figure 10.51 Ganglioneuroma comprised of large ganglion cells and neurofibrils.

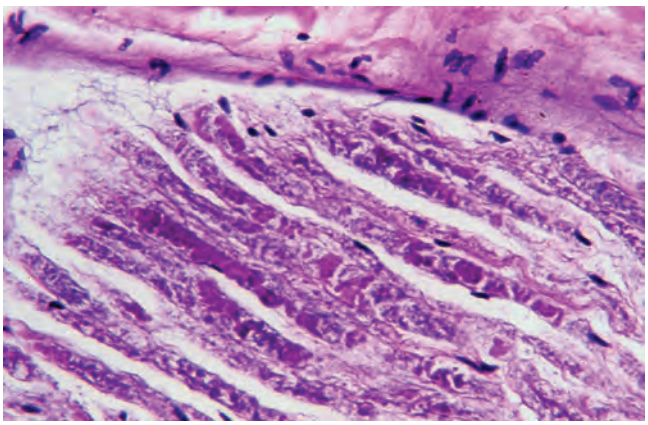

Figure 10.52 Swollen, degenerating axons seen in idiopathic peripheral neuropathy.

tumors comprise large ganglion cells, glial elements, and unmyelinated axons (Fig. 10.51).

Idiopathic lesions

Sporadic cases of peripheral nerve degeneration of undetermined cause are seen in pet avian species. There is no gross lesion, and microscopic changes consist of axonal degeneration and demyelination (Fig. 10.52).

Additional reading

Aguilar RF, Shaw DP, Dubey JP, et al. 1991. Sarcocystis-associated encephalitis in an immature northern goshawk (*Accipiter gentilis atricapillus*). *J Zoo Wildl Med* 22:466–469.

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11 Integument

The normal anatomy of the skin and feathers

All feathers are composed of keratin. They have a hollow central shaft (rachis) that ends in a quill or calamus, the tip of which anchors the feather to the feather follicle. The vane, which emanates from both sides of the shaft, is composed of long slender barbs and small hooklike barbules that project from the leading and trailing edges of the barbs. The barbules of the leading edge of the barbs interlock with the barbules of the trailing edge of its adjacent barb, causing the vane of the feather to act as a single flexible membrane. These elements of the feathers are modified to varying degrees at the base of the contour feathers, in down feathers, and in filoplumes. Birds typically molt once or twice a year. During the molt, old feathers fall out one at a time, and new feathers grow in their place. The base of the growing feather contains a vascular core and is surrounded by a partially opaque sheath. The bird breaks off the sheath, exposing the vane as the feather grows out. Powder-down feathers are specialized feathers that occur in dense tracts in a band cranial and dorsal to the legs. These feathers grow continuously. They are present in cockatoos and cockatiels.

Color is the result of two primary mechanisms: pigments and structural colors. Pigments include carotenoids, melanins, and porphyrins. While some birds derive their pigment coloration from the foods they consume, parrots synthesize all of their yellow to red pigment coloration *de novo*. The melanocytes in the skin and feathers produce the melanins (of which there is an entire family), while the psittacin pigments are usually manufactured by the liver. This is may be why strange color changes are observed in the plumage of birds with liver disease. The three types of pigments can combine to form several colors. Structural colors are the result of refraction and reflection of incident light which can change depending on the microscopic feather structure.

An axial artery enters the growing feather through the centrally located proximal umbilicus. The dermal papilla surrounds the proximal apex of the feather and fills the proximal umbilicus. The developing calamus is filled with a loose vascular mesenchymal reticulum (pulp). Surrounding the pulp is a thin layer of inner sheath cells: a broad layer of cells developing into the barbs and barbules (the zone of differentiation), the relatively thin, keratinized feather sheath, and the epidermis of the follicle wall. Surrounding the proximal umbilicus and forming the collar of the growing feather, from medial to lateral, is a thin layer of regenerative cells that are continuous with the follicular epithelium, a thicker layer of inner sheath cells that are continuous with the feather sheath, and the intermediate cell layer that is continuous with the layer of inner sheath cells. Feather follicles are surrounded by the dermis and attached to several bundles of muscle.

The epidermis of the bird is very thin, except on the beak and scales of the legs. The stratum germinativum has only two layers. Superficially there is a transitional layer and finally one or more layers of keratinized epithelium (stratum corneum). The stratum germinativum and corneum of the scales are markedly thickened. Lipogenesis takes place in the epidermis, which functions as a holocrine sebaceous gland.

Birds have a single skin-associated gland: the uropygial gland. The remaining skin is devoid of glands. The uropygial gland, which is found at the base of the dorsum of the tail, is bilobed and pear shaped. From its caudally directed nipplelike apex protrude short down feathers. The uropygial gland is a holocrine tubuloalveolar gland. Although present in most birds, it is larger in aquatic species. It is absent in most parrots, ratites, and pigeons.

External examination: skin and subcutis

The necropsy begins with an examination of the skin and feathers. Diseases of the skin and feathers can indicate either a primary disorder of the integument or an underlying systemic disorder. Skin and feather problems are common in pet avian species. Since the skin has a limited range of response to insults, a variety of causes will lead to similar clinical signs and, in many cases, similar lesions. The skin may vary from grossly normal to severely inflamed to necrotic. Feather disease or damage may occur with or without skin disease. Both skin and feather damage are commonly the result of, or at least complicated by, some degree of self-trauma. The distribution of the skin and feather disease and the presence of plaques, ulcers, or exudates on the skin may assist pathologists in reaching a diagnosis.

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

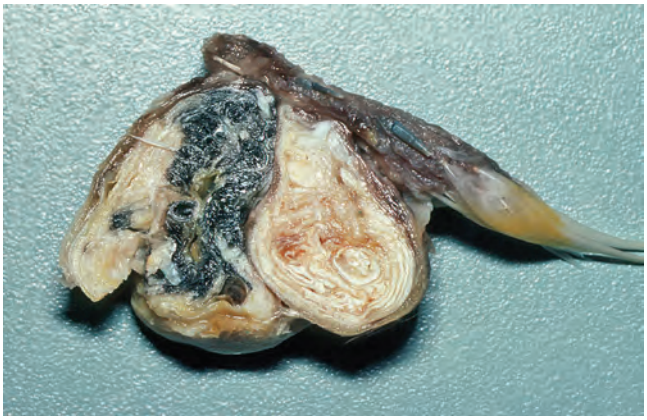

Figure 11.1 Typical appearance of follicular (epidermal inclusion) cyst.

Figure 11.3 Overgrown beak secondary to chronic liver disease.

Congenital and acquired malformations

True genetic disorders are poorly documented in pet birds. Occasionally feather cysts are seen in all species. Norwich and crested canaries have an apparent inherited predisposition to the development of feather cysts. Feather cysts grossly are oval or elongated swellings of the feather follicle. If the cyst is incised, it contains yellow-white dry layered material (keratin) (Fig. 11.1). The gross lesion must be differentiated from a follicular abscess.

Histologically, proliferated stratified squamous epithelium lines the keratin-filled cyst (Fig. 11.2). If there is secondary infection, inflammatory cells and possibly microorganisms may be seen. Although the cause of acquired cyst formation is usually not determined, infection, trauma, or any condition that interferes with normal growth of the feather may be responsible. A recently recognized condition of some species of eagles called "pinching-off" syndrome may have a genetic origin. This has not been reported in pet species.

Abnormalities of the beak, feathers, or claws can result from a variety of problems that interfere with the growth of the germinal epithelium of the beak, feather, or claw keratin. Vitamin deficiency, toxicity, and improper incubation temperatures all may lead to asynchronous growth or incomplete keratinization. Excessive growth of the beak is often associated with chronic liver disease (Fig. 11.3). Stress bars in feathers indicate possible unrecognized disease, nutritional problems, or environmental stressors (Fig. 11.4). Ectopic claws are occasionally seen (Fig. 11.5). History, physical examination, and laboratory profiles are necessary to determine the etiology of each individual case.

Constricted-toe syndrome is seen in nestling parrots. The etiology of this disease in not known. An annular band of what appears to be scar tissue completely surrounds a segmental section of the toe. The distal toe then becomes swollen, and, if constriction is not surgically repaired, the distal toe will undergo necrosis.

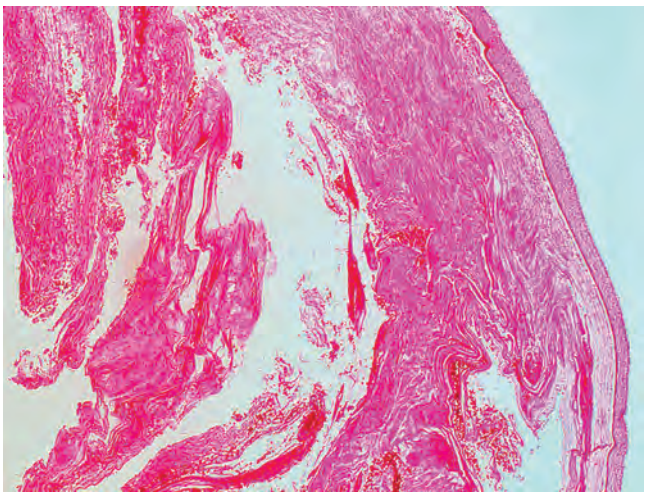

Figure 11.2 Follicular cyst containing keratin.

Figure 11.4 Stress bars in feathers. They are nonspecific responses to a variety of stressors.

Figure 11.5 Congenital ectopic claw in the skin of the neck.

Figure 11.6 Roughened beak and cere due to *Knemidocoptes* infection.

True genetic disorders are poorly documented in pet birds. So-called feather-duster disease is seen in budgerigars. There is continued, excessive growth of feathers, and the birds cannot fly. Several types of inherited beak malformation have also been described in budgerigars, including straight rhinotheca, abnormally curved rhinotheca, and excessively broad upper and lower beaks.

Color mutations of the feathers are highly sought after by aviculturists. As a result, species of birds that have been kept in aviculture for many years, such as the budgerigar, cockatiel, ringnecked parrot, and lovebird, are now available in many different colors. More recently color mutations have been selected for in other species such as the Quaker parrot and parrotlet. Many of these birds are, at least initially, highly inbred and often smaller, less robust, and possibly more susceptible to disease than the wild-type birds.

Figure 11.7 *Knemidocoptes* infection of the feet. Marked roughening and proliferation of the epidermis is seen.

Infectious disease

Parasitic disease

Knemidokoptic mites are found in budgerigars, canaries, and occasionally other species of companion birds. The cere and legs are commonly affected (Figs. 11.6 and 11.7), but feathered portions of the skin may also be involved in severe cases. Severe hyperkeratosis and acanthosis lead to variable gross thickening, irregularity, and flaking. Malformations of the beak can result in chronic cases. Mites are either superficial or deep, and with magnification may be seen moving in open spaces that occur in some extensive lesions. They are abundant and are readily seen in skin scrapings. *Dermanyssus* and *Ornithonyssus* mites are uncommon to rare in cage birds and, in our experience, are most likely to been seen on finches and birds that are housed outside. *Dermanyssus* only feeds on birds at night, and therefore diagnosis depends on finding the mite in the cage environment. Subcutaneous mites are found in some birds, but usually not in pet species. They live on the surface of skeletal muscle and in subcutaneous fat (Fig. 11.8).

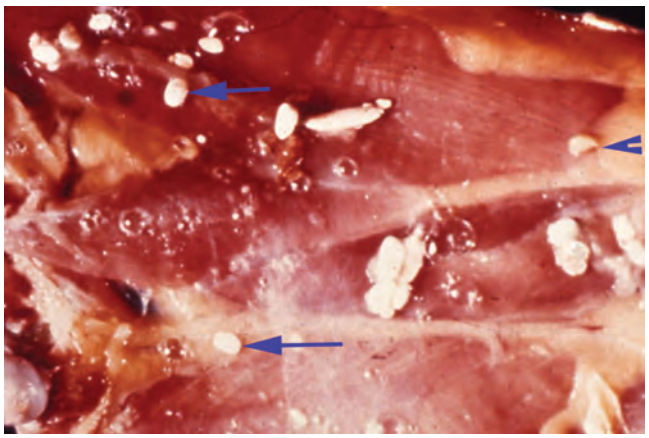

Figure 11.8 Subcutaneous mites on the surface of skeletal muscle.

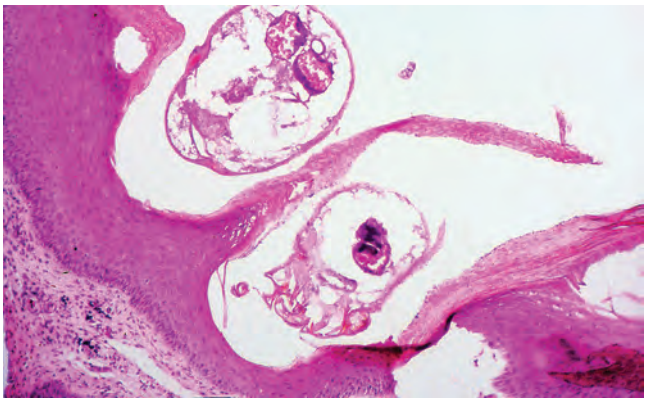

Figure 11.9 Superficial mite infection. The mites are present within the epidermis. There is hyperkeratosis and a mild dermal inflammatory response.

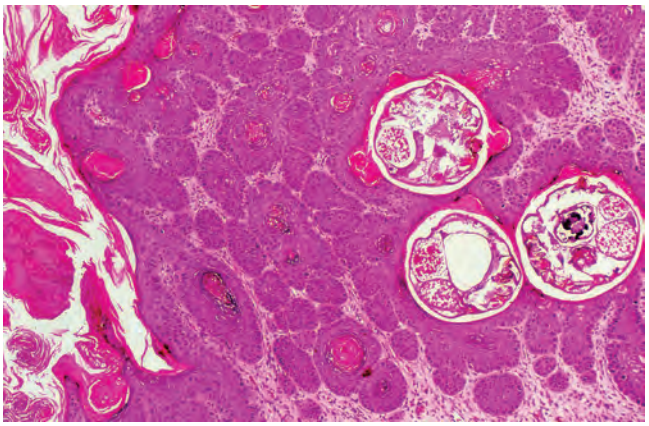

Figure 11.11 Deep mite infection with marked secondary acanthosis.

Histologically, mites are associated with a variable inflammatory infiltrate, including heterophils, macrophages, plasma cells, and, occasionally, giant cells (Figs. 11.9 and 11.10). Deep mite infection is often accompanied by markedly proliferative epidermis (Fig. 11.11). Occasionally numerous mites are seen in large cystic structures (Fig. 11.12). Mites can also be found in feather shafts (Fig. 11.13).

Filarid nematodes, both adults and microfilaria, can be found in the subcutis. Gross congestion and/or hemorrhage may be noted, and adult nematodes may be found. Microfilaria are usually found in the superficial subcutis, with essentially no inflammatory response.

Lice are uncommon in well-cared-for companion birds but are relatively common in domestic gallinaceous birds, pigeons, and wild birds. Unless the infestation is severe, no gross lesion is seen.

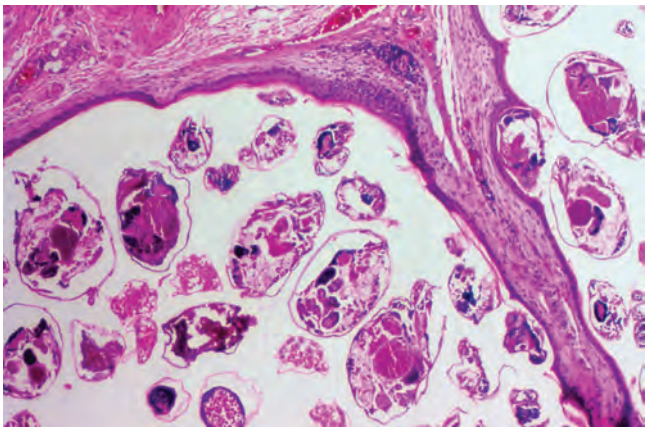

Figure 11.12 Large numbers of mites within a raised dermal mass.

Mycotic disease

There is relatively little in the literature about the types of fungi that may cause feather disease in companion birds. This issue is

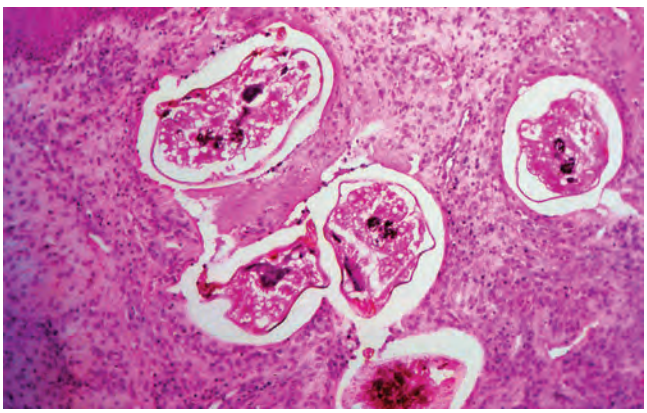

Figure 11.10 Deep mite infection with organisms in the dermis. Fibroplasia and a variable inflammatory infiltrate are seen.

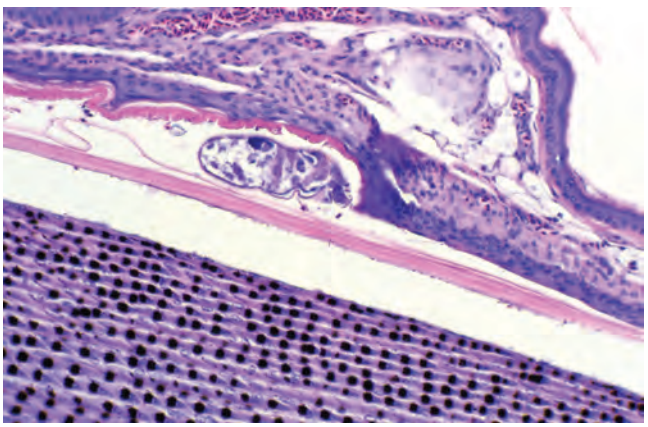

Figure 11.13 Sections of mites within the feather pulp.

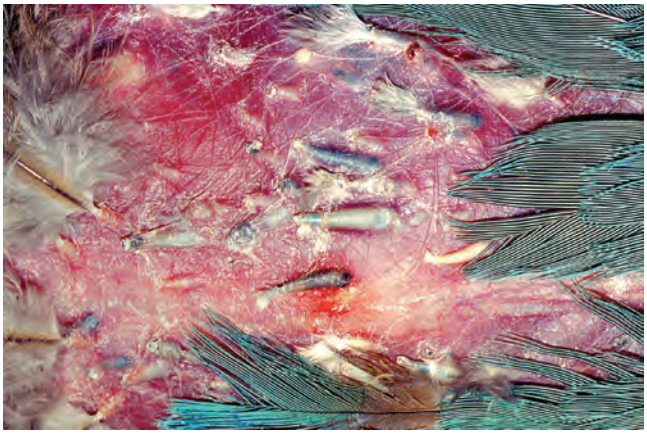

Figure 11.14 Follicular dermatitis with loss of feathers and generalized reddening associated with a fungal infection.

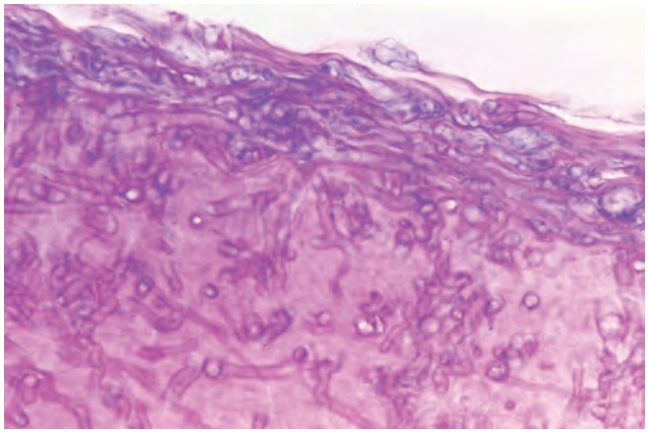

Figure 11.16 Periodic acid-Schiff stain to demonstrate fungal hyphae in the keratin.

complicated by the fact that many fungi are found on the feathers and skin of healthy birds, and heavy fungal growth may occur on old and soiled feathers without causing disease. Fungal organisms associated with skin or feather disease in companion birds include *Trichophyton* sp., *Microsporum gypseum*, several species of *Aspergillus*, *Mucor circinelloides*, *Rhizopus arrhizus*, *Penicillium chrysogenum*, *P. cyclopium*, and *Candida* sp.

Folliculitis due to dermatophytes appears to be less common in birds than is its counterpart in mammals, based on biopsy material. *Microsporum* sp. and *Trichophyton* sp. have been identified, and *Aspergillus* may occasionally be associated with skin/follicle problems. When present, there may be gross swelling and loss of follicles, with variable skin reddening, hyperkeratosis, and crust formation (Fig. 11.14). There is a pleocellular inflammatory infiltrate associated with necrosis and fungal hyphae, the latter giving the lesion its specificity (Figs. 11.15 and 11.16). Hyphae are also present in the follicular and surface keratin.

In some unusual severe cases of fungal infection, necrotizing lesions are seen not necessarily associated with feather follicles. These may appear as nodules with caseous centers (Fig. 11.17), and there is a pleocellular response. Fungal hyphae are found in the necrotic centers (Fig. 11.18).

Occasionally birds are seen with superficial infections by yeasts morphologically resembling *Malassezia* (*Pityrosporum*).

The organisms, which are present in superficial and follicular keratin, may cause problems due to inflammation or possibly due to a hypersensitivity response. Gross changes are usually not seen in psittacine birds, and, in small passerines, they are nonspecific, with some flaking, thickening of the skin, and possible reddening, particularly if there is pruritis and self-trauma.

In psittacine birds, there is usually a minimal perivascular dermal inflammatory infiltrate comprised primarily of lymphocytes and plasma cells, with organisms found in the keratin (Fig. 11.19). Small passerine birds may have significant superficial dermatitis, with a pleocellular infiltrate (Fig. 11.20).

Very rarely fungi have been associated with lesions of the beak and/or claws.

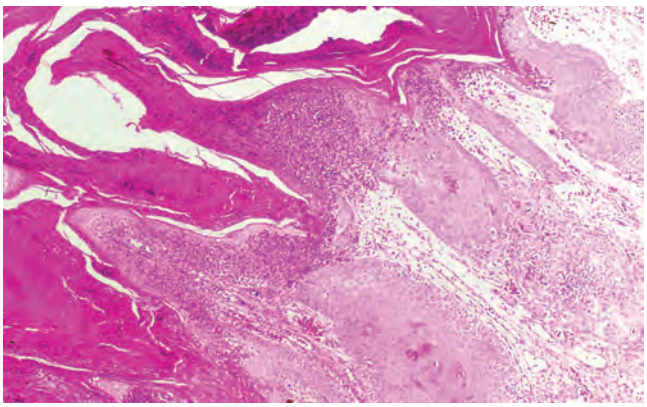

Figure 11.15 Acanthosis and severe hyperkeratosis due to fungal infection. Organisms are present in the keratin but may be difficult to see on routine stains.

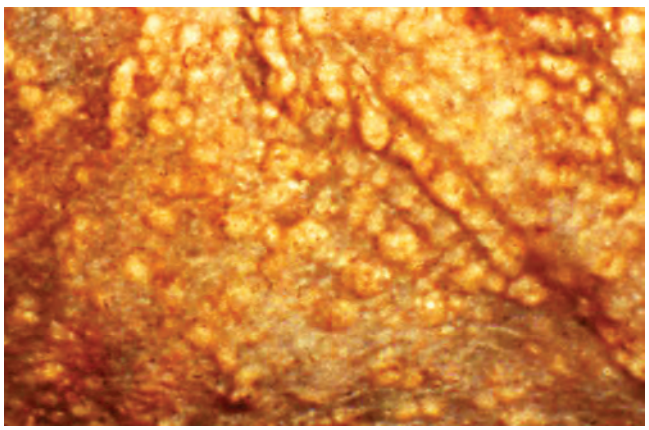

Figure 11.17 Multiple skin nodules due to mycotic infection.

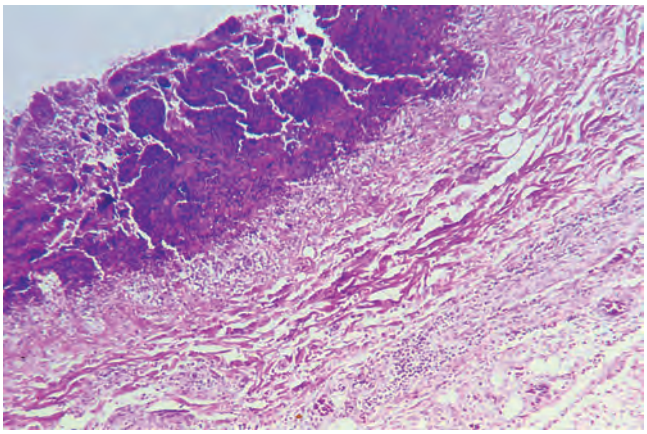

Figure 11.18 Mycotic granuloma within the dermis.

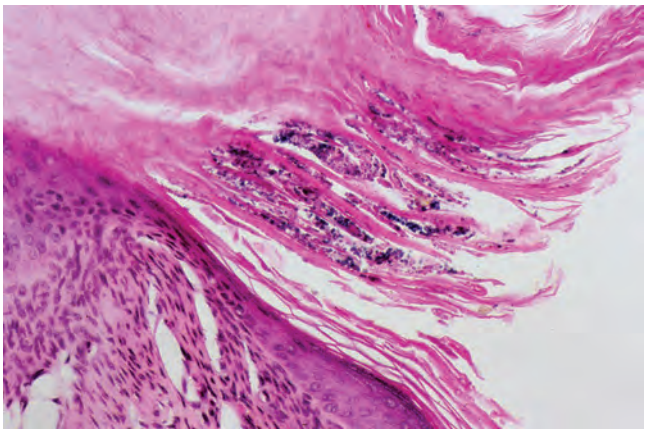

Figure 11.19 Hyperkeratosis associated with small yeasts consistent with *Malassezia* sp. in the keratin in a psittacine bird.

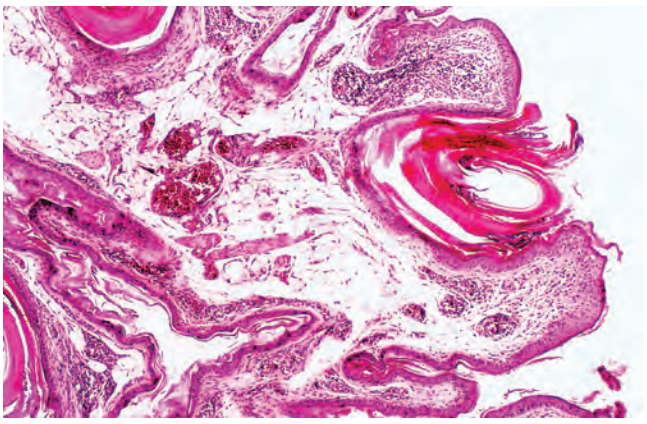

Figure 11.20 Hyperkeratosis, acanthosis, and diffuse dermatitis in a passerine bird with *Malassezia* sp. infection.

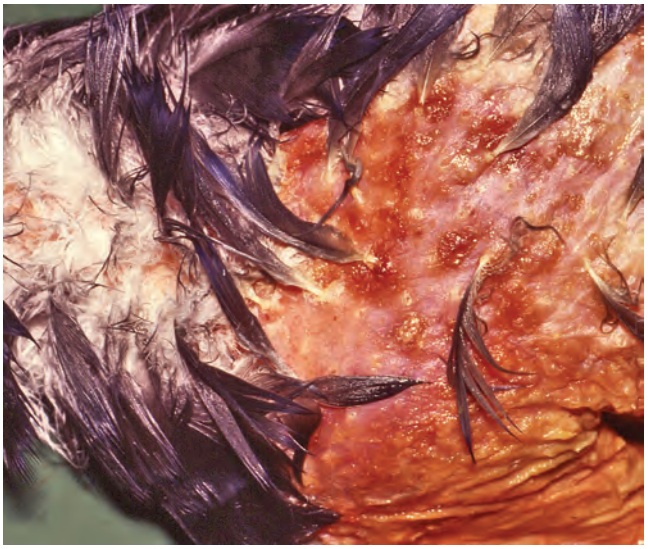

Figure 11.21 Severe bacterial follicular dermatitis with multiple foci of swelling and necrosis and generalized epidermal hyperemia.

Bacterial disease

Bacterial skin disease in pet birds may either be confined to the feather follicle or be generalized. *Staphylococcus* spp. are the most common bacteria associated with folliculitis. Grossly they cause a swelling of the perifollicular skin, with a variable amount of reddening (Fig. 11.21). Follicular abscessation and feather pulp inflammation may also occur (Fig. 11.22). Generalized bacterial dermatitis (pyoderma) may be pruritic, leading to self-trauma that results in a more severe lesion. Reddening, induration, and crust formation are grossly associated with necrosis.

Histologically a diffuse infiltration of heterophils and lesser numbers of plasma cells and macrophages are present. Necrosis extends through the epidermis into the dermis in severe cases (Fig. 11.23). Bacteria, usually gram-positive cocci, may present.

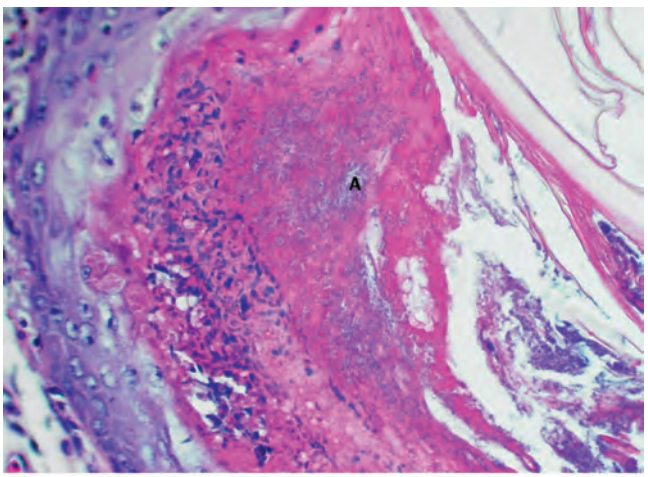

Figure 11.22 Bacterial folliculitis. Large numbers of organisms (A) within a necrotic, inflamed follicle.

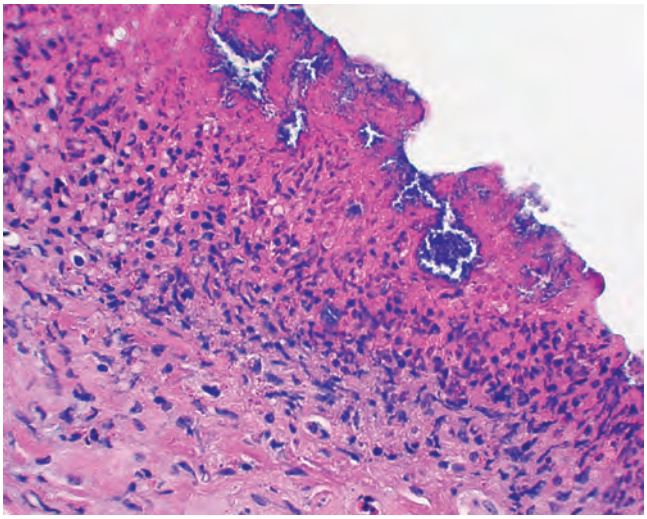

Figure 11.23 Severe superficial bacterial dermatitis with necrosis of the epidermis and large bacteria colonies.

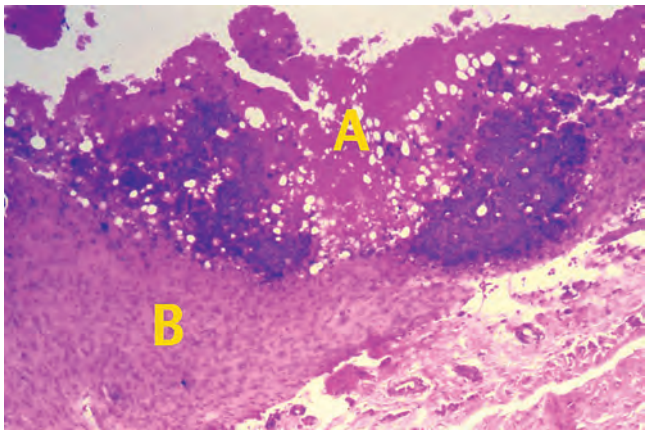

Figure 11.25 Severe pododermatitis with necrosis (A) and adjacent epidermal proliferation (B).

Secondary bacterial infections may follow skin trauma. If untreated, these usually result in abscess formation. Gross changes include localized swelling and necrosis, and a yellow, caseous exudate may be seen. The necrotic center of the abscess is usually surrounded by heterophils, lymphocytes, and macrophages, and giant cells are seen in some cases. Organisms are not always present.

Pododermatitis is usually secondary to trauma, with subsequent dermatitis and cellulitis leading to swelling and abscessation of the foot and toes (Fig. 11.24). Histologically areas of necrosis and inflammation are present, often containing numerous bacteria. The adjacent epidermis is usually acanthotic (Fig. 11.25). Birds of prey and waterfowl are highly prone to disease of the plantar surface of the feet (bumble foot). Disease occurs secondary to the use of improper perches in raptors and improper substrate in waterfowl. Injury to one leg that results in increased weight bearing on the other leg may also predispose some raptors to bumble foot. Damaged skin is infected with a *Staphylococcus* sp. that results in ulceration and infection of the underlying tissues. Secondary infections with *Escherichia coli* are common.

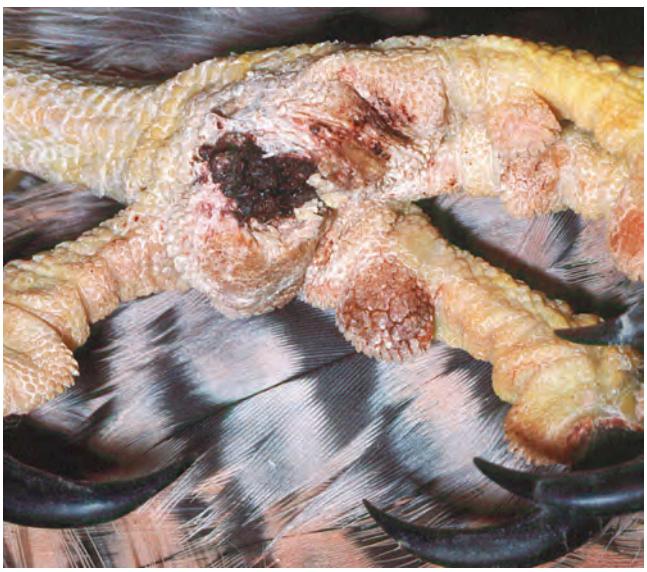

Figure 11.24 Swelling and ulceration in a severe case of pododermatitis.

Improper perch size and texture is a common cause of lesions of the bottom of the feet of parrots. Flattened patches of skin characterize these lesions. Additionally the roughened texture of the foot is lost, and the skin becomes pink to red and smooth. Birds that are housed on perches that are too large will bear weight on their hocks, and similar flat smooth skin lesions will develop on the ventral surface of the hocks. It is rare for the affected skin to become ulcerated.

Mycobacterial infections of the skin and subcutis may be primarily due to localized invasion but also may indicate systemic mycobacterial disease. The condition may present as single or multiple granulomas and grossly can resemble abscesses due to other bacteria or fungi, although in some birds nonpainful and nonpruritic nodules may be seen. It may also present as an area of localized thickening and induration (Fig. 11.26). Although *Mycobacterium avium* may be the cause, *M. genavense* and *M. tuberculosis* must be included as etiologic differentials in cutaneous mycobacteriosis.

The histologic lesion is characterized by the accumulation of numerous large macrophages with pale basophilic cytoplasm (Fig. 11.27). The cytoplasm of these cells contains acid-fast bacteria. Scattered heterophils and small macrophages will also be seen. Necrosis and caseation is minimal in most pet birds.

Although chlamydial infections do not cause primary skin lesions, occasionally a systemic chlamydial infection can lead to subcutaneous hemorrhage (Fig. 11.28). This can mimic the hemorrhage seen in polyomavirus infection (see polyomavirus below) and must be differentiated.

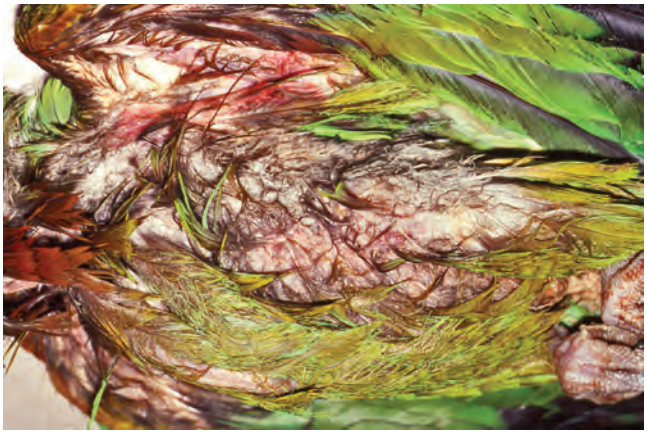

Figure 11.26 Mycobacterial skin infection. Note the thickening and nodularity of the skin in areas of feather loss.

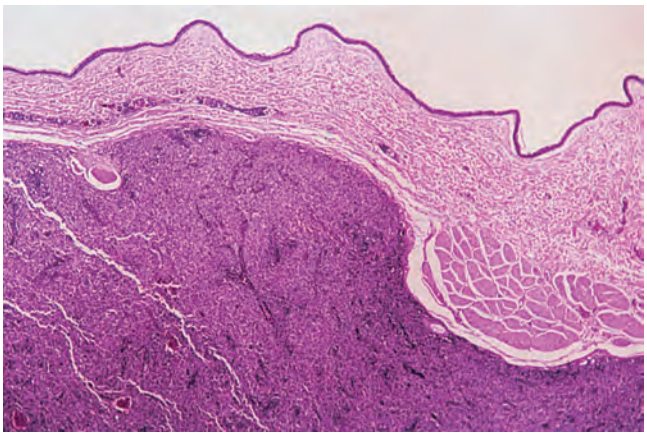

Figure 11.27 Mycobacterial dermatitis/cellulitis. There is diffuse infiltration of large macrophages with abundant cytoplasm. The cytoplasm is filled with the organisms that are difficult to identify with routine stains.

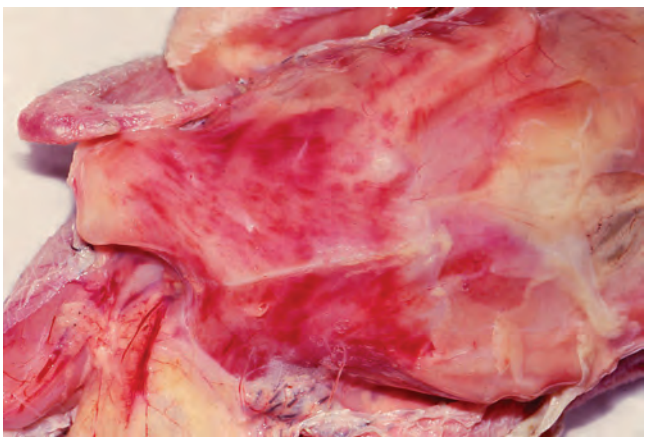

Figure 11.28 Subcutaneous hemorrhage in a bird with systemic chlamydiosis.

Viral disease

Papillomaviruses

These viruses are thought to cause cutaneous lesions in European finches, canaries, and the African grey parrot. Lesions in finches are found on the feet, the lesions in canaries are reported to be at the corner of the beak, and the lesions on African grey parrots are widely disseminated on the face (Fig. 11.29). Virus particles consistent in size and shape with a papillomavirus have been reported in the lesions of these birds, and a protein immunologically cross-reactive to the major capsid protein of a human papillomavirus has been reported to occur in cutaneous papillomas from an African grey parrot. The finch and African grey papillomaviruses have been sequenced. Grossly this disease is characterized by the presence of multiple proliferative skin lesions that superficially resemble those caused by mite infestations and poxvirus infections.

Histologically the lesions are fronds of hyperplastic epithelial cells supported by a vascular stroma (Fig. 11.30). Epidermal nuclei are often enlarged and homogeneous, suggestive of inclusion body formation. Well-defined inclusion bodies usually are not seen, but viral particles are demonstrated by electron microscopy. Similar lesions are seen in cockatiels but have not been characterized.

Figure 11.29 Viral-induced papillomatosis in an African grey parrot. This is the only psittacine bird with proven papillomavirus infection.

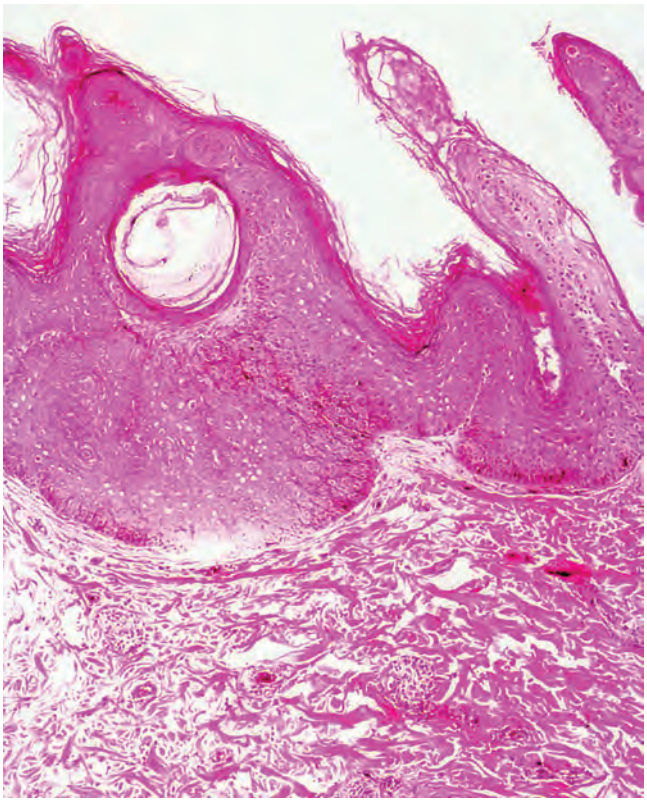

Figure 11.30 Virus-induced papilloma in an African grey parrot. Multiple fronds are seen.

Polyomavirus

Polyomavirus was originally reported as a disease of budgerigars, with feather loss one of the primary clinical signs.

Feather dysplasia is a common finding in fledgling budgerigars raised in large commercial aviaries. Breeders often call these birds runners or creepers. Grossly, primary wing feathers and tail feathers are either absent entirely or have thick sheaths, and there may be hemorrhage in their shafts (Fig. 11.31). These birds are typically infected with avian polyomavirus, psittacine beak and feather disease virus (PBFDV), or both. We have seen birds with these feather abnormalities that did not have either infection. However, novel circoviruses have recently been discovered, and they may not be picked up by traditional PCR-based diagnostic tests. It is speculated that giardiasis may also cause this type of lesion, but that has not been proved, and giardiasis is very common in budgerigars with and without feather disease.

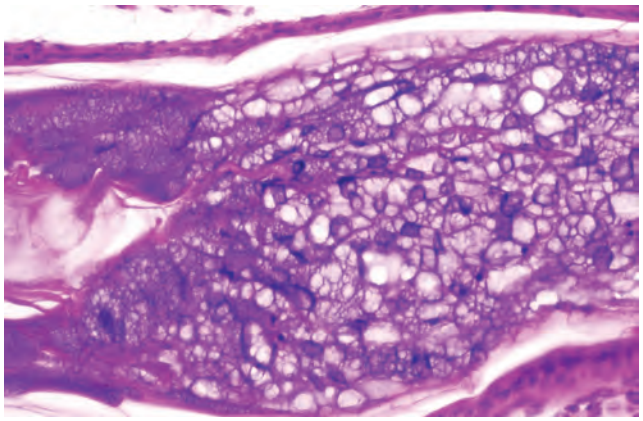

Figure 11.32 Polyomavirus-induced karyomegaly and intranuclear inclusion body formation in the epidermal collar.

Feather disease may be the only manifestation of avian polyomavirus in budgerigars, or it may accompany the systemic form of the disease seen in nestlings. Affected nestlings may have dysplasia of contour feathers, down feathers, flight feathers, or a combination of all of them. Within the growing feather, there is often massive infection of the cells in the zone of differentiation, with nearly every cell showing karyomegaly and containing the characteristic intranuclear inclusion bodies (Figs. 11.32 and 11.33). Inclusions in the epidermis of the skin are also usually present but are infrequent.

Figure 11.31 Feather loss and dystrophy due to polyomavirus infection.

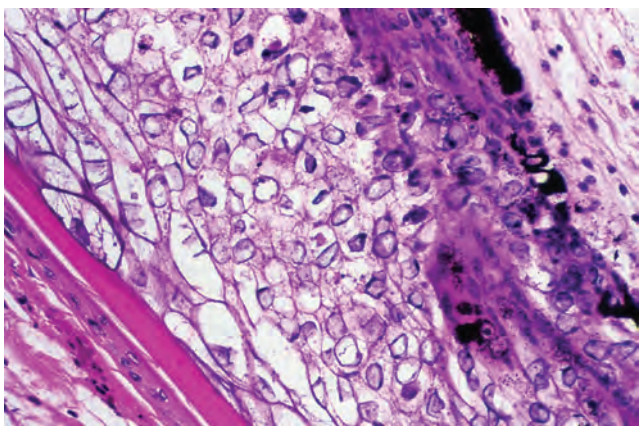

Figure 11.33 Detail of polyomavirus intranuclear inclusions. They are clear or lightly granular and basophilic.

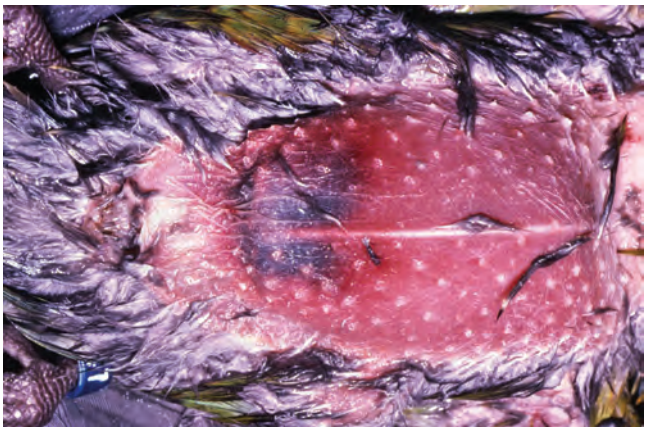

Figure 11.34 Skin hemorrhage in a psittacine bird with polyomavirus infection. With no history available, the lesion would have to be differentiated from trauma-induced hemorrhage.

Feather changes are rare in larger psittacine birds with avian polyomavirus. In some cases, however, these birds will have hemorrhage within the shaft of affected feathers. Skin and subcutaneous hemorrhage is a common feature of avian polyomavirus disease in nonbudgerigar parrots (Figs. 11.34 and 11.35). Nonpsittacine birds with polyomavirus infection rarely have gross feather changes.

Poxviruses

Poxviruses are large, enveloped DNA viruses. The biology of the poxviruses is complex. They have been isolated from many species of birds, but each virus has the ability to infect only a limited range of species. Disease is transmitted in most cases by biting insects; therefore, most affected birds are housed out of doors. Domestic birds that are commonly affected are the chicken, the ostrich, and the canary.

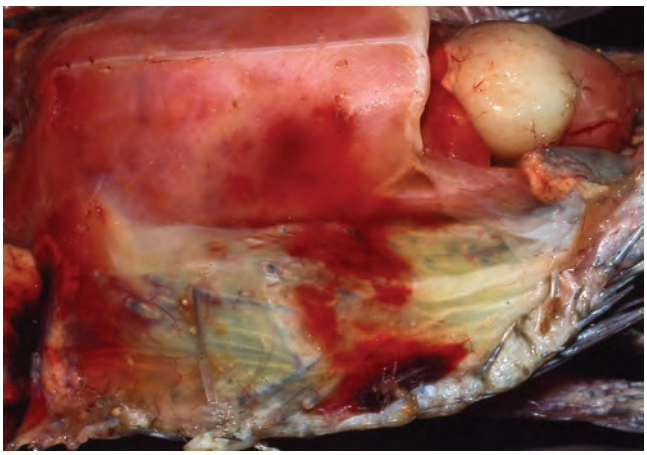

Figure 11.35 Severe subcutaneous hemorrhage due to polyomavirus in a large psittacine bird. Grossly this must be differentiated from possible chlamydial infection.

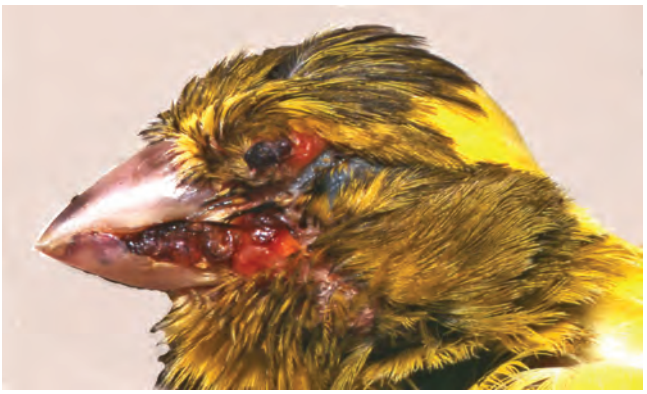

Figure 11.36 Proliferative and hemorrhagic lesion due to poxvirus infection. The face is a common location.

Historically this disease was a major problem in wild-caught blue-fronted Amazon and Pionus parrot nestlings held in quarantine. Some of these birds would be infected with the virus prior to capture, and then the use of common feeding instruments between birds would result in its dissemination. Since the end of the importation of wild-caught parrots, this disease is no longer seen in these birds.

Poxvirus infections are a very common problem in nestling and fledgling wild birds, particularly doves, grackles, and mockingbirds in North America, Australian magpies in Australia, but are found in many species of birds, including the chicken, around the world. The so-called dry or cutaneous form of the poxvirus infection is confined predominantly to the skin. Lesions are common on the head, face, and feet, but can also be present in feather tracts in severe infection. The lesions are proliferative, presenting as papules, pustules, and nodules. These lesions may ulcerate and crust over.

Grossly the lesions can have rough or smooth surfaces, depending on the duration of the lesion, self-trauma, and the degree of secondary bacterial infection (Figs. 11.36 and 11.37).

Figure 11.37 Typical poxvirus lesion involving the foot.

Figure 11.38 Early poxvirus infection with minimal or no proliferative change.

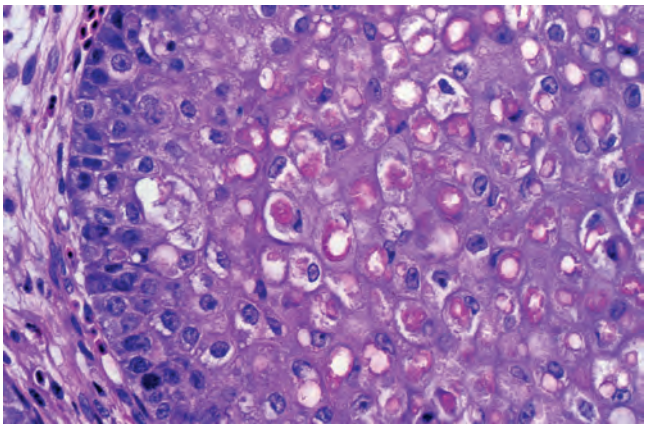

Figure 11.40 Detail of poxvirus infection illustrating ballooning degeneration and eosinophilic, intracytoplasmic inclusion bodies.

The lesions may be massive, causing the eye to close and interfering with prehension. Severe lesions may be mistaken for neoplasia. In some early cases, birds present with blepharospasm, excessive conjunctival fluid production, and swelling of the periocular tissues, but little or no obvious proliferative lesion (Fig. 11.38).

Histologically there may be epidermal ulceration and superficial bacterial infection. There is severe hyperplasia of the epidermis, with intraepithelial vesicle formation, ballooning degeneration, and large eosinophilic intracytoplasmic inclusion bodies (Bollinger bodies) that may cause the nucleus to have a crescent shape and be displaced to the side of the cell. Inclusion bodies are often abundant but in some cases are uncommon (Figs. 11.39 and 11.40). Ultrastructurally virus particles are present in the inclusions (Fig. 11.41).

Herpesvirus

Pacheco's disease typically causes systemic infection that can occasionally include involvement of the epidermis of the skin or feather, leading to necrosis. Inclusion bodies can be seen in the cells surrounding the necrosis. Since the generalized disease is usually catastrophic, little attention is paid to what may be grossly minimal skin lesions.

Proliferative lesions of the lower legs and feet are seen in a number of species of psittacine birds, particularly cockatoos and macaws. An uncharacterized herpesvirus is the one possible cause of these lesions, because virus particles can be seen with electron microscopy of this tissue.

In cockatoos, this disease presents as solitary proliferative nodule or as multiple proliferative nodules. The lesion in macaws is typically a roughening of the skin and/or a flat, raised plaque. Depigmentation of the diseased tissue is common (Fig. 11.42). These lesions are very dry, and the thickened skin is readily scraped away.

Microscopically there is epidermal hyperplasia and marked acanthosis, with large intranuclear inclusion bodies that fill the nucleus, which is often surrounded by a clear halo (Fig. 11.43).

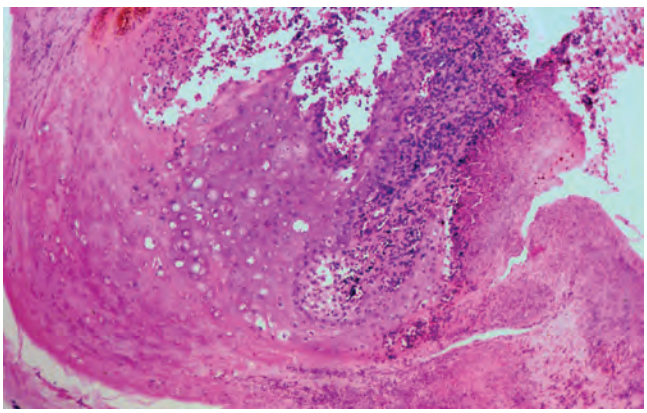

Figure 11.39 Typical poxvirus lesion with marked epidermal hyperplasia and associated necrosis and hemorrhage.

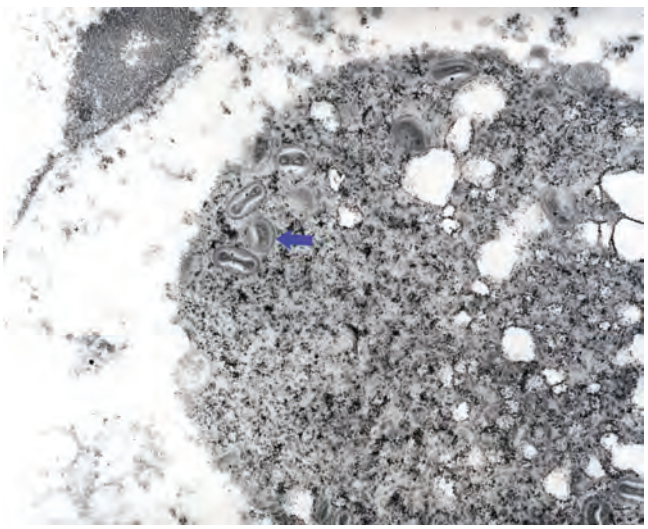

Figure 11.41 Electron photomicrograph of poxvirus particles (arrow) within an inclusion body.

Figure 11.42 Cytomegalic herpesvirus infection. The skin of the feet is typically affected, being thickened, and depigmented.

Psittacid herpesvirus-2 is found in African grey parrots. Most infections do not cause disease; however, this virus is associated with mucosal papillomas of the cloaca and oral cavity and a periophthalmic skin thickening.

Circoviruses

Unique circoviruses have now been identified in ostriches, domestic ducks, domestic geese, swans, chickens, parrots, gulls, finches, starlings, the canary, and an Australian Raven (Chapter 8). Feather lesions reported to be caused by circovirus infections occur in the ostriches, in parrots, infrequently in geese, in the Australian raven, and infrequently in finches.

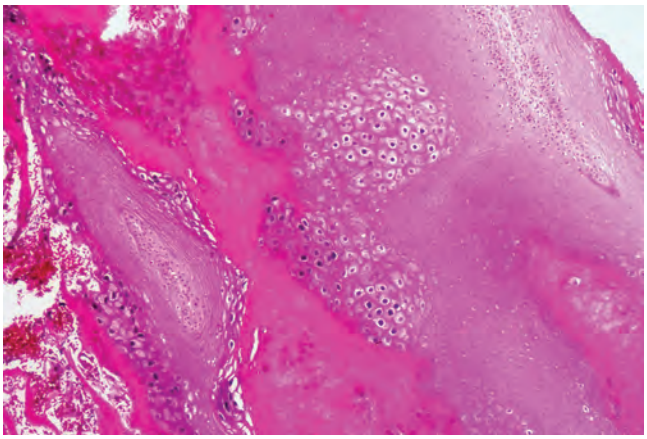

Figure 11.43 Cytomegalic herpesvirus infection. Marked parakeratosis is seen, and basophilic inclusion bodies fill the nucleus, which is surrounded by a clear halo.

The PBFDV is a circovirus that is enzootic in many species of wild Australian parrots and is found in wild African parrots and has spread widely into naïve populations of parrots as the result of the parrot trade. It causes an acute fatal infection in nestling cockatoos and, less frequently, nestlings of other species and a chronic disease in young adult birds, including cockatoos, lovebirds, lorikeets, neophemas, African grey parrots, and, rarely, New World parrots. The disease in psittacine nestlings is acute in onset and generalized so that it affects all growing feathers. Flight feathers take longer to develop than contour feathers; therefore, if nestlings are somewhat older when infected, only the flight feathers may be involved.

Affected birds typically die within 2 weeks of the onset of the disease. The chronic form of disease is generally seen in birds 8 months to 3 years old and is first recognized when birds go through their first molt. Dystrophic feathers replace normal ones during the molt. Powder-down feathers may be first affected in cockatoos.

Currently PBFDV is most commonly seen in lovebirds, budgerigars, lories, lorikeets, and eclectus and African grey parrots. Feather lesions in lovebirds are rarely as florid as those seen in cockatoos. Many affected lovebirds show only dull plumage or have an increased number of broken or worn feathers. Advanced cases may show some feather dysplasia, or new feathers may simply not develop, leaving portions of the bird unfeathered. A significant percentage, perhaps the majority of lovebirds infected with PBFDV, shows no signs of disease at all.

A generalized feather disease is seen in African grey parrots, but often it is confined to the tail feathers, or there may be no feather involvement at all. Young African grey parrots may not thrive and may die with no specific signs/lesions or may have marked secondary bacterial or fungal infections. In these birds specific lesions are often confined to the bursa of Fabricius (Chapter 8). Eclectus parrots do not show typical feather lesions of PBFDV, but affected birds may have a delayed molt and poor-quality feathering.

PBFDV appears to be widespread in lories and lorikeets in North American collections. Many birds with this infection do not show signs of disease, but a certain percentage develops characteristic feather lesions. In Australia, many wild rainbow lorikeets fledglings are presented to carers every year with PBFDV infection. These birds are typically missing their tail feathers and primaries and are unable to fly. Approximately, one third of these will develop normal feathers after the first molt and the other two thirds will either die or have persistent feather dysplasia.

Grossly there is necrosis and annular constriction of the base of the feather shaft and hemorrhage in the feather pulp. There may be severe shedding of affected feathers (Fig. 11.44). Affected feathers are stunted and may have thickened, hyperkeratotic sheaths, pulp hemorrhage, annular constrictions of the calamus, curling, or stress lines on the vanes (Fig. 11.45). The apex of the sheath and the ensheathed feather may be necrotic. Affected feathers may only grow out partially and may be clubbed. Discoloration of feathers may be the initial sign in some birds. African

Figure 11.44 Severe feather loss due to circovirus infection.

grey parrots may develop red feathers, and yellow feathers have been seen to replace green feathers in other species of parrots.

Beak lesions are less common than feather changes but are a prominent feature of this disease in sulfur-crested, umbrella, and Moluccan cockatoos (Chapter 3). Variable necrosis and loss of keratin can be seen. Although this form of the disease is still common in Australia, since the importation of wild-caught birds has ceased, it is uncommon in captive-raised parrots. External gross lesions are usually not seen in nonpsittacine birds. Feather dystrophy similar to that seen in psittacines has been reported in pigeons, doves, and finches.

Figure 11.45 Dystrophic feathers in a bird with circovirus infection.

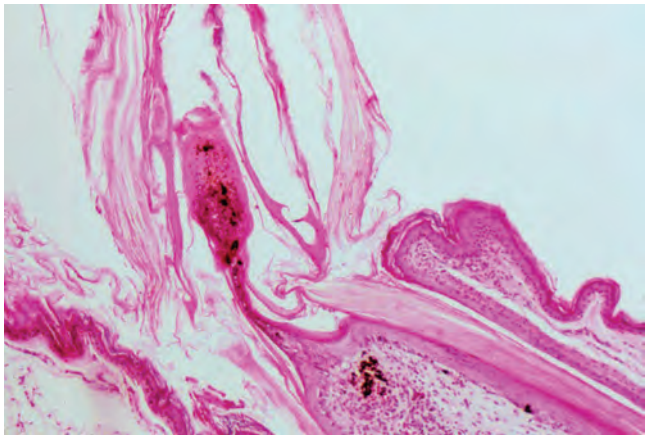

Figure 11.46 Circovirus-induced epidermal collar necrosis leading to constriction of the feather shaft.

Follicular epidermal hyperplasia, hyperkeratosis, and degeneration of germinal cells are seen histologically. There is ballooning and patchy degeneration of cells of the epidermal collar. Although considered to be an example of necrosis, the process may actually be apoptosis. The feather-shaft constriction noted grossly is secondary to the necrosis in the epidermal collar. An associated infiltration of macrophages, which may contain large, globular, basophilic, cytoplasmic inclusion bodies, is seen. Similar cells are seen in the pulp, and there may also be hemorrhage and a heterophilic infiltrate, particularly if there has been self-trauma. In chronic cases, small granulomas with keratin fragments and giant cells are seen (Figs. 11.46, 11.47, 11.48, and 11.49). Multifocal to confluent inflammation may be present in the superficial dermis, with lymphocytes and plasma cells predominating. A few epithelial cells of the epidermis or epidermal collar may contain structures resembling intranuclear inclusion bodies.

With electron microscopy, non-membrane-bound paracrystalline arrays representing the small 12- to 26-nm virus are

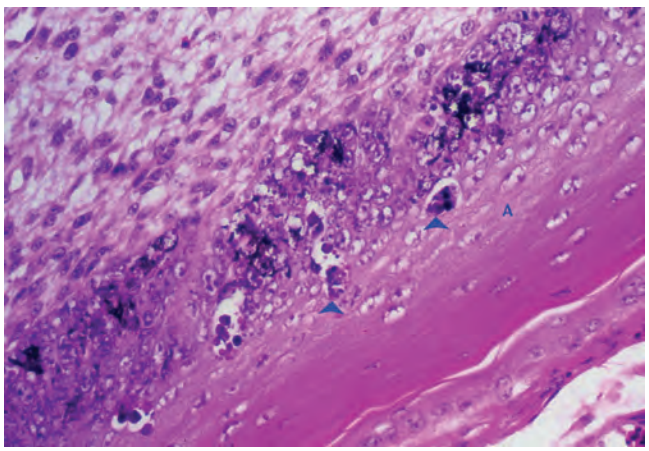

Figure 11.47 Epidermal collar (A) necrosis and scattered intracytoplasmic inclusion bodies (arrowheads) in circovirus infection.

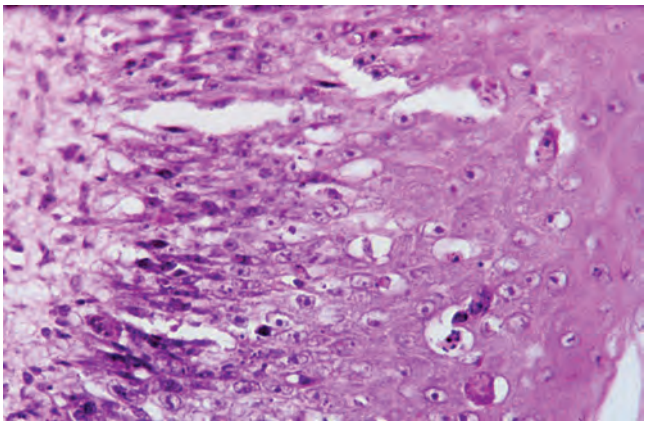

Figure 11.48 Detail of epidermal collar necrosis or possible apoptosis.

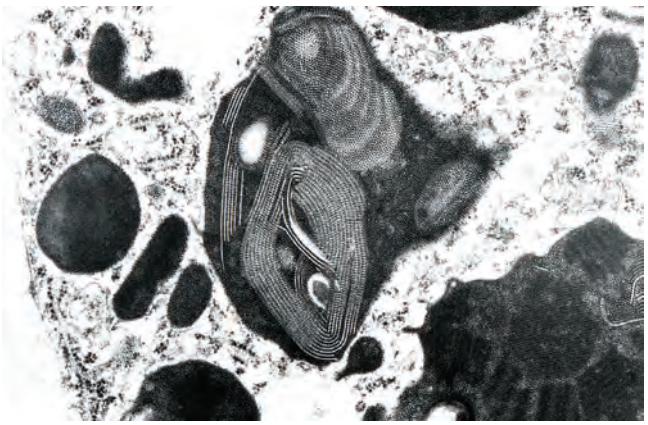

Figure 11.50 Electron photomicrograph of circovirus intracytoplasmic inclusion bodies. Note the nonmembrane-bound paracrystalline arrays.

seen (Fig. 11.50). Definitive diagnosis can also be done with PCR assays, DNA *in situ* hybridization, and immunoperoxidase staining.

In some psittacine birds, mixed infections with polyomavirus and circovirus are found. Grossly there are a variety of feather and skin changes as previously described (Fig. 11.51). Histologic changes consistent with both diseases are seen.

Although there have been reports of circovirus infection in geese and gulls, nonpsittacine circovirus infection is more often seen in passerines (finches and canaries) and columbiformes (pigeons and Senegal doves). The viruses feather dystrophy and loss has been reported in affected birds in these groups, but rarely in pigeons. Gross lesions in these birds are often limited to atrophy of the bursa of Fabricius or associated with secondary infections due to immunosuppression. Histologically lesions are similar to those described previously. These viruses are genetically different from the psittacine virus and a different PCR must be done for identification.

Young pigeon syndrome is the constellation of diseases seen in pigeons with underlying immunosuppressions caused by infection with the pigeon circovirus. These birds often have severe trichomoniasis, oral lesions associated with pigeon herpesvirus, as well as, a high prevalence of candidiasis of the crop, helminth infections, and systemic bacterial disease.

Noninfectious disease

Nutritional/metabolic disease

Specific and nonspecific nutritional problems that can result in poor feathering and skin disease include vitamin, mineral, and amino acid deficiencies, as well as generalized malnutrition. Depigmentation, altered pigmentation (Fig. 11.52), improper

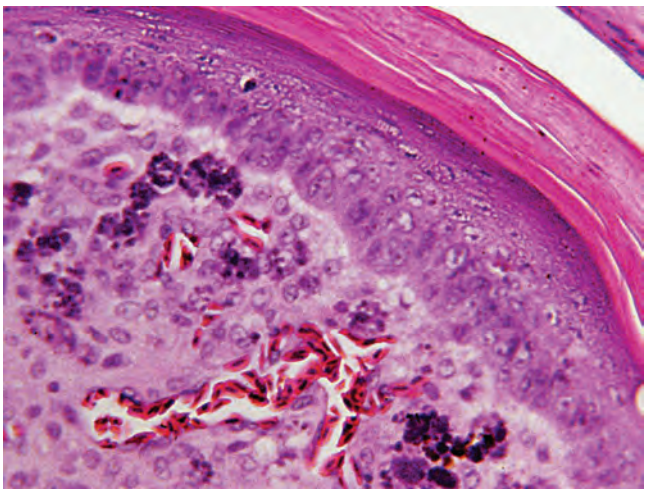

Figure 11.49 Numerous globular intracytoplasmic inclusion bodies in circovirus infection.

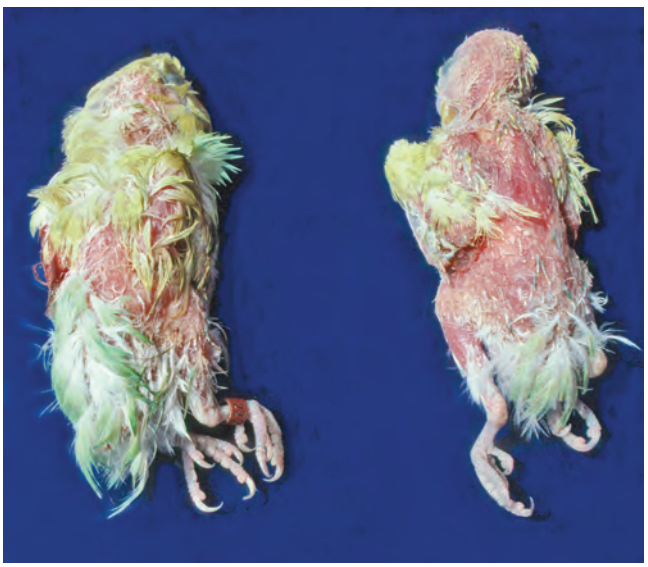

Figure 11.51 Severe feather loss associated with mixed infection by polyomavirus and circovirus.

Figure 11.52 Abnormal feather color which can be the result of a number of nutritional problems.

molting, and poor-quality feathers can be seen. Gross changes are rarely specific, and, in many cases, mild hyperkeratosis and acanthosis may be the only histologic changes noted.

Vitamin A deficiency may lead to scaly skin, poor feather quality, and focal hyperkeratosis, particularly of the feet. The uropygial gland may become enlarged, with yellow caseous-appearing material present instead of the typical secretion product. Squamous metaplasia is seen microscopically, with hyperkeratosis a primary contributor to the gross appearance (Fig. 11.53).

African grey parrot nestlings fed a diet that was misformulated to contain no vitamin A had pronounced transverse ridges develop on their beaks. The lesions resolved once the diet was corrected.

Lack of carotenoids in the diet can lead to dilution of skin and feather color, because carotene is a component of yellow, orange, red, and green feather colors. Tyrosine deficiency can lead to poor melanin production and color changes. Protein or specific amino acid imbalances can result in alterations in feather structure leading to color changes due to changes in light scattering.

Horizontal, 1- to 2-mm, dark, dysplastic bands are a common lesion seen in hand-fed nestling birds. These bands are segmental sections of the vane that did not form barbules. Empirically it appears that these bands are the result of a short period of stress that occurs while the feather is growing in. (See Fig. 11.4). In this case, stress is broadly defined to include such things as being chilled, not eating, and illness. A few dysplastic bands are a common finding on the feathers of most nestling parrots. However, multiple bands suggest that the bird suffered from a prolonged illness or an extended period of improper husbandry. Dysplastic bands are particularly obvious on young birds, because all their feathers grow in simultaneously and, thus, if one feather is affected, most others will be also affected. After the first molt, dysplastic bands will generally be confined to only few feathers.

Physical/environmental agents

Trauma, burns, excessive cold, and other physical factors often cause skin lesions. Loss of feathers, varying degrees of hemorrhage, necrosis, and superficial crust formation are seen (Fig. 11.54). Severe necrosis and sloughing of epidermis and possibly portions of dermis can be seen in injuries due to both heat and cold. Discoloration of the lesions is variable. Severe frostbite may lead to complete loss of digits.

Histologically there is severe coagulative necrosis, with an active, well-defined inflammatory margin between necrotic and live tissue. Traumatic injuries are characterized by variable amounts of hemorrhage, edema, and inflammation, depending on the severity of the insult and time elapsed prior to examination.

Self-trauma of the feathers and the skin is a common problem in parrots and may occur in other species. Self-trauma may be due to a primary disease of the skin or feathers, a multisystemic disease, or it may be psychogenic in nature. In these birds, typically the head feathers are unaffected, and there are varying

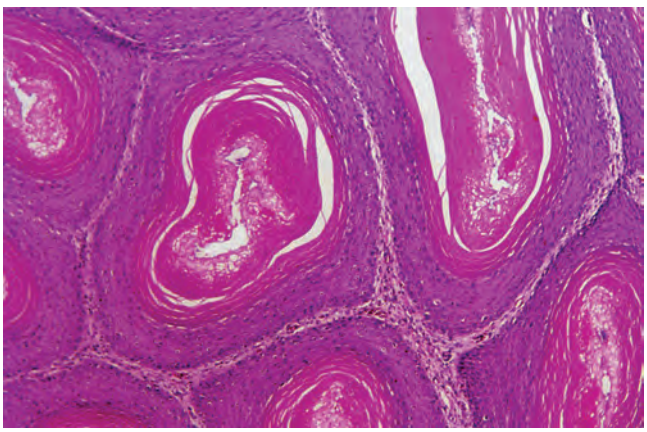

Figure 11.53 Squamous metaplasia and hyperkeratosis of the uropygial gland due to vitamin A deficiency.

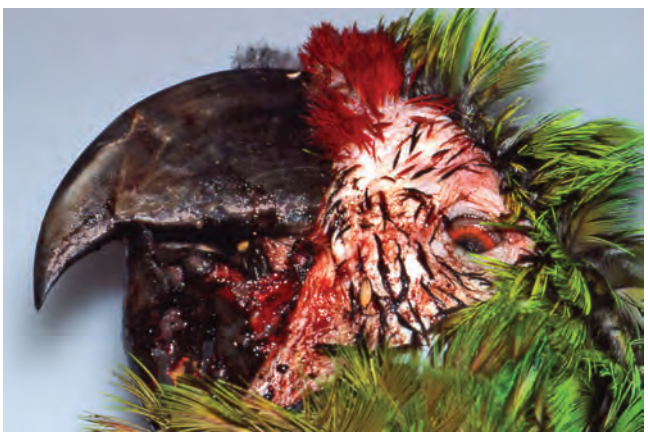

Figure 11.54 Traumatic hemorrhage and beak damage.

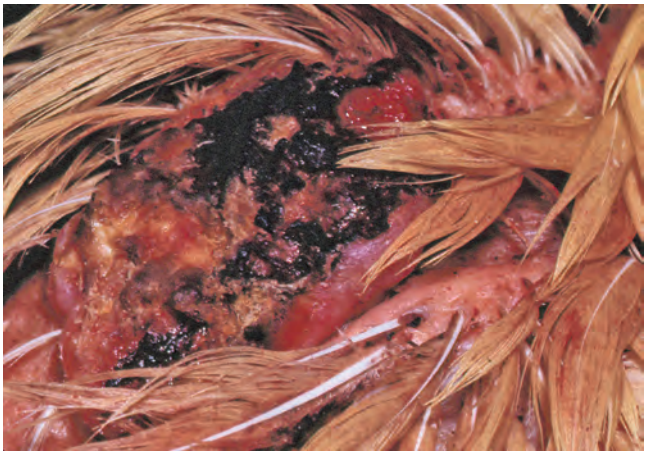

Figure 11.55 Severe focal ulceration and hemorrhage due to self-trauma.

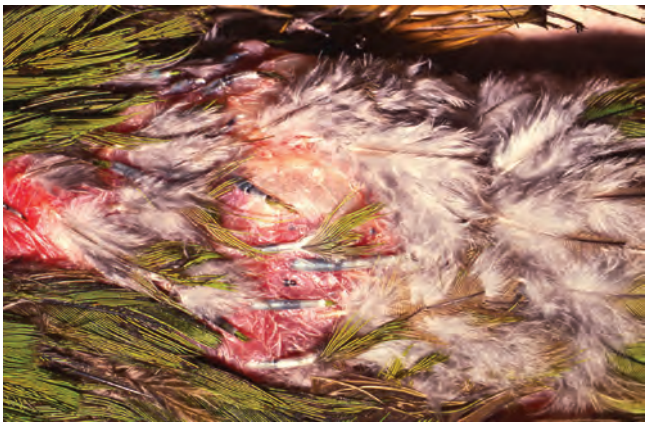

Figure 11.57 Loss of mature feathers in a bird with clinical hypothyroidism.

degrees of damage to other feathers. There are many patterns of feather picking. Some birds confine their attention to wing feathers and some to contour feathers, whereas, others will damage both. Some birds will chew only on the feathers; others will pull them out entirely. Some birds will even pull out growing feathers or bite them off at the level of the feather follicle.

Self-trauma to the skin is less common and often associated, initially, with an underlying disease. As birds damage the skin, the problem escalates to the point that large areas of skin are destroyed, sometimes including underlying muscle (Fig. 11.55). Traumatic wounds over the sternum are often aggravated by self-trauma and may result in osteomyelitis of the keel of the sternum.

Trauma of any sort may result in hematoma formation in the skin/subcutis (Fig. 11.56). Organized hematomas must be differentiated from abscesses and neoplasms.

Endocrinopathies

Although estrogen and testosterone may influence feather development, hypothyroidism is the only described endocrine disease affecting pet birds, and there is only one published report of this disease. In this bird and those seen by us, there is no specific pattern of feather disease or feather lesions that are specific for endocrine disease. Instead, these birds have a generalized loss of feathers, a failure of new feathers to grow in, and the absence of observable skin lesions (Fig. 11.57). Similar lesions are reported in a case of thyroid carcinoma in a cockatiel.

Histologic changes can be poorly defined, with generalized follicular inactivity and atrophy associated with epidermal thinning and atrophy of dermal collagen (Fig. 11.58). In some cases of hypothyroidism, excessive mucin deposition is seen in the dermis. To confirm a diagnosis of endocrine-related skin disease, appropriate clinical laboratory testing is necessary. Confirmation can also result from finding appropriate endocrine gland lesions at necropsy.

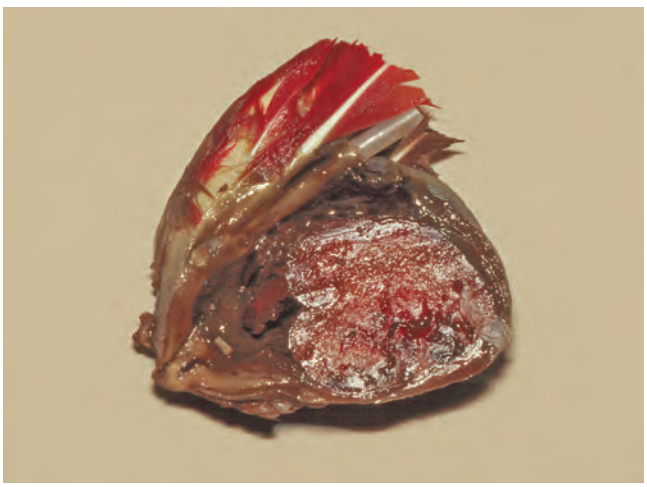

Figure 11.56 Organized hematoma that must be differentiated from a neoplastic process.

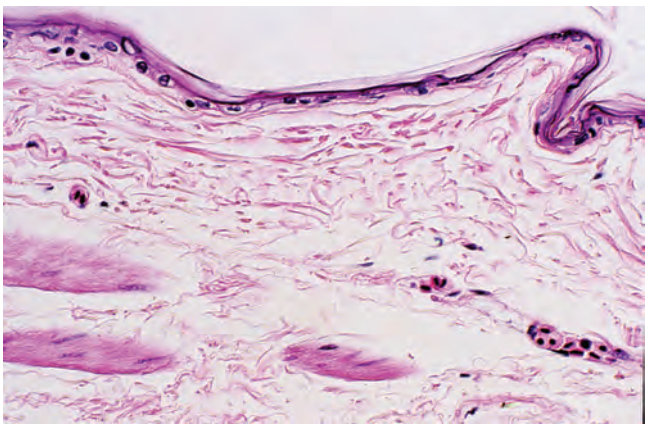

Figure 11.58 Mild hyperkeratosis associated with epidermal atrophy and dermal edema in a hypothyroid bird.

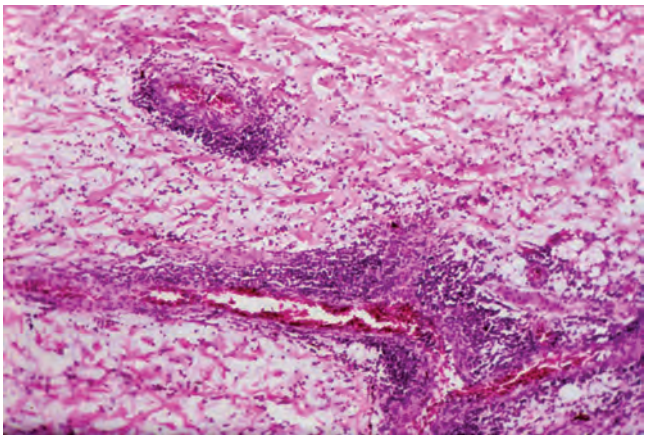

Figure 11.59 Severe angiocentric dermatitis consistent with hypersensitivity.

Figure 11.60 Amazon foot necrosis. The affected area is swollen and hemorrhagic.

Hypersensitivity

Allergic skin disease in birds is occasionally reported but is not well documented and confirmation can be difficult. Gross changes that may be associated with allergic skin disease include feather loss, reddening of the skin, and, occasionally, surface exudates. Some of the gross lesions may be secondary to self-trauma.

Histologic lesions are not definitive, because there are still an insufficient number of cases with follow-up information. Perivascular inflammatory cell foci are seen in the dermis and subcutis. These foci usually consist primarily of mononuclear cells, with a few granulocytes in some cases (Fig. 11.59). In severe lesions in some species, large numbers of granulocytes and a variable amount of degranulation have been noted. A pleocellular inflammatory infiltrate is often present in the feather pulp. Severe superficial necrosis, variable acanthosis, and dermal fibrosis are often associated with self-trauma. Secondary infection is possible. It is important to note that this is the most common lesion seen in skin biopsies of feather- and skin-damaging birds. Whether it is a primary lesion or a secondary lesion and how it might be related to allergens are not known.

A condition known as "Amazon foot necrosis" is seen in Amazon parrots. Affected birds suddenly begin chewing at their feet and lower legs. The pathogenesis of this lesion is not known, but there is a speculation that it represents a delayed hypersensitivity reaction following staphylococcal dermatitis. Owners of many of these parrots smoke cigarettes, and it is also postulated that nicotine or some element in tobacco smoke may initiate this disease. Gross lesions are seen in unfeathered skin of the leg and foot and begin as erythematous areas. There is usually severe self-trauma leading to swelling and ulceration (Fig. 11.60). In some cases, staphylococci are found in the lesion.

Chronic internal disease

Feather loss and poor-quality feathering are nonspecific findings in many cases of chronic internal disease, including infectious, degenerative, and neoplastic conditions. All of these can lead to feather-destructive behavior.

Miscellaneous conditions

Calcinosis circumscripta, which is an unusual condition in birds, presents as nodular lesions that may have a white, chalky appearance grossly. Histologically, a chronic inflammatory reaction and variable fibrosis surround mineralized foci (Fig. 11.61).

Follicular malformations and dystrophy are occasionally seen. The most recognized is the so-called polyfolliculitis, which is a misnomer, as in many cases there is no inflammation. The condition is seen in budgerigars, cockatiels, and lovebirds. Multiple feather shafts appear to grow from a single follicle. Feathers are thick and short and may have retained sheaths. Histologically the feather follicles appear to coalesce due to an atrophy of the skin between the follicles, leading to what appear to be multiple shafts and epidermal collars within a dilated follicle (Fig. 11.62).

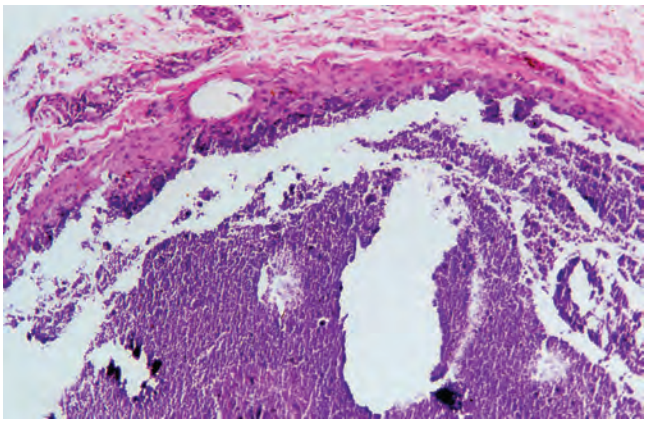

Figure 11.61 Calcinosis circumscripta. Multiple foci of dermal mineralization and a variable inflammatory reaction are seen.

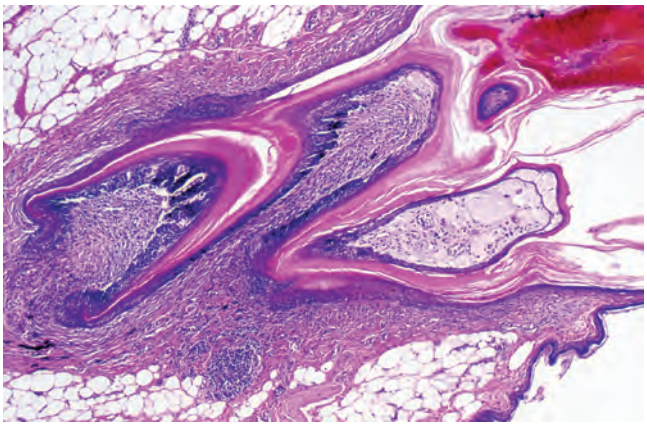

Figure 11.62 Feather dystrophy typical of polyfollicle formation. Several feather shafts appear to be arising in an area of one feather follicle.

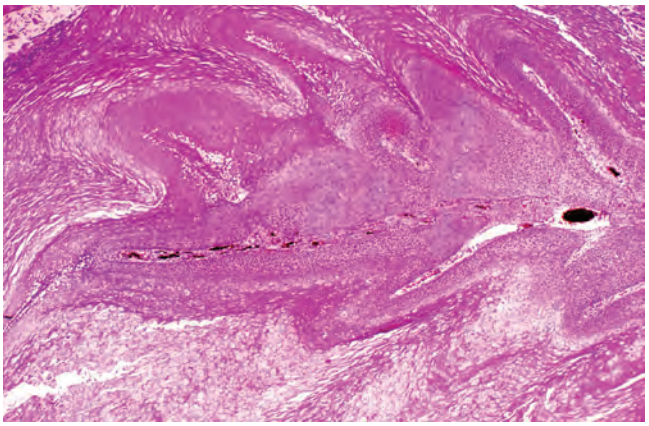

Figure 11.63 Squamous papilloma. Multiple epithelial fronds are seen. Other than in African grey parrots, viral causation has not been proven.

Occasionally, structures morphologically consistent with adventitial bursa formation are found. Grossly they present as fluctuant subcutaneous swellings that contain slightly viscid fluid. Histologically, synovial-like cells usually line the structures. The wall is usually chronically inflamed with an infiltrate of macrophages, heterophils, and plasma cells.

Collagen necrosis associated with a severe granulocytic response is occasionally seen in dermal lesions. Although many of the granulocytes may be eosinophils, they are difficult to distinguish from heterophils histologically. The lesion is similar to idiopathic collagenolytic inflammation seen in several mammalian species.

Autoimmune skin disease has not been documented in birds, but several cases with intraepidermal pustule formation and acantholysis have been seen. Unfortunately these few cases were lost to follow-up.

Perifollicular lymphoid aggregates and perivascular lymphoid cuffing are common findings in the birds with specific feather disease and in the birds that are self-mutilating. This may be a nonspecific finding associated with antigen stimulation when there is inflammatory skin disease. However, it is not clear why these lesions are commonly seen in the birds that are damaging their feathers but do not have other obvious skin disease.

Proliferative disease

Neoplastic disease

Epithelial tumors

Papillomas of the skin are not common and may be virally induced in African grey parrots (see the section on viral disease). In other birds, particularly cockatiels, these tumors usually present as papillary growths on the face. Histologically the lesions are similar, but viral causation has not been proved. They comprise fronds covered by proliferative, hyperkeratotic epidermis (Fig. 11.63). There is a delicate vascular stroma.

Squamous cell carcinomas are often ulcerated and hemorrhagic as well as infiltrative. They tend to grow slowly and can become large if not treated (Fig. 11.64). They can arise anywhere in the skin and also within the uropygial gland, where they must be differentiated from primary tumors of the gland.

The microscopic appearance of squamous cell carcinomas is variable. Many are fairly well differentiated, with cells forming nests and cords that may contain keratin centers (Fig. 11.65). Others are poorly differentiated, with no keratin differentiation. The cells will form diffuse sheets that are infiltrative (Fig. 11.66). Metastasis is possible but seldom reported.

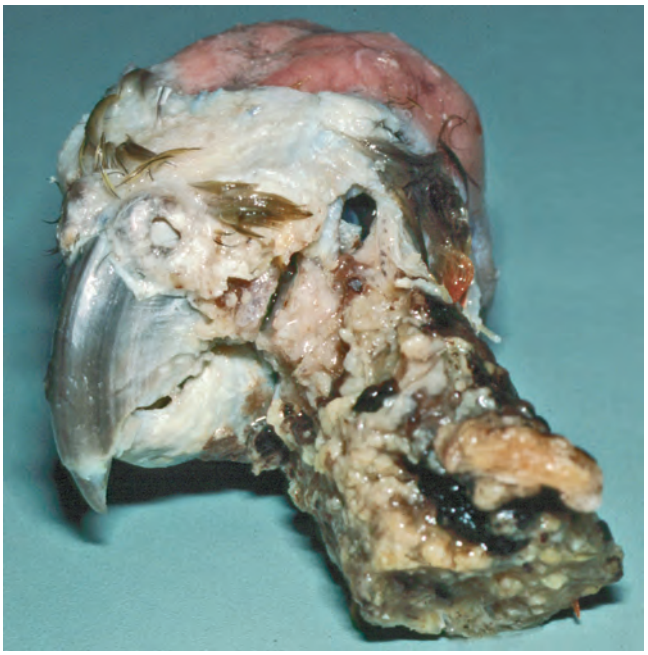

Figure 11.64 Squamous cell carcinoma involving a large area of the face and neck.

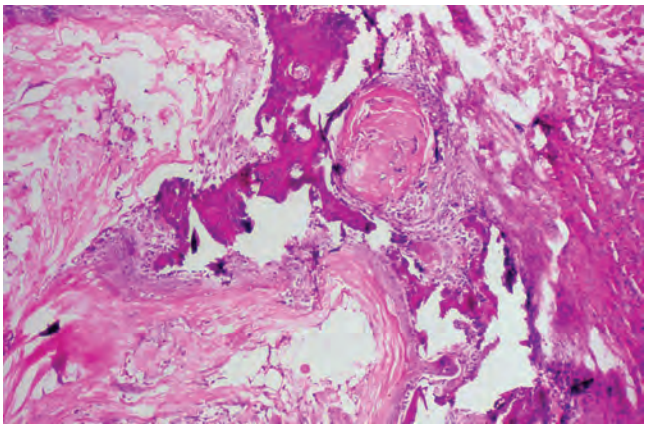

Figure 11.65 Squamous cell carcinoma with keratin pearls that is invasive into bone.

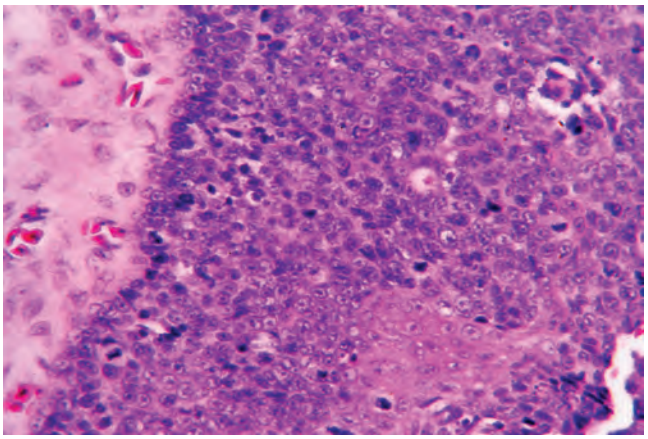

Figure 11.67 Sheet of neoplastic cells in basal cell tumor.

Basal cell tumors can present as solitary nodules, may also originate in feather cysts, and, although expansile, are histologically benign, forming sheets, cords, or nests. Basal cell tumors associated with attempted feather formation have been called "feather folliculomas" and may be the avian equivalent of trichoepitheliomas. The proliferative basal cells form nests and ridges that grow by expansion in the wall of the cyst (Fig. 11.67).

Basal cell carcinoma is rare but can be invasive, with a high potential for recurrence or possible metastasis.

Keratoacanthomas are occasionally reported in psittacine birds. They usually are seen involving the beak or base of the claws. Grossly the masses are not diagnostic, but they may lead to deformities in either beak or claw (Fig. 11.68). Histologically there are cyst-like structures filled with keratin (Fig. 11.69). The structures are lined by fairly well-differentiated squamous epithelial cells. Although histologically benign, these tumors will grow by expansion and can efface normal structures.

Uropygial gland tumors can be either adenomas or carcinomas, and gross differentiation is difficult. Grossly there is an

Figure 11.68 Deformed beak associated with a keratoacanthoma.

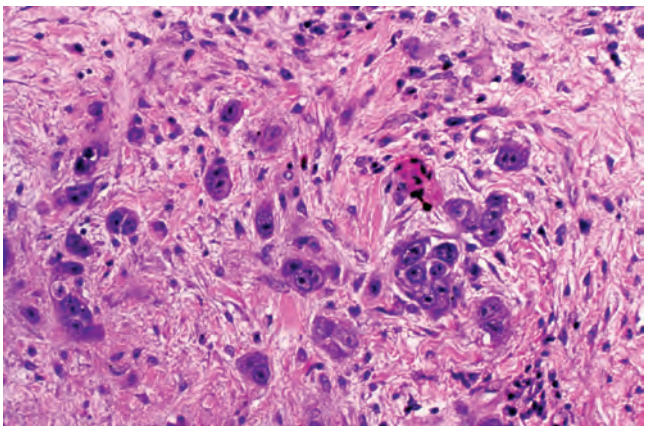

Figure 11.66 Poorly differentiated squamous cell carcinoma with individualization of tumor cells and a scirrhous response.

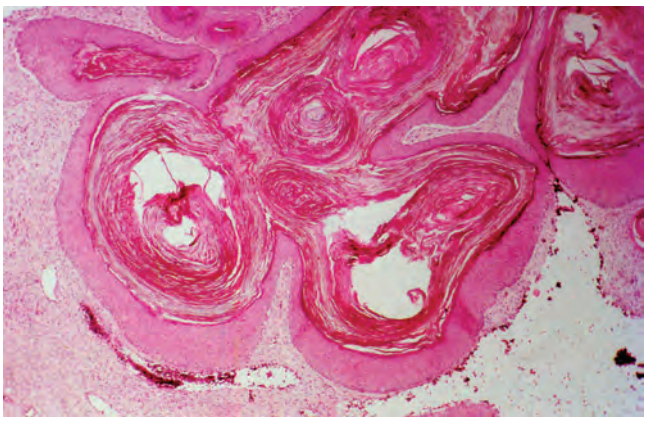

Figure 11.69 Typical histologic appearance of keratoacanthoma. Cyst-like structures are filled with keratin.

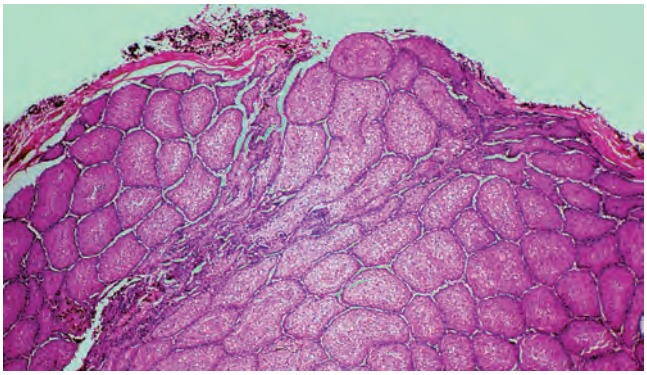

Figure 11.70 Uropygial gland tumor with lobules of well-differentiated epithelial cells.

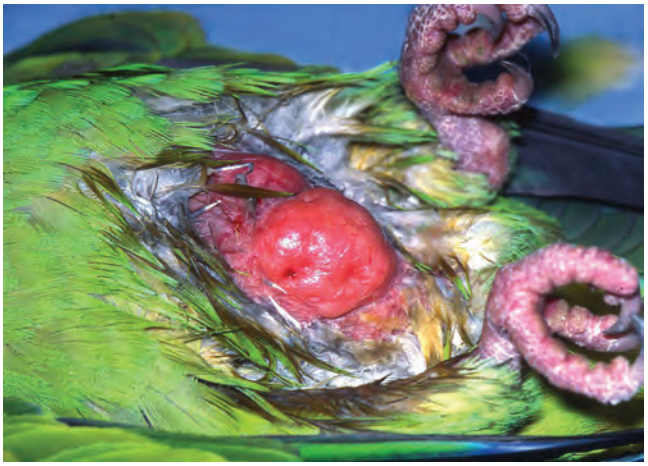

Figure 11.72 Large subcutaneous abdominal mass typical of lipoma.

enlarging mass in the region of the uropygial gland. The mass is ulcerated in some cases.

Adenomas are usually well circumscribed and encapsulated and are comprise fairly well-differentiated glandular epithelial cells (Fig. 11.70). Carcinomas contain less well-differentiated cells that are infiltrative into surrounding tissue (Fig. 11.71). Carcinomas are more likely to be necrotic, hemorrhagic, and secondarily inflamed.

Mesenchymal tumors

Mesenchymal tumors include those of vascular origin, fibrous and adipose connective tissue, and myxomas. In addition, lymphosarcoma and mast cell tumors may be found. Gross differentiation can be difficult with both benign and malignant tumors.

Lipomas are common and have the gross appearance of a mass of normal fat (Fig. 11.72), although they can be hyperemic and there may be areas of inflammation. Histologically the typical lipoma comprises a sheet of well-differentiated adipose cells (Fig. 11.73). Several variants have been noted on histologic examination. Myelolipomas, in addition to the adipose cells, contain multiple foci of extramedullary hematopoiesis. Sections of these tumors resemble normal bone marrow.

Osteolipomas and hemangiolipomas have also been identified. They are characterized respectively by the formation of either normal bone spicules or numerous well-differentiated capillaries.

Infiltrative lipomas comprise histologically normal-appearing adipose cells, but they will infiltrate into surrounding fibrous connective tissue and skeletal muscle behaving as a locally aggressive malignant tumor.

Liposarcomas are less common. They are usually fatty-appearing, poorly demarcated masses (Fig. 11.74).

Hemangiomas and hemangiosarcomas occur in the skin and subcutis with essentially the same frequency in pet birds. Lymphangiomas are rarely seen. These tumors are described in Chapter 1.

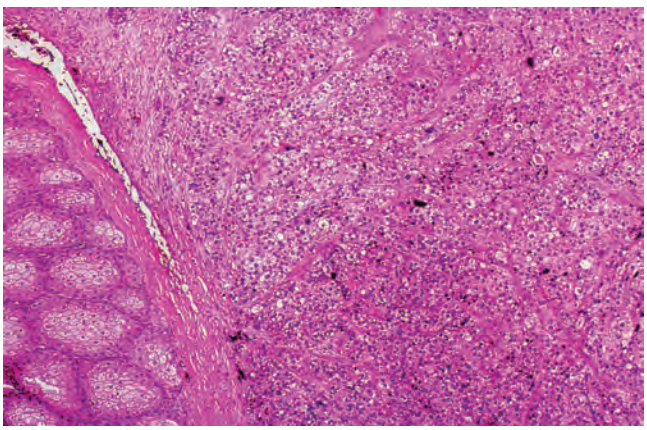

Figure 11.71 Poorly differentiated cells of uropygial gland carcinoma. Normal gland on left.

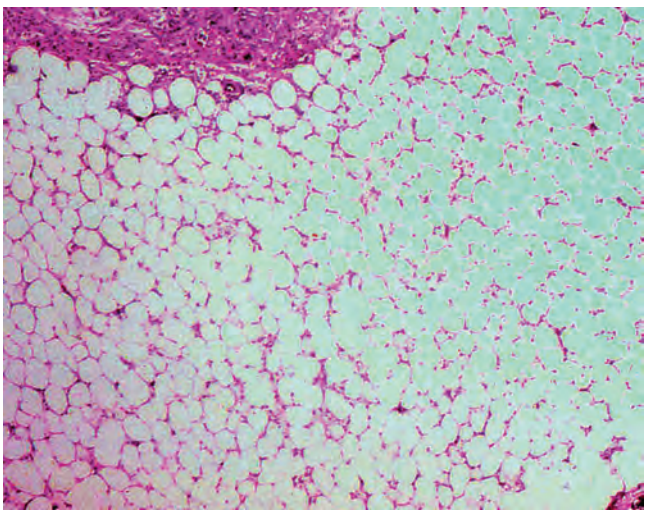

Figure 11.73 Typical subcutaneous lipoma composed of a sheet of well-differentiated adipose cells.

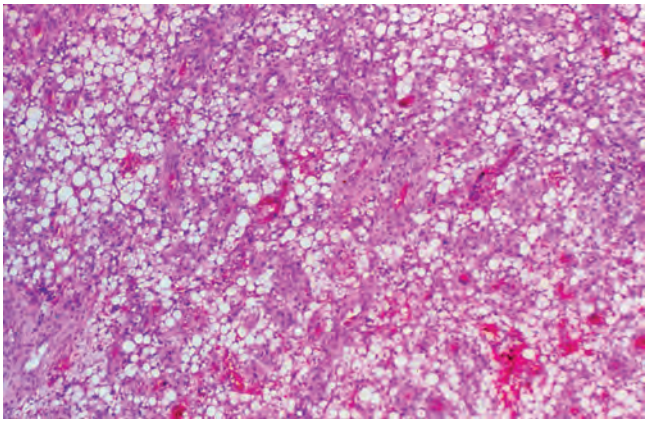

Figure 11.74 Liposarcoma. Moderately undifferentiated to poorly differentiated adipose cells and minimal stroma.

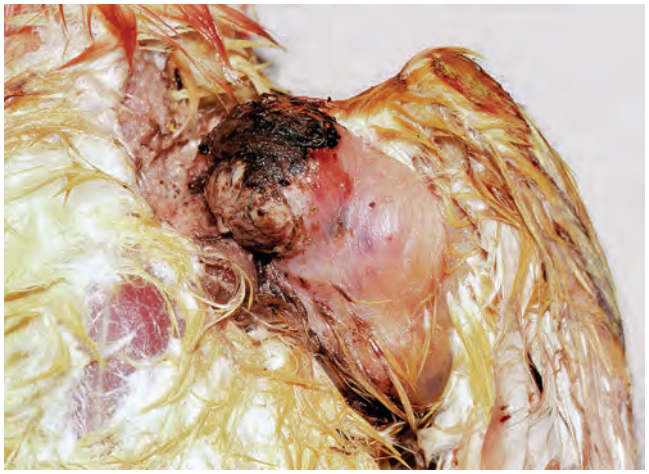

Figure 11.76 Large irregular mass that was a fibrosarcoma. Hemorrhage and necrosis are more common in the malignant tumors.

Fibrosarcomas are common tumors of the skin of pet birds, but fibromas are infrequently diagnosed. Both tumors present as firm nodules or masses. Benign tumors are encapsulated, but sarcomas may have indistinct margins (Figs 11.75 and 11.76). These tumors present as firm nodules or masses.

Histologically fibromas comprise interlacing bundles of well-differentiated collagen (Fig. 11.77). Fibrosarcomas are very cellular, with fusiform cells forming interlacing bundles and sheets (Fig. 11.78). Numerous mitotic figures are usually seen. Cytologic preparations will contain mesenchymal cells, but may be poorly cellular (Fig. 11.79).

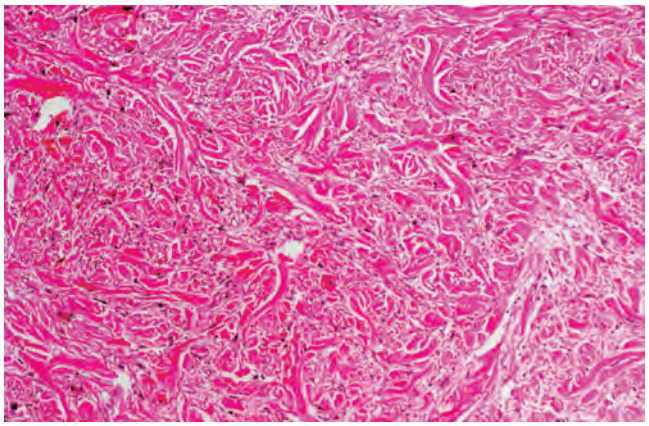

Figure 11.77 Bundles of well-differentiated collagen typical of fibroma.

Figure 11.75 Fibroma. Note the smooth borders.

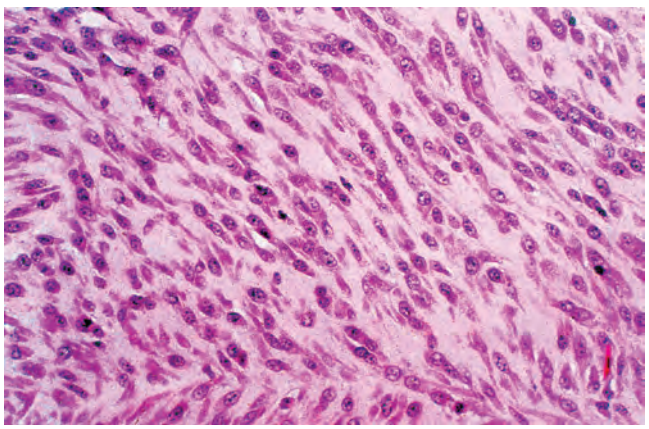

Figure 11.78 Highly cellular fibrosarcoma common in pet birds. Scattered mitotic figures are seen.

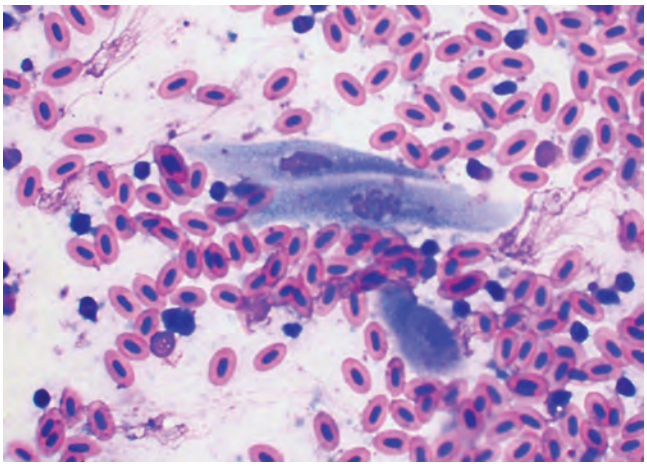

Figure 11.79 Cytology of fibrosarcoma. Minimal numbers of mesenchymal cells are seen.

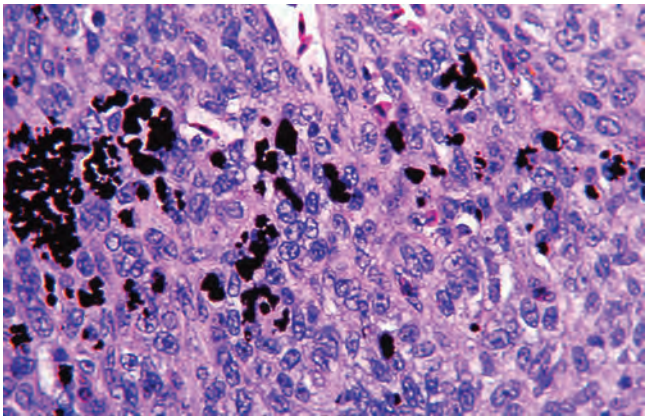

Figure 11.81 Undifferentiated sarcoma associated with the site of a skin tattoo. The dark pigment is tattoo ink.

Tumors morphologically similar to mammalian hemangiopericytoma are occasionally diagnosed. They comprise whorls of fusiform cells that appear to surround blood vessels (Fig. 11.80).

Some connective tissue tumors contain large amounts of extracellular mucin and morphologically are called myxofibromas or myxomas, depending on the cell-to-ground substance ratio. Mitotic activity is usually minimal.

Undifferentiated sarcomas are occasionally found at the site of skin tattoos. Histologically tattoo ink is present in the lesion (Fig. 11.81).

Dermal lymphosarcoma can present as solitary or multiple masses or as diffuse thickening of the skin with loss of feathers (Fig. 11.82). Neoplastic lymphoid cells form diffuse sheets, and there is variable mitotic activity (Figs. 11.83 and 11.84). Histochemistry can be used to differentiate the exact cell type (Fig. 11.85). Multifocal infiltration of feather follicles, is often seen in Marek's disease in chickens. Grossly the skin may contain

Figure 11.82 Mass in the skin and subcutis diagnosed as malignant lymphoma. Histology or possibly cytology is necessary to differentiate from other neoplasms.

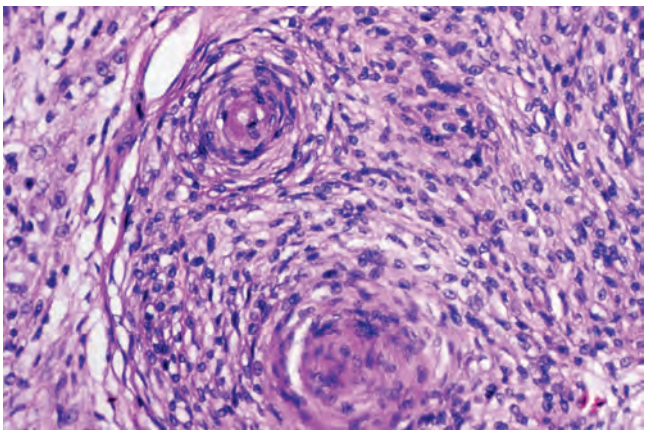

Figure 11.80 Pattern of fusiform cells consistent with probable hemangiopericytoma. These tumors are uncommon in birds.

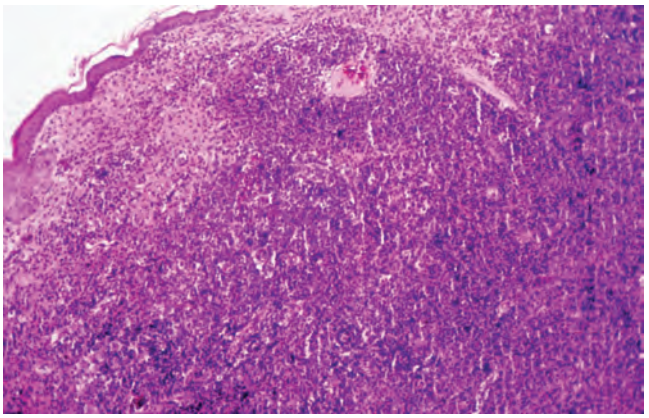

Figure 11.83 Dermal lymphosarcoma composed of a sheet of neoplastic lymphoid cells.

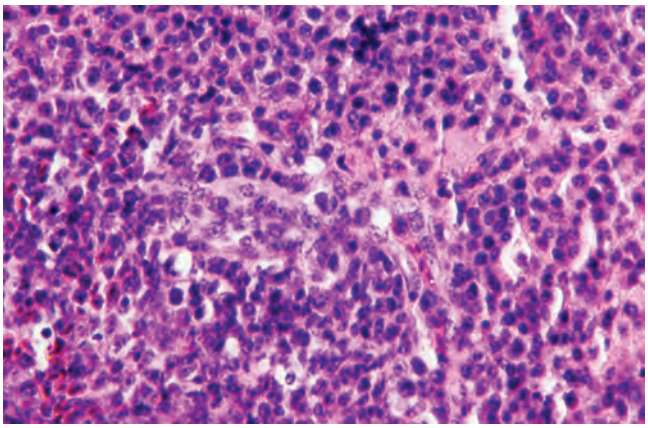

Figure 11.84 Dermal lymphosarcoma. The cells have indistinct cytoplasmic boundaries and are minimally pleomorphic.

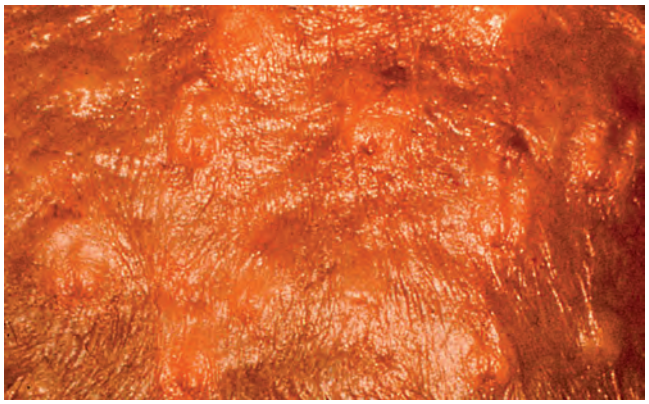

Figure 11.86 Skin nodules due to Marek's disease in a chicken.

multiple nodules (Fig. 11.86). Epitheliotropic lymphoma similar to Marek's disease occurs sporadically in pet birds. An etiologic agent has not been identified.

Melanocytic tumors

Melanoma has been diagnosed in several psittacine birds. The tumor is not common and is usually malignant. These tumors, which often occur on the face and may involve the beak, are brown-black, raised masses, with poorly defined margins (Fig. 11.87). Histologically they comprise pleomorphic melanocytic cells that form nests and sheets (Fig. 11.88).

Mast cell tumors. These have been primarily reported in chickens and owls, and we have rarely diagnosed one in a psittacine bird. They are grossly nonspecific, but impression smears can be diagnostic, as the mast cell granules usually readily stain (Fig. 11.89). Histologically they present as diffuse sheets of mast cells. Special stains may be necessary to illustrate the granules.

Figure 11.87 Malignant melanoma (arrows) deforming the beak.

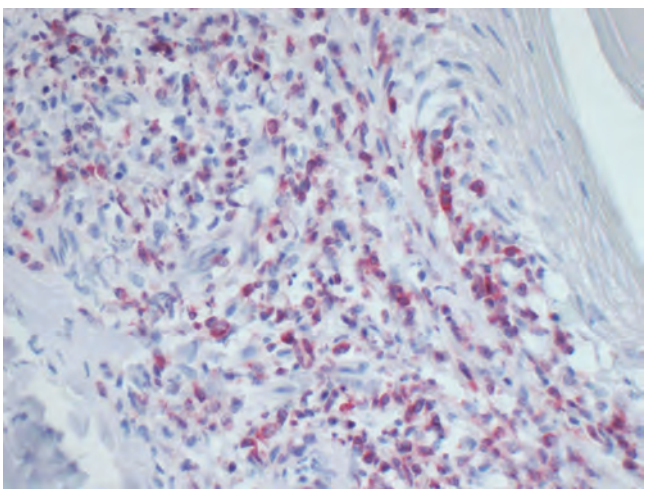

Figure 11.85 Histochemical stain illustrating a T-cell lymphoma in the skin of an African grey parrot. Positive neoplastic cells stain red-brown.

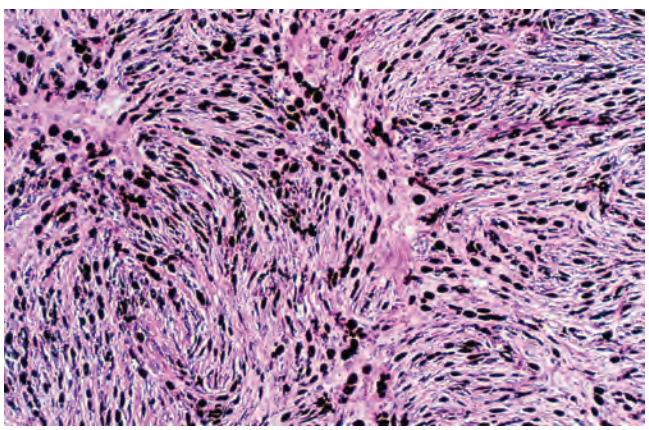

Figure 11.88 Malignant melanoma composed primarily of fusiform cells.

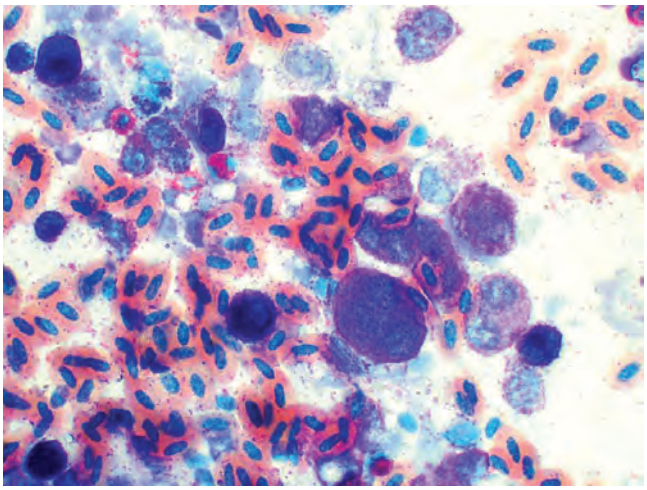

Figure 11.89 Cytologic preparation of avian mast cell tumor.

Tumors of uncertain origin

Granular cell tumors are infrequent in birds and are seen primarily in psittacine birds, particularly Amazon parrots. They are small, smooth nodules composed of pleomorphic cells with abundant pale eosinophilic cytoplasm containing distinct granules (Fig. 11.90). The granules are periodic acid-Schiff positive and, in one bird, were histochemically positive for muscle actin. Although they are morphologically distinct, the cells may not have a distinct histogenesis.

Nonneoplastic proliferative lesions

Xanthomatosis is a condition of uncertain etiology. Xanthomas are seen most commonly in cockatiels and budgerigars and are usually present on the wing as a variably sized, yellow mass (Fig. 11.91). The lesion is often extensive and often bothers the bird, causing it to self-mutilate, resulting in a further increase in lesion size.

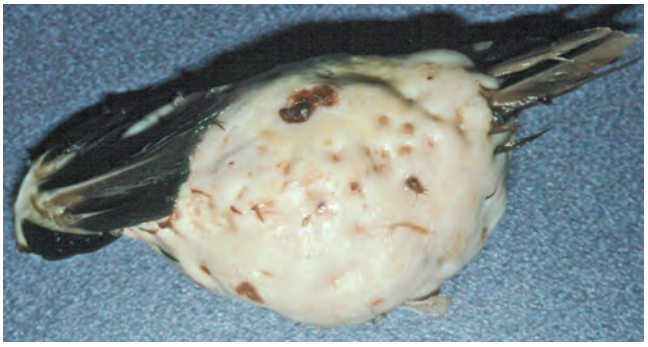

Figure 11.91 Typical nodular appearance of xanthoma.

Xanthomas comprise numerous large macrophages with abundant foamy cytoplasm. The cytoplasmic material is lipid, and there may also be free lipid and cholesterol cleft formation (Fig. 11.92). There can be variable inflammation and necrosis, with infiltration of heterophils and lymphocytes as well as giant cell formation. Superficial ulceration may occur.

Atypical granulomatous disease in moluccan cockatoos has recently been reported, however sporadic cases have been seen for sometime. The condition is systemic, but skin lesions can be the presenting sign. Multiple variable-sized masses are seen grossly, and histologically there are irregular multinucleated giant cells present (Fig. 11.93), as well as macrophages and granulocytes. A causative agent has not been identified in tissue sections.

A condition termed "pseudolymphoma" is sporadically seen, primarily in macaws. This is usually a proliferative lesion of the face that usually presents as a swelling occasionally accompanied by reddening of the skin. Histologically it comprises lymphoid cells that may appear more hyperplastic than neoplastic; however, delineating between these possibilities may be difficult in

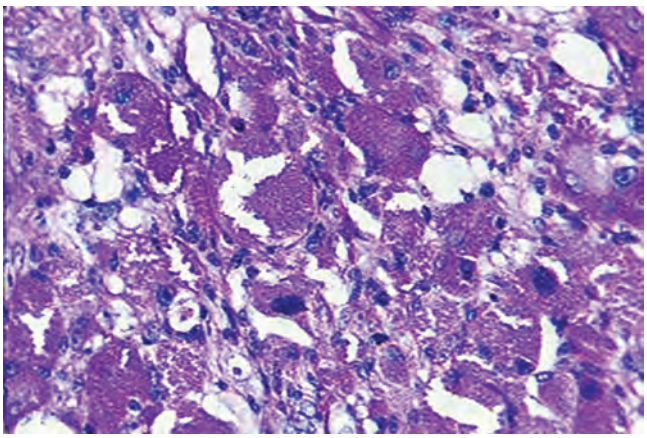

Figure 11.90 Granular cell tumor with distinct granules seen on periodic acid-Schiff-stained section.

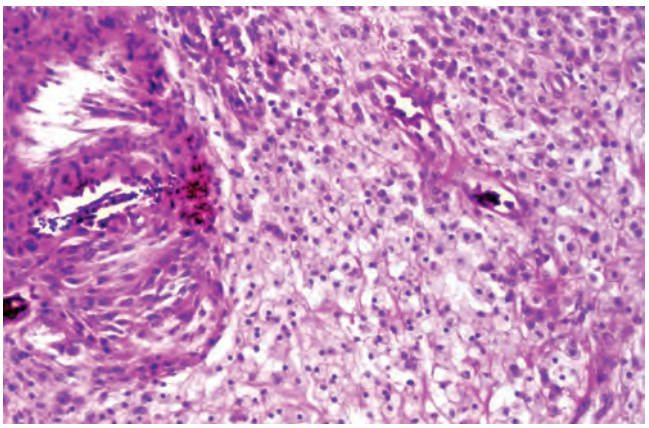

Figure 11.92 Large macrophages with abundant foamy cytoplasm and cholesterol cleft formation typical of avian dermal and subcutaneous xanthoma.

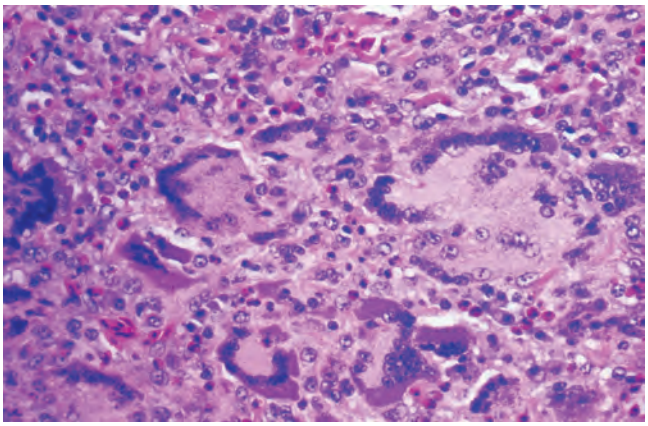

Figure 11.93 Appearance of atypical granulomatous disease lesion in the skin of a moluccan cockatoo.

cytologic preparations or small needle biopsies. The cause of the condition is not known.

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12 Special Sense Organs

Eye

Normal structure

Relative to most other animals, birds have large eyes. They are recessed in the skull and fill most of the space in the rostral skull. The shape of the eye varies significantly between species but in most companion birds is spherical with an anterior to posterior flattening. The eye is surrounded dorsally, rostrally, ventrally, and medially to some extent by the infraorbital sinus. Two muscular eyelids and the third eyelid cover the eye. The lower eyelid contains a fibroelastic tarsal plate. There are no meibomian glands. A harderian gland is present at the base of the third eyelid. The eyelash-like filoplumes of the upper lids are modified feathers. Avian eyelids close mostly in sleep, as the nictitating membrane is responsible for blinking. Two striated muscles move the nictitating membrane, which in diurnal birds is usually transparent.

The lacrimal apparatus includes a gland of the nictitating membrane (harderian gland) that is a compound tubular or tubuloalveolar gland located on the ventromedial surface of the eye. It contains plasma cells derived from the bursa of Fabricius that produce specific antibodies to local antigenic stimulation. The lacrimal gland, which is smaller than the harderian, is located in the area of the caudal or lateral temporal commissure and is attached to the orbital ring. Secretions drain via lacrimal ostia of upper and lower eyelids to a lacrimal canaliculus and finally to a nasolacrimal duct that extends to the nasal cavity.

The cornea and sclera comprise the fibrous tunic of the eye. The cornea is composed of an outer stratified squamous epithelial layer, and a thick inner lamina propria comprises collagen fibers. Both Bowman's and Descemet's membranes are present in some birds, but in others the anterior limiting membrane is not differentiated. At the junction of the anterior and posterior chambers, the sclera is reinforced by ring of overlapping bones called the scleral ossicles. Their number varies from 10 to 18 depending on species. The sclera surrounding the posterior chamber is thick and has two layers: a cartilage layer and a thick fibrous layer. In some species, the scleral cartilage around the optic nerve is ossified.

The vascular tunic comprises the choroid, ciliary body, and iris. The choroid is very vascular and pigmented. A tapetum lucidum is seen in only a few nocturnal birds. The choroid continues as the ciliary body and iris. The lens is suspended by the zonular fibers of the ciliary body. Small folds—ciliary processes—produce the aqueous humor and are pressed against the rim of the lens by the ciliary muscles. In birds, these muscles are striated rather than smooth.

The avian lens is softer than the mammalian lens, having a fluid-filled lens vesicle between the annular pad and body of the lens. The anterior surface of the lens is flatter in diurnal species than in nocturnal and aquatic birds. In diurnal birds, the cornea and lens are clear and will transmit wavelengths of light to about 350 nm, making near-ultraviolet radiation visible.

The neural tunic (retina) is relatively thick and, unlike in mammals, does not contain blood vessels. As in mammals, it comprises inner optic fiber layer, the ganglion cell layer, the inner plexiform layer, the bipolar (inner nuclear) layer, the outer plexiform layer, the neuroepithelial layer (outer nuclear and rod and cone layers), and the pigment epithelium. Visual cells of the avian retina include rods that lack oil droplets, cones, and double cones. Avian cones contain oil droplets that may be red, yellow, yellow-green, or multiple colors. Oil droplets comprise one or more stable carotenoid pigments. There are thin chief cones and short, broad accessory cones. Oil droplets are consistently found in the chief cone but are not present in the accessory cones of all species. Diurnal birds have far more cones than rods, and the rods are confined to the periphery of the retina. The retina of nocturnal birds contains mostly rods. The central portion of the retina may have a fovea whose depth may increase visual acuity. Some birds have patches where the retina is thickened by densely packed cells (foveas). These areas are thought to be locations of improved visual acuity. Birds that pursue moving prey or feed in flight have both central and temporal areas.

The pecten, which projects from the retina into the vitreous at the exit of the optic nerve, is markedly vascular and may be active in nutrition of inner retinal layers. Its size and morphology vary by species. Conical pectens are seen only in the kiwi; vaned pectens are found in rheas, ostriches, and tinamous; and pleated pectens are present in most other birds.

Three striated muscles control the eyelids: the levator of upper eyelid (third cranial nerve), depressor of lower lid (fifth cranial nerve), and sphincter muscles that encircle the lids. Extraocular

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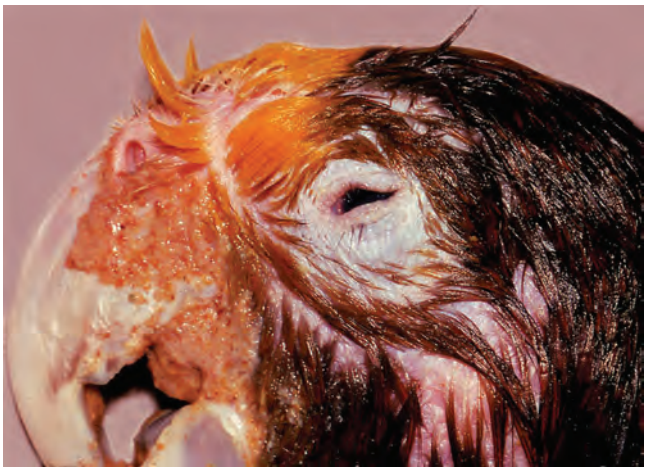

Figure 12.1 Slightly small orbit and sunken, small globe in a bird with microphthalmia.

Figure 12.2 Marked swelling and reddening of eyelids due to poxvirus infection.

muscles in birds include the dorsal and ventral oblique, and dorsal, medial, ventral, and lateral rectus. Eye movements are independent (unlike in mammals).

Disease of the eye and adnexa

Developmental anomalies include cryptophthalmos (continuous skin over the globe with no evidence of lid formation) and agenesis of eyelids, symblepharon, improperly draining nasolacrimal ducts, and corneal dermoids. Microphthalmia is probably the most commonly reported anomaly, with a small globe being obvious grossly. In cases of microphthalmia pectin defects, colobomas and orbital cysts have been reported in chickens. The region of the choroid fissure may be where the primary abnormality occurs. There is also often reduction of cells in the ganglion cell layer. Grossly, the eye and orbit and globe appear small (Fig. 12.1), and possibly malformed in serious cases. Microphthalmia has been reported in gyrfalcon chicks that were hatched from eggs that were mistakenly incubated at higher than normal temperatures.

There may be anomalies of all segments of the eye, associated with disturbances of optic vesicle involution or embryonic fissure closure. Congenital cataracts are infrequent, and their underlying cause is not known. Retinal dysplasia results as a nonspecific altered response of the retina at certain stages of development. There are variable histologic changes and different etiologies. Coloboma is a focal absence of ocular tissue that can occur anywhere in the eye. Colobomas are secondary to defective differentiation of mesenchyme leading to problems in the choroid and iris.

Ocular adnexa

Blepharitis is often an extension of periocular dermatitis due to a variety of causes. Viruses that may affect the eyelids include poxvirus, psittacine beak and feather disease virus (PBFDV), polyomavirus, Psittacid herpesvirus-2, and finch and parrot papillomaviruses. Acute changes in poxvirus infection include mild inflammation and edema with a serous ocular discharge. With chronicity, there is ulceration of the lids, and a proliferative mass may form (Fig. 12.2). The exudate may become purulent due to secondary bacterial infection. Histologic lesions are typical and are described in Chapter 11.

Chemosis is a characteristic feature of poxvirus infections of canaries. PBFDV infection can lead to acute lesions in the periorbital skin that may be difficult to differentiate from poxvirus infection grossly. Histologic lesions are consistent with those previously described (Chapter 11). Polyomavirus can cause blepharitis as part of generalized infection in budgerigars. Intranuclear inclusion bodies are seen. Papillomas that can be caused by either papillomaviruses or Psittacid herpesvirus-1 are in rare instances found on the skin of the face and eyelids of African grey parrots (Chapter 11).

Bacterial infection can be primary in the eyelid or secondary to dermatitis of the periorbital skin. Gross changes are variable, from reddening and swelling to ulceration. Histologic examination may be necessary to rule out underlying poxvirus infection.

Knemidokoptes sp. infections present as crusts and/or scales and commonly involve the periorbital skin. Histologically mites can be found in the chronic inflammatory response.

Fungi can cause nonspecific inflammation just as in any other location. Organisms are usually found on histologic examination. Deep lesions have been associated with *Cryptococcus* infection (Fig. 12.3).

Noninfectious disease

Vitamin A deficiency may cause periorbital epidermal hyperplasia and hyperkeratosis, with secondary infections possible. Histologically the lesion is characterized by marked proliferation of keratin without an inflammatory response.

Neoplastic lesions of the eyelids potentially include all of the tumors reported in the skin of birds (Chapter 11). Xanthomas are also seen in the eyelids, including the third eyelid (Fig. 12.4).

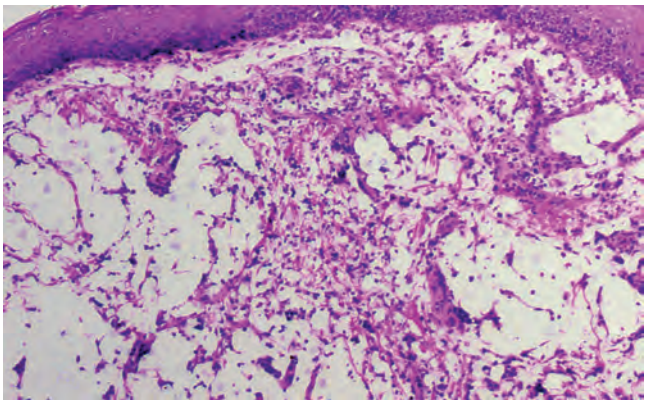

Figure 12.3 Mycotic blepharitis due to *Cryptococcus* sp. Organisms with large mucinous capsules are present.

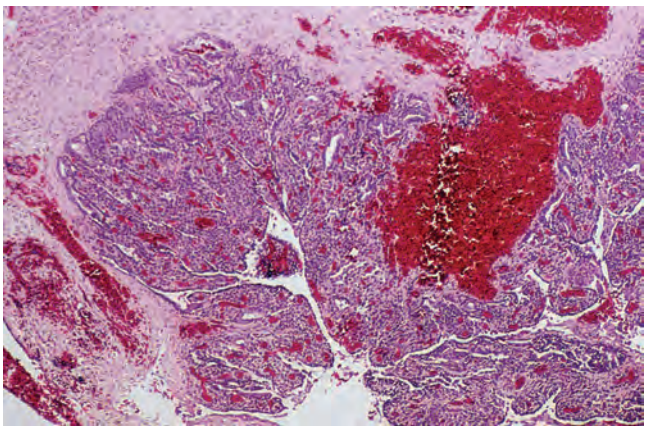

Figure 12.5 Lacrimal gland carcinoma composed of numerous trabecular and tubular structures.

Lacrimal glands

Lacrimal glands may become infected with bacteria, leading to swelling and abscess formation. The swelling must be differentiated from possible gland or periorbital neoplasia. Grossly the lesion is fluctuant, and purulent material may be expressed. Histologically, variable necrosis is seen associated with a pleocellular inflammatory infiltrate. Organisms must be found for etiologic specificity.

Lacrimal gland neoplasia is seen infrequently in birds. Based on our experience, carcinoma appears to occur most commonly. The tumors present as firm gray-white masses. Histologically there are acini, trabeculae, and tubular structures lined by moderately undifferentiated epithelial cells. There can be variable necrosis and inflammation (Figs. 12.5 and 12.6).

Conjunctiva

Lesions of the conjunctiva may be primary or associated with diseases of the lids and periorbital skin. They can involve palpebral or bulbar conjunctiva or the nictitating membrane. Secondary lesions are most commonly associated with sinusitis and therefore may be due to a variety of infectious agents including viruses, bacteria, *Chlamydia psittaci*, and *Mycoplasma* spp. In some cases, conjunctival lesions may indicate a generalized infection or septicemia.

Primary disease may be infectious or noninfectious. Infectious diseases may have similar gross signs, including blepharospasm, reddening and ocular discharge, regardless of cause (Fig. 12.7). Poxvirus infection causes lesions that are similar to those of the eyelids. The finding of intracytoplasmic inclusion bodies in proliferative conjunctival epithelial cells is diagnostic.

An alpha herpesvirus is the cause of conjunctivitis in Gouldian finches. Grossly the conjunctiva is swollen due to edema and congestion. There is a serous exudate in the conjunctival sac. Histologically, conjunctival epithelial cells are hypertrophied, hyperplastic, and variably necrotic. Karyomegalic nuclei contain basophilic inclusion bodies. A submucosal infiltrate consisting primarily of lymphocytes and plasma cells is seen. The lesions are usually associated with systemic disease particularly of the respiratory system (Chapter 2).

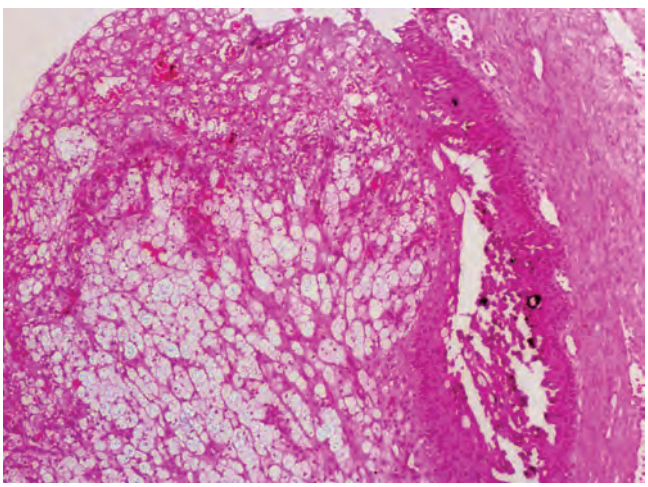

Figure 12.4 Xanthoma of the eyelid. The mass comprises numerous large cells with foamy, granular cytoplasm.

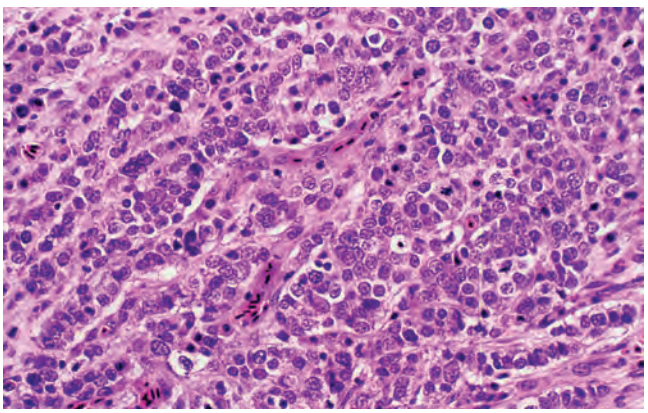

Figure 12.6 Higher magnification of lacrimal gland carcinoma.

Figure 12.7 Swelling, blepharospasm, and exudation typical of conjunctivitis.

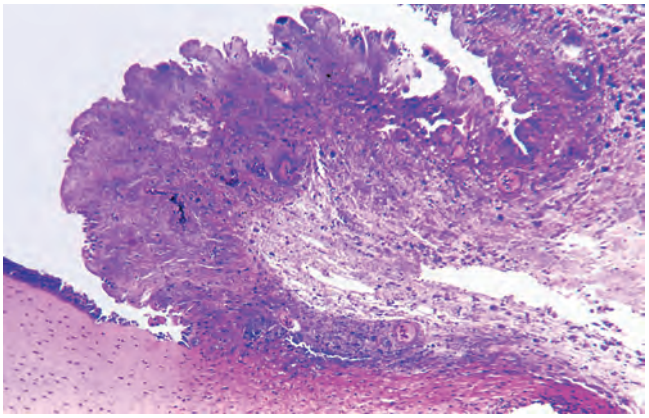

Figure 12.9 Conjunctival necrosis and inflammation due to bacterial infection.

Adenoviral conjunctivitis is occasionally seen as a part of generalized disease. Lesions are nonspecific unless intranuclear inclusions consistent with adenovirus are found. Conjunctivitis can also be caused by paramyxovirus 2. Inclusion bodies are not seen, and the lesions are nonspecific, with variable necrosis and a lymphoplasmacytic inflammatory infiltrate noted.

Bacterial conjunctivitis has been associated with a variety of organisms. Affected conjunctival surfaces are variably proliferative and reddened. In chronic cases, multifocal to confluent yellow-white foci are seen (Fig. 12.8). Necrosis and a pleocellular infiltrate with numerous heterophils are histologic characteristics of acute inflammation. With chronicity, granulomatous foci containing macrophages and giant cells are seen associated with fibrin deposition, necrotic debris, and proliferation of the mucosa (Fig. 12.9). Organisms must be found to characterize the lesion definitively.

Avibacterium paragallinarum causes a significant disease of chickens characterized by inflammation of serous membranes including the conjunctiva. Grossly severe blepharospasm and conjunctival exudate may be associated with sinusitis and facial swelling (Fig. 12.10). A mixed inflammatory infiltrate is seen in early cases (Fig. 12.11), with eventual necrosis of mucosa.

Mycobacterial infection leads to proliferative lesions that have necrotic centers surrounded by giant cells, macrophages, and heterophils. Mineralization may be present. Acid-fast bacteria are seen in giant cells and macrophages. The lesions are usually part of a systemic disease process. Mycobacterial granulomas of the conjunctiva are particularly common in cockatiels.

Conjunctivitis is a fairly common feature of *Chlamydia psittaci* and *Mycoplasma* spp. infections in birds. *Chlamydia psittaci* causes conjunctival reddening with a serous or purulent

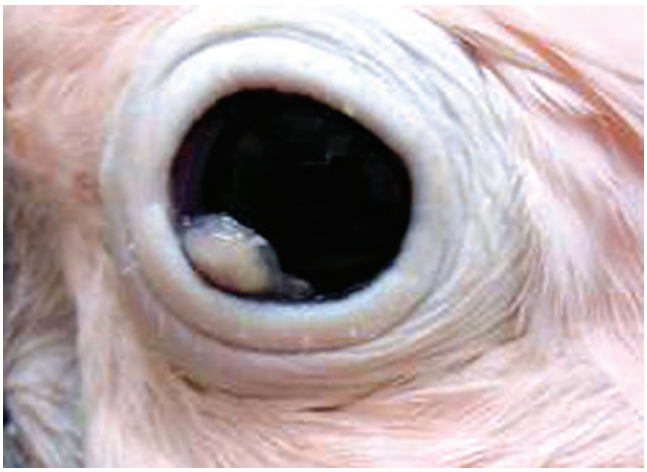

Figure 12.8 Focal lesion characteristic of chronic granulomatous conjunctivitis.

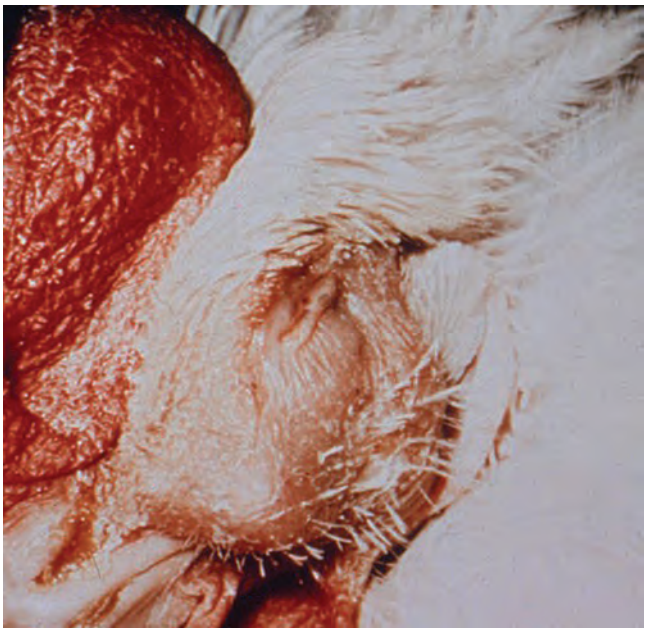

Figure 12.10 Conjunctival exudation and facial and sinus swelling in a chicken with *Avibacterium paragallinarum* infection.

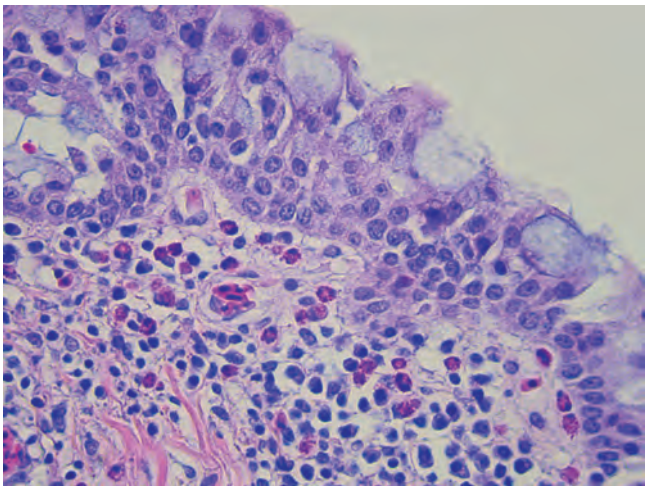

Figure 12.11 Typical mixed inflammatory infiltrate in early conjunctivitis due to *Avibacterium*.

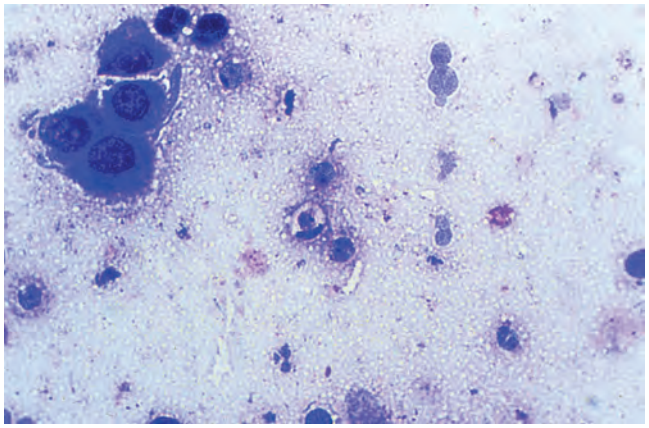

Figure 12.12 Cytology of conjunctival smear from a bird with cryptococcal infection. Note the budding yeasts with a clear capsule.

exudate. Histologically there is necrosis associated with a lymphohistiocytic infiltrate. Unless organisms are found, a definitive diagnosis cannot be made based on the conjunctival lesion. Conjunctivitis may be the only clinical sign of *C. psittaci* infection in cockatiels.

Mycoplasmosis is seen occasionally in individual companion birds, and we have seen it in flocks of commercial budgerigars. It is also suspected to be one of the causes of the chronic conjunctivitis seen in cockatiels, but this remains to be proven. *Mycoplasma gallisepticum* is widespread in wild house finches in North America. Several other species of native American birds are also reported to be susceptible to disease caused by this organism, and subclinical infections also occur. These house finches are potential sources of *M. gallisepticum* for companion birds housed outdoors. Affected birds have swollen conjunctival membranes and a serous to mucopurulent discharge. Histologically there is a chronic lymphoplasmacytic inflammatory infiltrate. Variable epithelial hyperplasia is noted. Similar lesions are often seen in the upper respiratory tract. *Mycoplasma gallisepticum* is a common cause of conjunctivitis in backyard chicken flocks and in pheasants.

Fungi causing conjunctivitis include *Aspergillus* spp., *Candida* spp., and *Cryptococcus neoformans*. Gross lesions are similar to those of bacterial infections. Cytologic examination of smears of the exudate may contain organisms and can provide a provisional differential diagnosis in some cases (Fig. 12.12). Histologic changes include necrosis, pleocellular inflammation including giant cells, and the presence of intralesional organisms (Fig. 12.13). Cryptosporidial conjunctivitis is occasionally seen. It may indicate an underlying immunosuppression and systemic disease. Gross changes are minimal and nonspecific. Histologically there is epithelial hyperplasia and a mild lymphoplasmacytic infiltrate. Organisms are found on the surface of epithelial cells (Fig. 12.14).

Nematodes that can cause conjunctivitis include *Oxyspirura mansoni*, which irritates the conjunctiva and may enter the lacrimal ducts, and *Thelazia* sp., which can be found in the conjunctival sac of birds with mild inflammatory changes. *Oxyspirura mansoni* has an indirect life cycle with cockroaches as intermediate hosts. Larvae travel from the crop to the esophagus and eventually up the nasolacrimal duct. Both of these parasites would be expected to be found only in wild-caught birds and are relatively rare findings.

Philophthalmus gralli is a trematode that is the cause of severe chronic conjunctivitis, primarily in waterfowl. Gross lesions include swelling and reddening of the conjunctiva. Generally, multiple flukes are present, and they are large enough to be seen with the unaided eye (Fig. 12.15). A chronic inflammatory reaction with numerous macrophages, lymphocytes, and plasma cells is present histologically. The conjunctival epithelium may be proliferative, however organisms may or may not be seen. (Figs. 12.16 and 12.17).

Noninfectious causes of conjunctivitis include foreign bodies that lead to reddening and discharge, which is generalized or

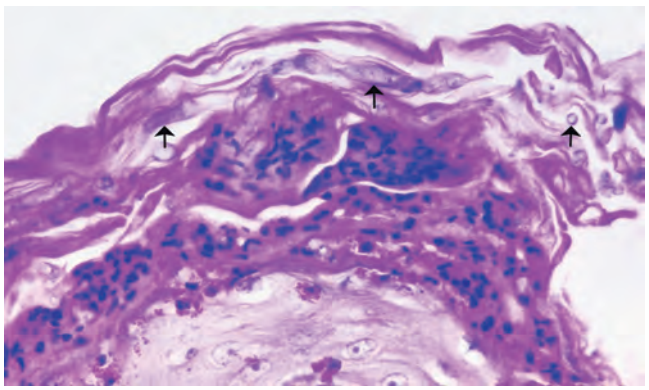

Figure 12.13 Mycotic conjunctivitis with hyphal fragments in necrotic debris (arrows).

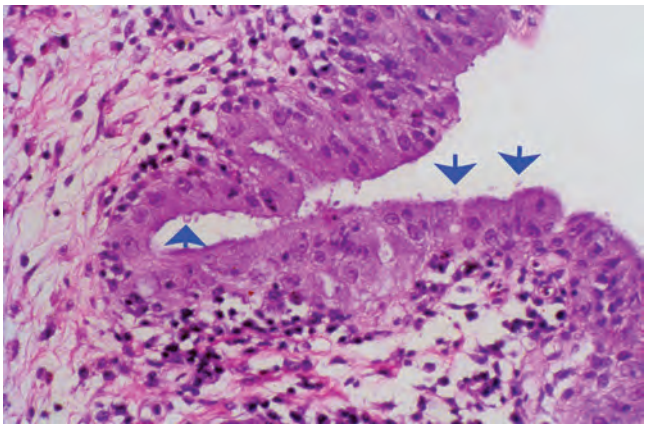

Figure 12.14 Proliferative conjunctival epithelial cells with cryptosporidial organisms adhering to their surface (arrows).

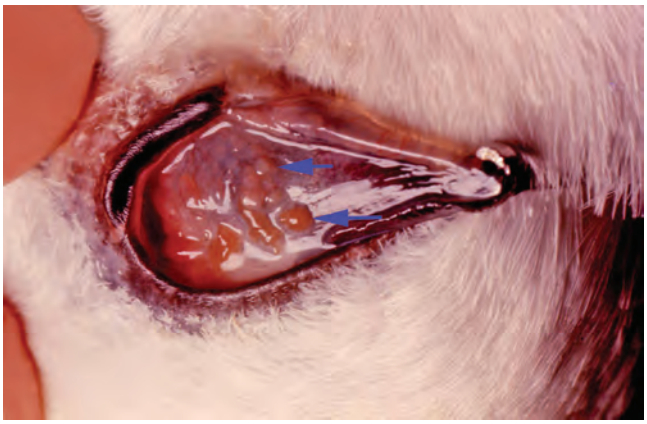

Figure 12.15 Numerous conjunctival swellings due to infection by *Philophthalmus gralli* (arrows).

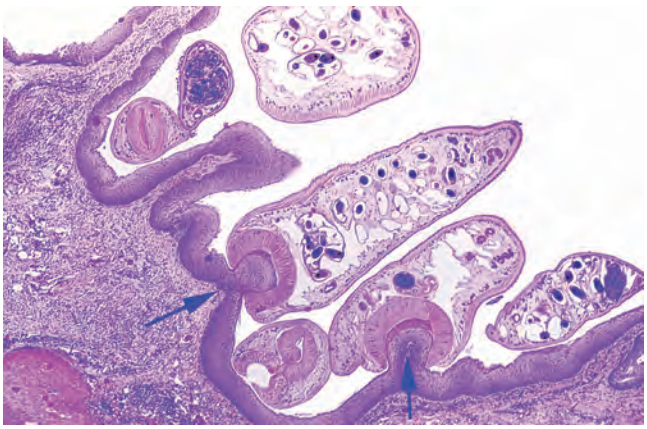

Figure 12.16 Conjunctivitis due to *Philophthalmus gralli*. There is marked proliferation and chronic inflammation. Organisms are present (arrows).

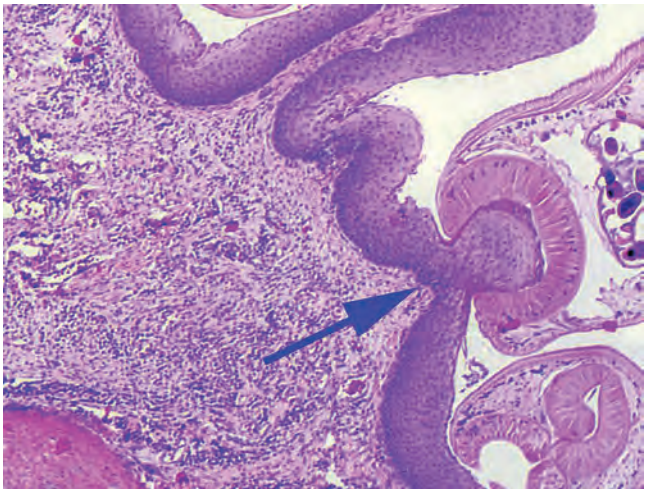

Figure 12.17 *Philophthalmus gralli* infection of the conjunctiva. Detail of attachment site of one fluke is obvious (arrow). The mucosa is proliferative and a diffuse inflammatory reaction is seen in the submucosa.

localized. The latter may present as a focal swelling due to a granulomatous reaction. Physical irritants such as smoke aerosols or chemical fumes can cause nonspecific conjunctival inflammation. Vitamin A deficiency can result in metaplasia and hyperkeratosis of conjunctival epithelium. Advanced causes of vitamin A deficiency will result in the accumulation of large semicircular plaques of sloughed squamous cells in the ventral conjunctival recesses. Amyloid deposition is sometimes seen associated with systemic amyloid deposition (Fig. 12.18).

Proliferative lesions include conjunctival papillomas (Fig. 12.19) and tumors such as squamous cell carcinoma and melanoma (Figs. 12.20 and 12.21). The papillomas are similar to those of the skin, and the possibility of a viral etiology has been considered but not proved.

Cornea

Keratitis will present grossly as corneal opacity, with possible reddening if there is vascularization. In severe cases, there may be ulceration. It can be associated with a variety of causes.

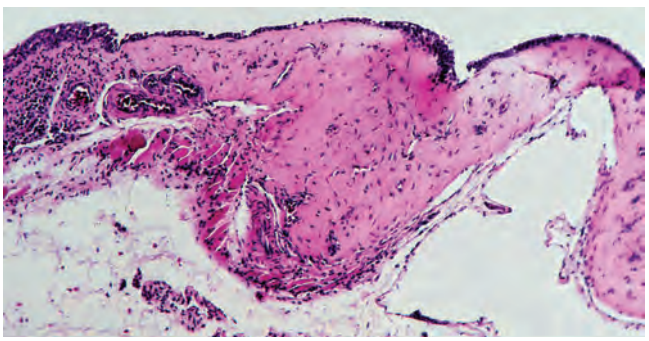

Figure 12.18 Conjunctival thickening due to diffuse amyloid deposition.

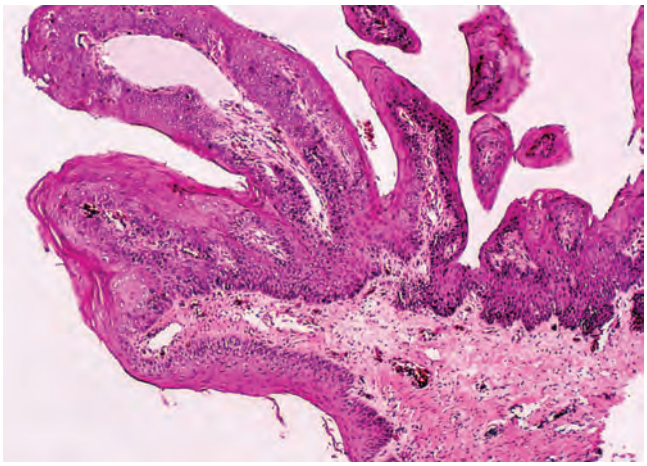

Figure 12.19 Conjunctival papilloma. The cause of these lesions has not been determined.

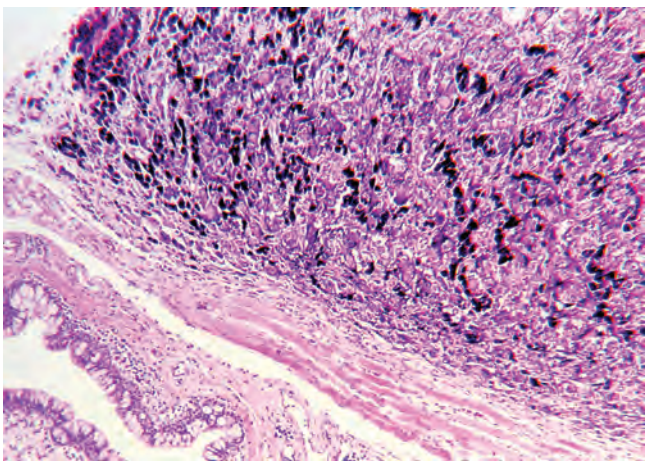

Figure 12.20 Malignant melanoma infiltrating a portion of the conjunctiva.

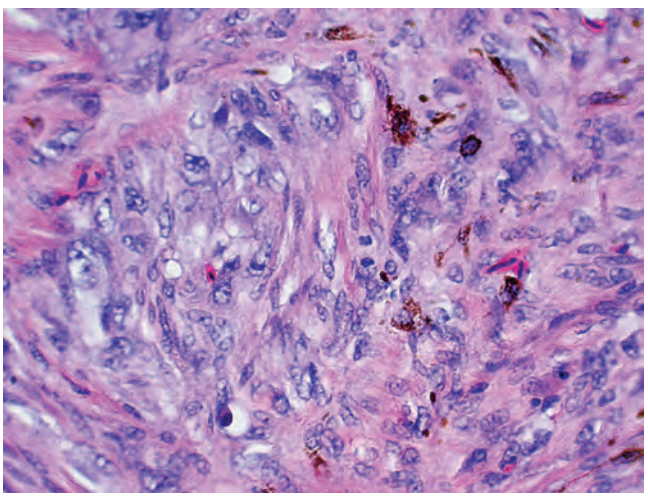

Figure 12.21 Detail of conjunctival malignant melanoma.

Figure 12.22 Chronic bacterial keratitis leading to corneal opacity.

Infectious keratitis can be due to any of the agents described as causes of conjunctivitis. In birds, bacterial infection (Figs. 12.22 and 12.23) and mycotic infection are the most common. Gross changes are similar, but there may be yellow-white or greenish, fluffy exudate in mycotic infections (Fig. 12.24).

Histologically, the lesion comprises a pleocellular infiltrate with varying proportions of heterophils, macrophages, lymphocytes, and giant cells, depending on the exact organism and duration. Finding organisms in the lesion gives specificity (Figs. 12.25 and 12.26).

Microsporidial keratitis is occasionally seen in psittacine birds. Gross changes include conjunctival reddening and corneal opacity. Histologically there is stromal infiltration by heterophils, lymphocytes, and macrophages associated with stromal necrosis. Protozoal organisms are found in the lesion (Fig. 12.27). *Microsporidia* stain best with Gram stains and trichrome stains. These birds may have a history of a chronic nonhealing conjunctivitis that is refractory to traditional antimicrobial treatment. Organisms are more common on the cornea than they are in the adjacent conjunctiva, which will also be inflamed. Conjunctival smears stained with calcofluor MR2 and viewed with ultraviolet light is the most specific way to identify

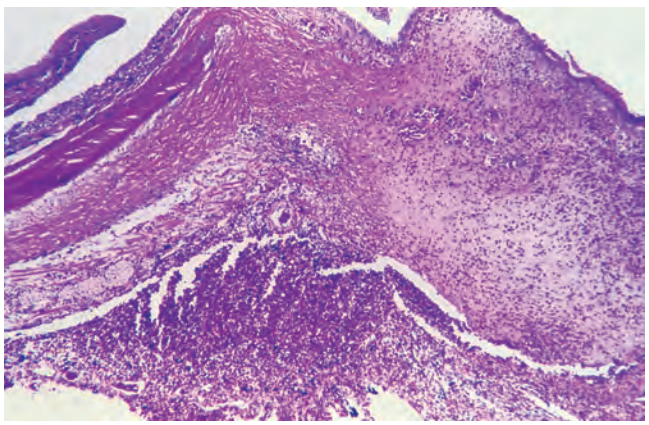

Figure 12.23 Severe necrotic keratitis due to bacterial infection.

Figure 12.24 Proliferative yellow exudate seen in mycotic conjunctivitis.

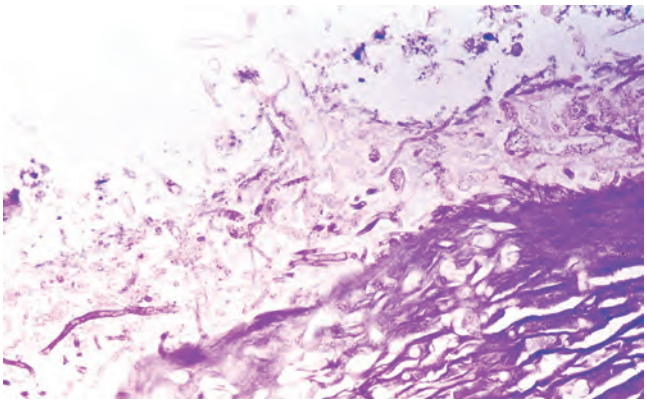

Figure 12.25 Mycelial fragments present in mycotic keratitis. The exact organism cannot be determined histologically.

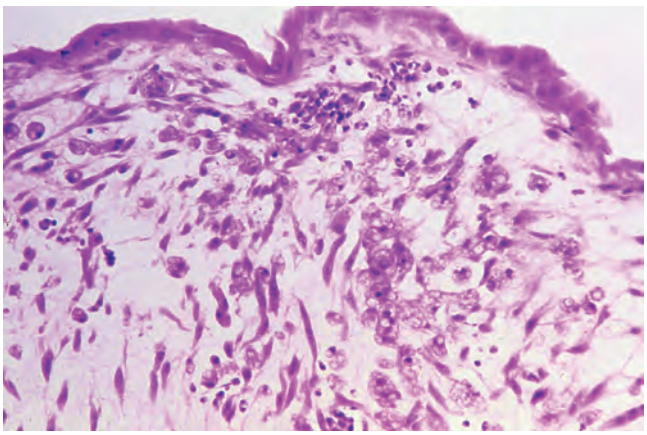

Figure 12.26 Deep mycotic keratitis. Numerous macrophages contain organisms morphologically consistent with *Histoplasma* sp.

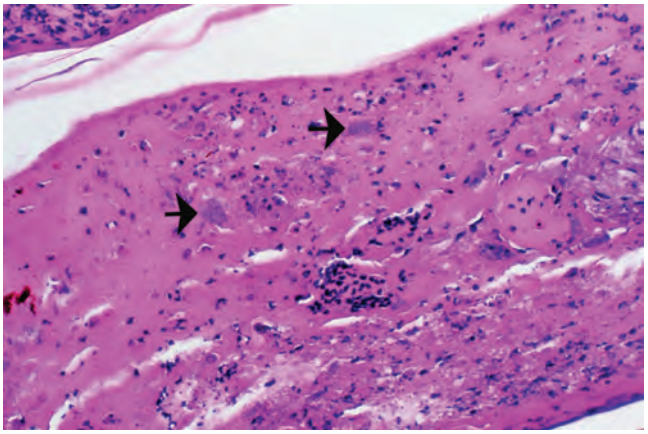

Figure 12.27 Necrosis and an infiltrate of macrophages in microsporidial keratitis. The small dark foci within many of the macrophages are organisms (arrows).

these organisms in live birds. Use of PCR assays of conjunctival swabs or biopsies may be the only way to detect microsporidia in some ocular infections.

Noninfectious keratitis is usually secondary to trauma; however, unless there is foreign material found in the lesion, the cause is usually inferred due to a lack of any infectious agent. Chronic keratitis results in corneal epithelial hyperplasia and stromal hypercellularity (Fig. 12.28).

Noninflammatory corneal lesions are infrequently seen. Stromal dystrophy would imply a primary inherited condition and is not documented in pet birds. Stromal degeneration secondary to previous inflammation is seen in a variety of pet species. Grossly there is corneal opacity, and histologically, stromal inflammation associated with lipid deposition and cholesterol cleft formation are noted (Fig. 12.29).

Lens

Lens luxation may be secondary to trauma or inflammation leading to zonule lysis. Careful gross sectioning of the eye is necessary to be sure that the lens was not displaced artifactually.

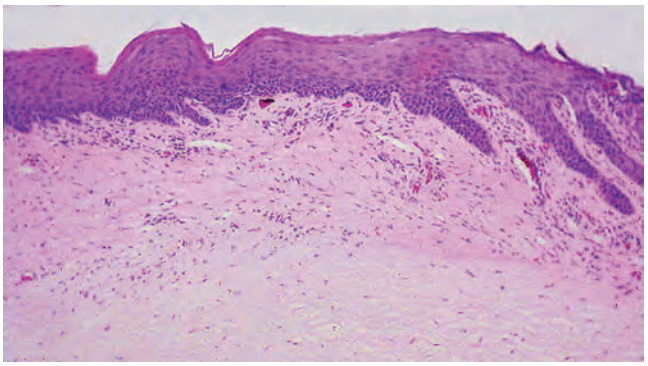

Figure 12.28 Chronic keratitis with marked epithelial hyperplasia and stromal fibroplasia.

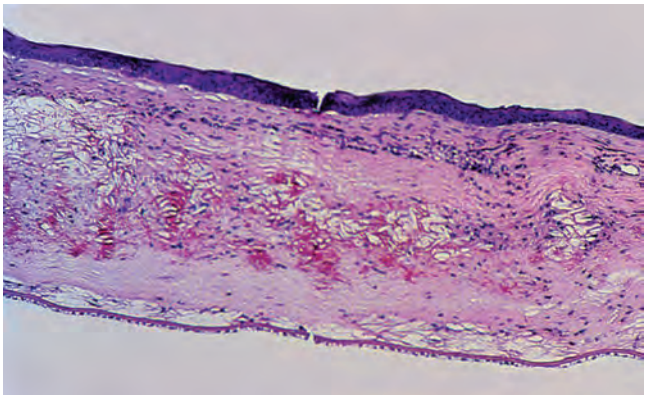

Figure 12.29 Corneal stromal degeneration with the formation of numerous cholesterol clefts.

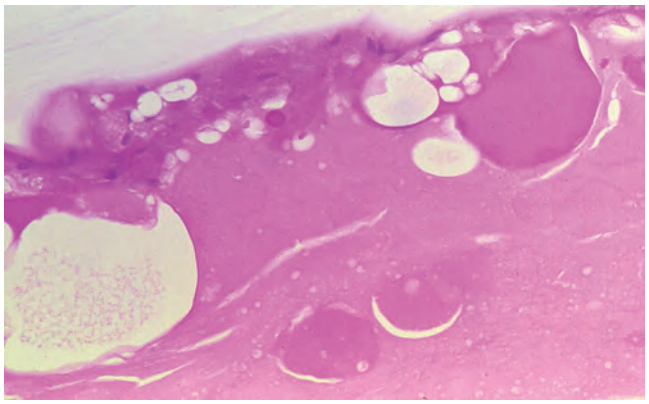

Figure 12.31 Early cataract formation. The capsule is irregular, and there is cystoid degeneration.

Cataracts may be congenital or acquired. They are hereditary in some canaries (Yorkshire and Norwich). The condition appears to be caused by an autosomal recessive gene. Acquired cataracts have been associated with nutritional deficiencies, trauma, toxins, infection, electrocution and inflammation of the eye, and aging. Many older psittacine birds will have cataracts, and falcons appear to have a higher incidence than many other birds. Cataracts are opacities of the lens secondary to altered lens metabolism usually following some injury to lens epithelium and/or capsule (epithelial basement membrane). Cataracts can be classified according to age of onset or location within the lens. Morphologically the usual structure of the capsule and lens fibers is altered.

Grossly, cataracts present as lens opacities (Fig. 12.30). Histologically, early changes may be limited to swelling of lens fibers with bladder cell formation. There may be epithelial hyperplasia and foci of capsular thinning. With progression, cystoid spaces can develop and lens protein will coagulate and fibers fragment (Figs. 12.31 and 12.32). The epithelium will become necrotic, and the capsule may rupture. Occasionally mineralized foci are noted. In some cases, the lens liquefies and lens fibers fragment (Fig. 12.33). Mature cataracts involve the entire lens. Hypermature cataracts develop when necrotic cortical material is lost, leading to a small lens with a wrinkled capsule. Fragments of lens material may be seen (Fig. 12.34).

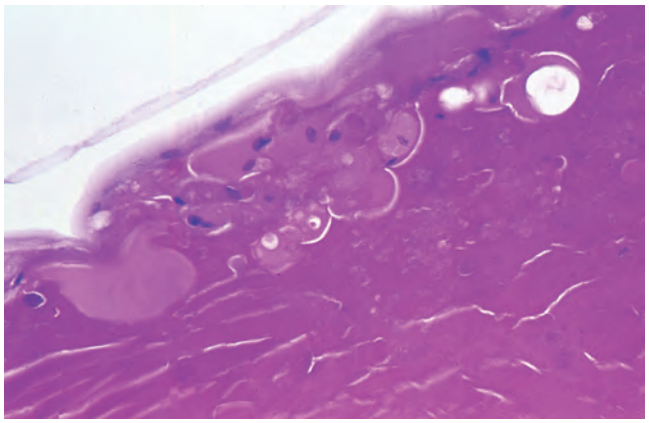

Figure 12.32 Bladder cell formation and lens fiber fragmentation in a cataract.

Figure 12.30 Cataract formation. Grossly this must be differentiated from corneal cloudiness.

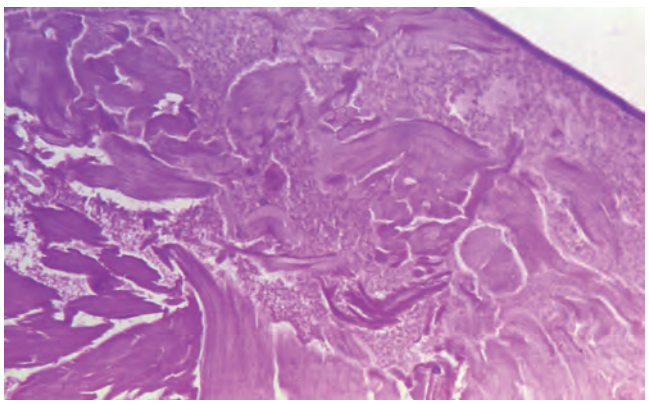

Figure 12.33 Morgagnian cataract with severe lens fragmentation and partial liquefaction.

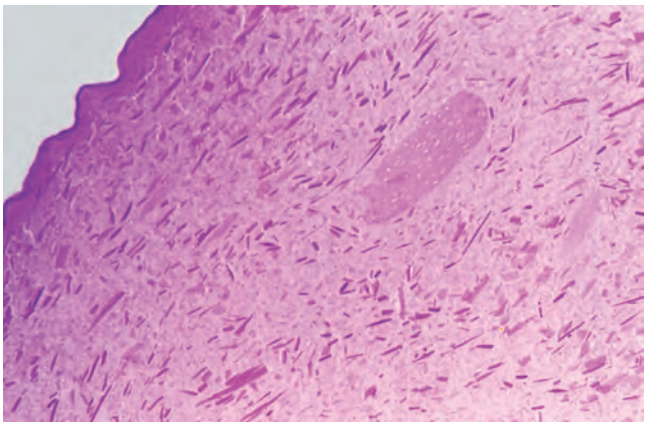

Figure 12.34 Hypermature cataract. A shrunken lens with a wrinkled capsule is noted. Lens fragments are present.

Uveal tract (iris, ciliary body, and choroid)

In some avian species there may be color changes as the bird ages. Color changes can be abnormal, however, and may be related to problems in pteridine (the most common pigment that affects iris color) synthesis. Irregularities in the shape of the iris may be due to colobamas. These have been reported in some types of chicken. Uveitis may be anterior, posterior, or diffuse, involving the entire uveal tract. Suppurative uveitis may be secondary to penetrating trauma, extension from the corneal or sclera, or the result of localization of systemic infections. Grossly there may be fibrin clots in the anterior chamber, hemorrhage, hypopyon, and hyphema.

Histologic lesions depend on the exact cause and location but will include fibrin deposition, necrosis, and a reaction that is primarily heterophilic initially (Fig. 12.35). Eventually there may be typical granuloma formation. Nonsuppurative uveitis due to an immune-mediated reaction may occur in birds but is rarely seen.

Synechia is adherence of the iris to either the cornea (anterior) or the lens (posterior). It is a sequela to an inflammatory lesion in the anterior chamber. Histologically there will often be evidence of the underlying cause.

Retina

Retinitis may be caused by a variety of infectious agents, be secondary to trauma, or be associated with diseases of the central nervous system. Gross lesions are usually not seen unless severe. West Nile virus infection of raptors may cause intraocular hemorrhage in some affected birds. Several viral infections can lead to a nonsuppurative inflammatory infiltrate, but this is infrequent, possibly due to the avascularity of the retina. Histologically West Nile virus can cause necrosis of the retinal pigment epithelium and retina, lymphoplasmacytic inflammation, and eventually atrophy. There may also be pectinitis. Antigenic material can be seen in the retina. Bacterial infections that involve the retina result in inflammation that is primarily heterophilic early in the disease, with chronicity leading to abscess formation and granulomas. Specificity is associated with demonstration of specific etiologic agents (Fig. 12.36). *Toxoplasma gondii* infection may involve the eye in birds. Chorioretinitis characterized by numerous tachyzoite-containing macrophages and tachyzoite accumulation in the nerve fiber layer have been reported.

Avian bornavirus occasionally causes blindness in infected birds. It infects multiple cells within the retina but does not induce inflammation. How it causes blindness is not known, but its impact may be on the central nervous system. The vitreous of infected birds often contains a high titer of virus particles.

Retinal degeneration is potentially due to a variety of causes (toxins, nutrition, and hypoxia), but no specific conditions are reported in birds. In many cases, areas of degeneration are found incidentally on histologic examination of grossly normal eyes. The severity of the lesion may vary, but outer retinal segments seem to be more commonly affected (Figs. 12.37, 12.38, and 12.39).

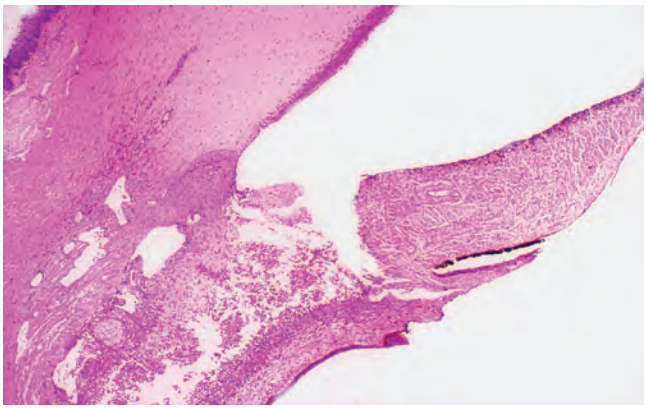

Figure 12.35 Necrosuppurative iridocyclitis involving the base of the iris. This lesion is seen with systemic localization of infection or traumatic globe puncture and secondary infection.

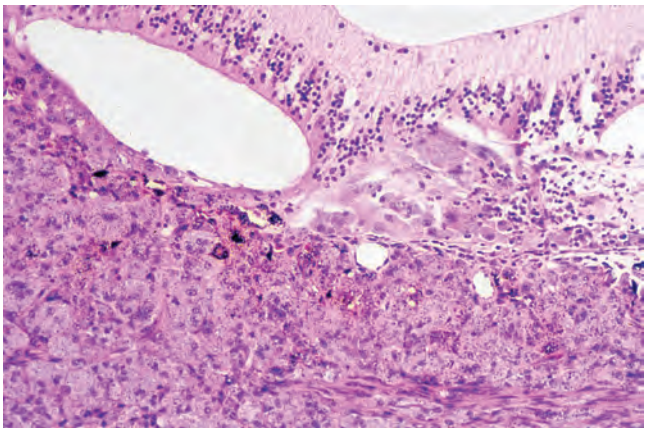

Figure 12.36 Chorioretinitis due to *Mycobacterium* sp. infection. Numerous large macrophages are infiltrating the tissues, leading to a partial retinal detachment.

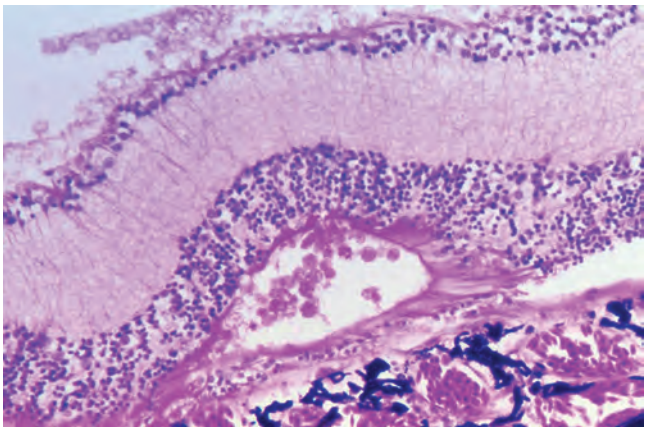

Figure 12.37 Focal area of retinal degeneration with loss of photoreceptor outer segments. The cells in the area of detachment may be reactive retinal pigment epithelial cells.

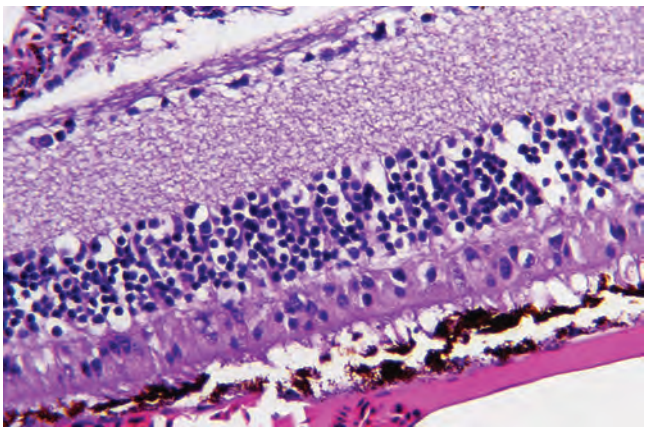

Figure 12.38 Retinal degeneration characterized by loss of photoreceptors and detachment.

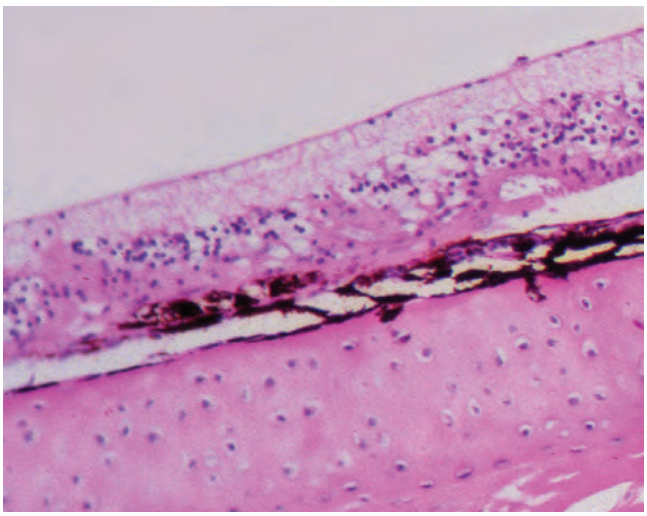

Figure 12.39 Severe retinal degeneration. The inner plexiform layer is present, but only scattered unidentified nuclei are seen in the remaining portion of the retina.

Congenital retinal dysplasia is sporadically reported, and the cause is usually not known.

Retinal detachment can also be secondary to trauma or inflammation of the retina and/or choroid. Depending on the duration of the detachment, there will be variable degeneration. The pigment epithelium is usually reactive, with hypertrophy and individualization of cells. Retinal tears, hemorrhage, and detachment are very common lesions in birds of prey that are struck by vehicles. Tearing or rupture of the pecten is also very common when trauma occurs to the eye.

Optic nerve

Lesions of the optic nerve are similar to those seen in the brain and are due to the same causes. Optic neuritis can be seen in cases of proventricular dilatation disease, and birds with this disease may have a history of blindness. Similar microscopic lesions occur in West Nile virus infection. A lymphoplasmacytic infiltrate characterizes this lesion. Any cause of nerve fiber degeneration in the brain can also cause degeneration of the optic nerve. Pituitary tumors may cause pressure and secondary optic nerve degeneration at the chiasm. Optic nerve demyelination of unknown cause is seen sporadically (Fig. 12.40).

Eye as a whole

Panophthalmitis may result from trauma or a variety of infectious agents as listed for the various segments of the eye. It represents spread of the infection and/or inflammatory process throughout the eye. A sequela of chronic panophthalmitis is phthisis bulbi (Fig. 12.41). Affected eyes are shrunken, and histologically there is evidence of chronic inflammation, fibroplasia, and loss of normal components of the globe (Fig. 12.42).

Glaucoma

Glaucoma is occasionally reported in birds. It is usually secondary to trauma, but primary glaucoma is infrequently

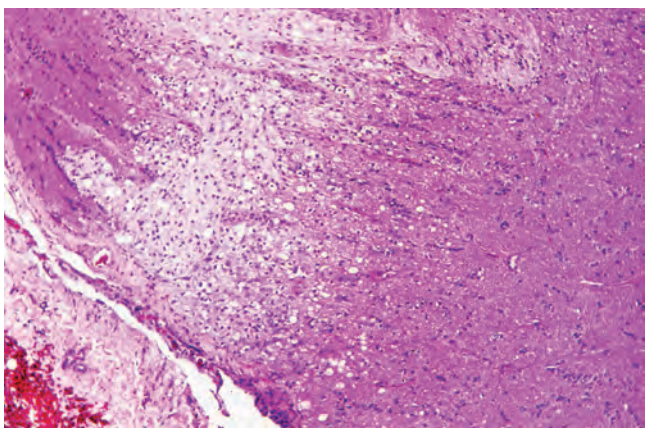

Figure 12.40 Focal demyelination of unknown cause affecting the optic nerve.

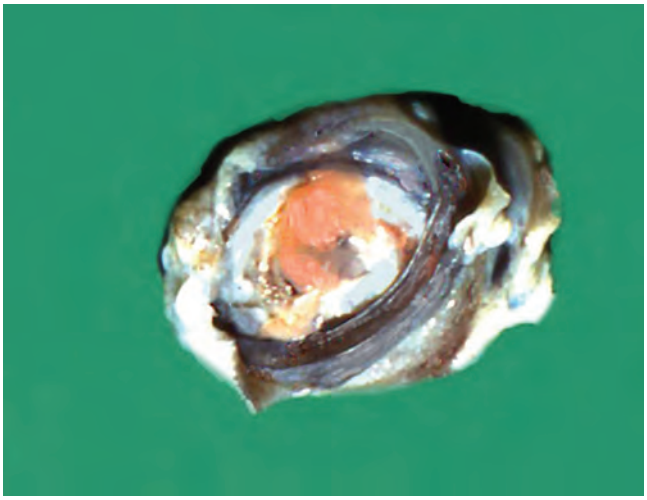

Figure 12.41 Phthisis bulbi. The globe is collapsed and normal structures are not recognized.

suspected. Grossly the affected eye is enlarged. The lens may be luxated. Grossly and histologically there may be changes indicative of the underlying cause.

Ocular neoplastic disease

Tumors of skin and subcutis affecting the eyelids have been previously mentioned. Squamous papilloma, squamous cell carcinoma, malignant melanoma, and basal cell tumors are seen.

Adnexal tumors include adenomas and adenocarcinomas of the lacrimal gland and were previously described. Orbital neoplasia seen in birds includes chondroma, infiltrative carcinoma (Fig. 12.43), lymphosarcoma (Figs. 12.44 and 12.45), and teratoma (Fig. 12.46). The gross appearance is of an orbital mass that displaces the eye. Histologically they are similar to the tumor type in any other location.

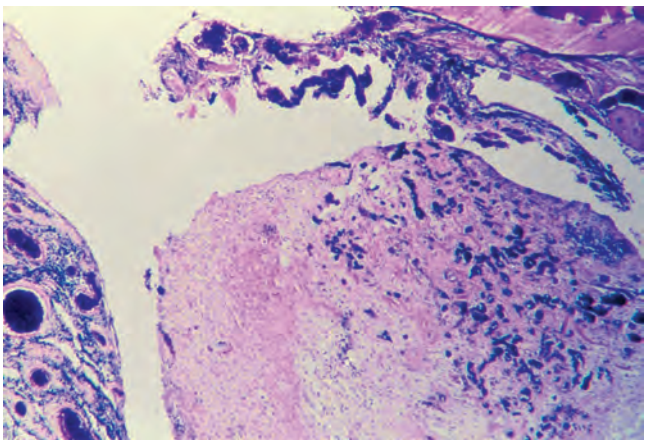

Figure 12.42 Unrecognizable mass of inflamed fibrous tissue and neovascularization consistent with phthisis bulbi.

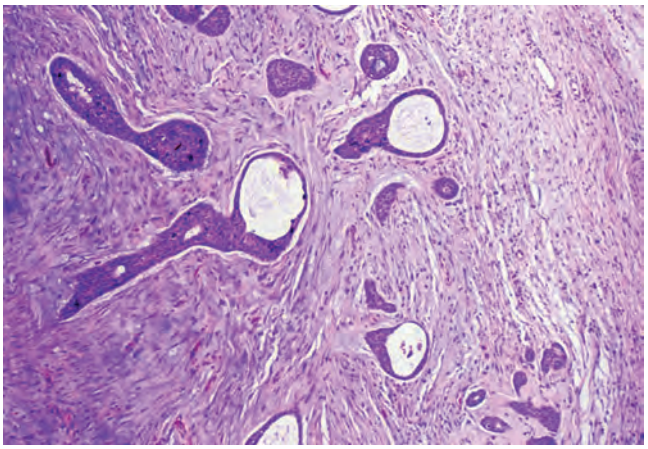

Figure 12.43 Infiltrative orbital squamous cell carcinoma. The centers of many of the nests and trabeculae are necrotic.

Figure 12.44 Lymphosarcoma obliterating the eye and orbit.

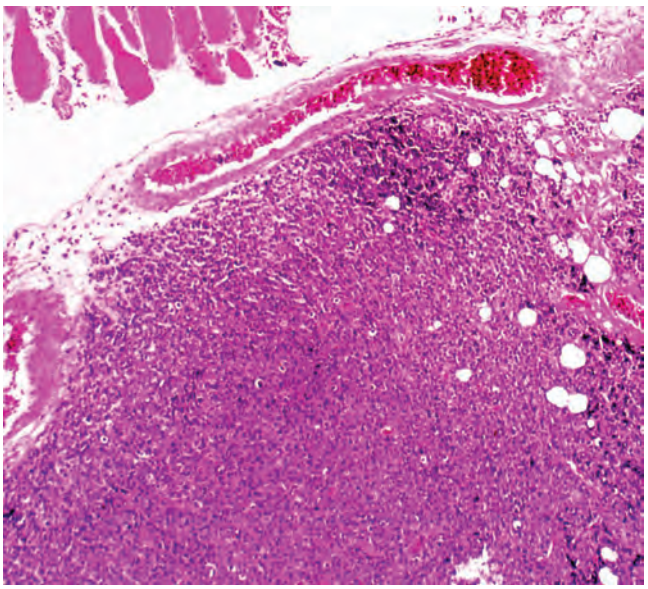

Figure 12.45 Typical appearance of lymphosarcoma.

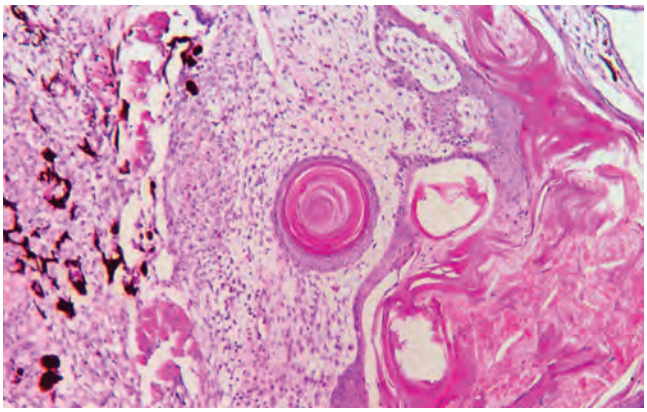

Figure 12.46 Orbital teratoma with several tissue types present.

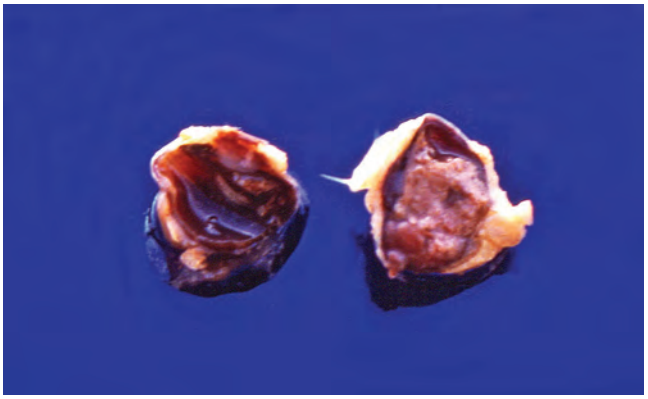

Figure 12.48 Medulloepithelioma filling the globe.

Intraocular malignant melanoma can arise in the uveal tract. These tumors may or may not be grossly pigmented and histologically comprise poorly differentiated cells that form an infiltrative sheet (Fig. 12.47).

Primary intraocular tumors are rarely reported in birds. Medulloepithelioma, an embryonic tumor of the central nervous system and retina, is reported in cockatiels. This tumor usually presents as an undiagnosed gray-white and somewhat friable intraocular mass (Fig. 12.48). The tumor extends through the orbit and impinges on the brain. Histologically the tumor comprises tubular structures lined by tall neuroepithelial cells. Structures resembling rosettes are also seen. Less well-differentiated areas comprise nests and sheets of neoplastic cells (Figs. 12.49 and 12.50). Marek's disease can involve the eye in chickens. The iris is often infiltrated, leading to discoloration and an irregular pupillary opening (Fig. 12.51). Microscopically in Marek's disease there is a lymphoreticular cell infiltration.

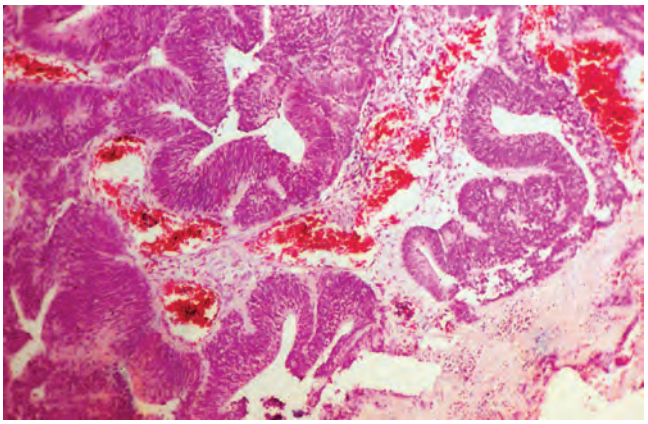

Figure 12.49 Medulloepithelioma. Bands of poorly differentiated columnar epithelium resemble embryonic retina.

Orbital disease

Inflammation or neoplasia in the orbit can impact the eye even if the fibrous tunic is not penetrated. Trauma and localization of systemic disease can lead to retrobulbar abscess formation (Fig. 12.52).

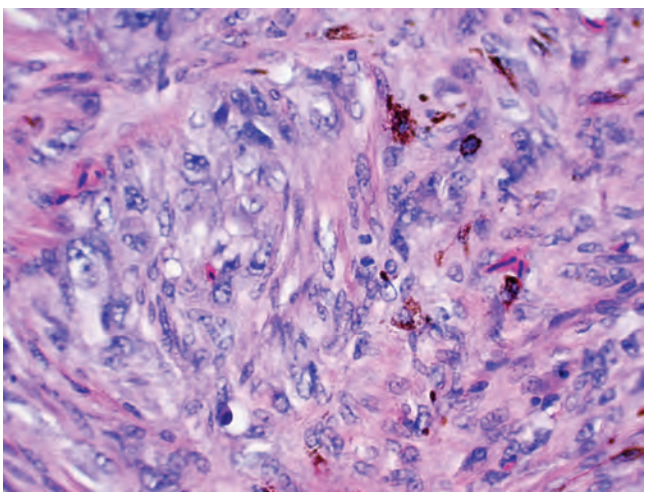

Figure 12.47 Malignant melanoma diffusely infiltrating the choroid.

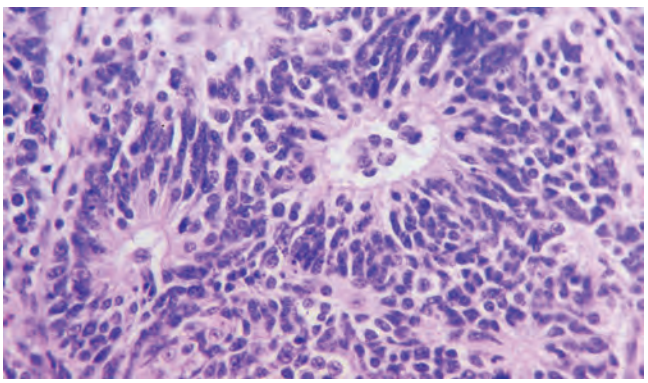

Figure 12.50 A portion of medulloepithelioma with rosette formation.

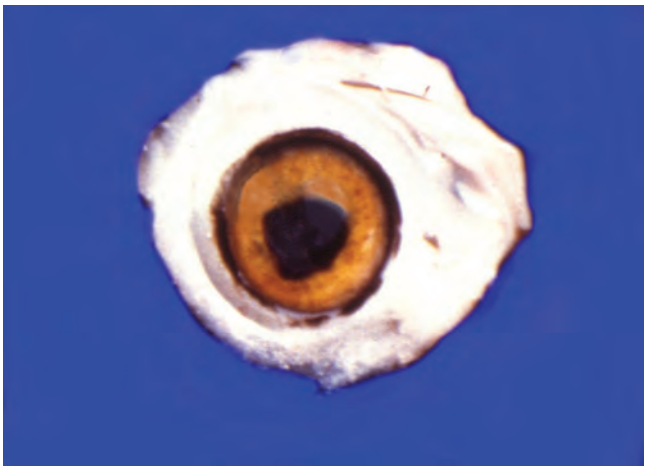

Figure 12.51 Irregular, discolored iris in a chicken with Marek's disease.

Ear

Normal structure

The avian external ear has a short canal extending vertically and caudally from the external acoustic meatus to the tympanic membrane. The external meatus is small, usually circular, and opens on the side of the head. In most birds, it is usually covered by specialized contour feathers called ear coverts that reduce drag caused by turbulence and diminish the masking of sound by noise from turbulence in the external ear. Macaws and eclectus parrots have a membrane over the opening that normally disappears in about 3 weeks. Many owl species have a skin flap (operculum) on the rostral margin of the external ear.

The external surface of the tympanic membrane is covered by epidermis continuous with the external auditory meatus. The internal surface is covered by epithelium continuous with the tympanic cavity and pharyngotympanic tube. The tympanic membrane projects outward in birds rather than inward as in mammals.

The middle ear is the air-filled cavity between the tympanic membrane and the inner ear that transmits acoustically induced vibrations of the tympanic membrane to the vestibular window. It contains a single ossicle called the columella, which is the homolog of the mammalian stapes. The columella extends across the tympanic cavity to form a direct connection between the tympanic membrane and the perilymph of the inner ear. The paratympanic organ, which is within the dorsomedial wall of the tympanic cavity, is not present in owls or psittacine birds. It contains tall cells in contact with nerves from the geniculate ganglion, but its exact sensory function has not been determined.

The inner ear has two major portions and two functions. The bony labyrinth is formed by compact bone and comprises the vestibule, semicircular canals, and cochlea. It encloses the membranous labyrinth. Perilymph is present between the bony and membranous labyrinths, and endolymph is present within the cavities of the membranous labyrinth. The membranous labyrinth contains the utricle, saccule, and semicircular ducts concerned with position and movement of the head in space, and the cochlear duct involved in hearing.

Disease

External ear

Occasionally the membrane covering the external ear in macaws and eclectus parrots is retained and must be opened surgically.

Otitis externa is uncommon in birds. Potential causes include bacteria, fungi, and arthropod parasites. There may be problems associated with extension of skin disease. The gross appearance may be altered by self-trauma. Hemorrhage, necrosis, and exudate are seen (Fig. 12.53). Chickens with fowl cholera may have diffuse edema and swelling of the face including the external ear area. A definitive etiologic diagnosis of external otitis depends on finding an organism on culture or histologic examination.

Carcinoma of the glands of the external ear canal is occasionally seen. It may present as a chronic condition with thickening

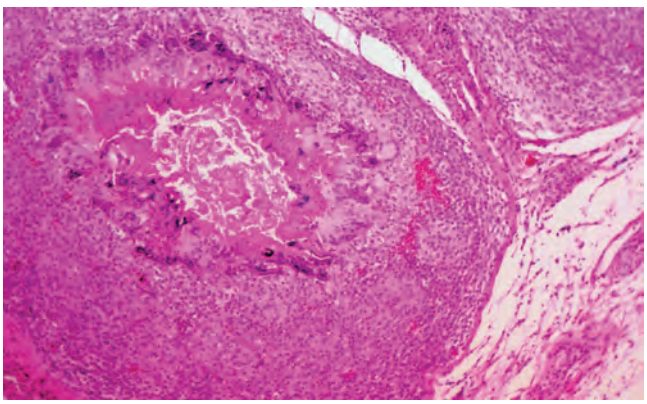

Figure 12.52 Retrobulbar abscess with multifocal areas of necrosis surrounded by giant cells and numerous macrophages.

Figure 12.53 Otitis externa. There is loss and discoloration of feathers and exudate on the skin surrounding the ear opening.

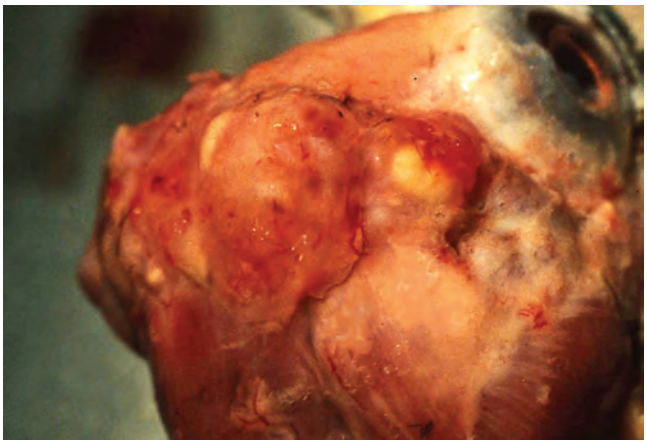

Figure 12.54 Carcinoma of the glands of the external ear canal. An irregular lobular mass with destruction of surrounding tissue is seen.

of the ear canal, as well as a localized mass lesion (Fig. 12.54). Microscopically these tumors comprise moderately undifferentiated to poorly differentiated cells that form infiltrative nests and cords. There may be moderate amounts of fibrous stroma (Fig. 12.55). These tumors must be differentiated from carcinoma of nasal or sinus origin.

Middle ear

Otitis media is rarely reported. A variety of infections are possible, and it may be secondary to oral/pharyngeal disease with extension via the pharyngotympanic tube.

Inner ear

Congenital lesions have been reported in Belgian Waterslager canaries. There are often multiple abnormalities associated with dysgenesis of the pars inferior of the otocyst. These include stunting of tall hair cells of the organ of Corti, loss of short hair cells, and narrowing of the tectorial membrane.

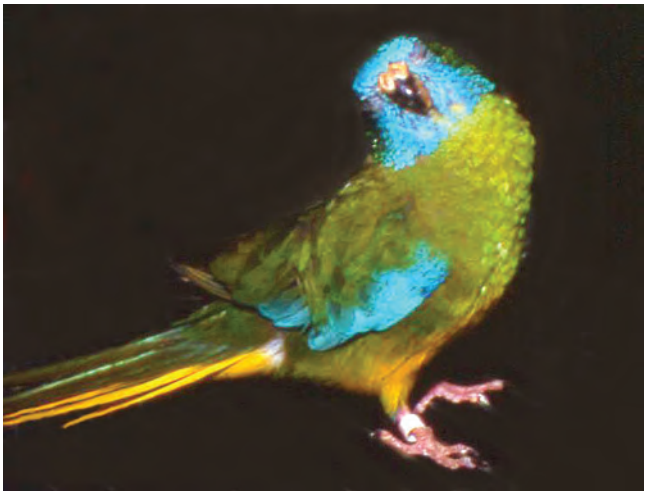

Figure 12.56 *Neophema* sp. with a paramyxovirus infection of the inner ear leading to a twisted neck and "star gazing".

Otitis interna can be due to paramyxovirus infection, particularly in Australian grass parakeets (*Neophyma* sp.). Lesions can lead to "twisted neck," "stargazing," and similar syndromes (Fig. 12.56). Inner ear disease can be associated with brain lesions but also may occur in the absence of central nervous system involvement. Gross changes are usually not apparent. Histologically there is nonsuppurative inflammation, loss of normal structures, and intranuclear inclusion bodies within hair cells of the crista basilaris in some cases (Figs. 12.57, 12.58, and 12.59).

Psittacid herpesvirus-3 causes hyperplasia of the epithelial lining of the inner ear and syncytial cell formation. Intranuclear inclusions may be common. A mild inflammatory response to infection may also occur.

Poxvirus can also affect the inner ear. There may be ballooning degeneration of epithelial cells and intracytoplasmic inclusion body formation (Fig. 12.60).

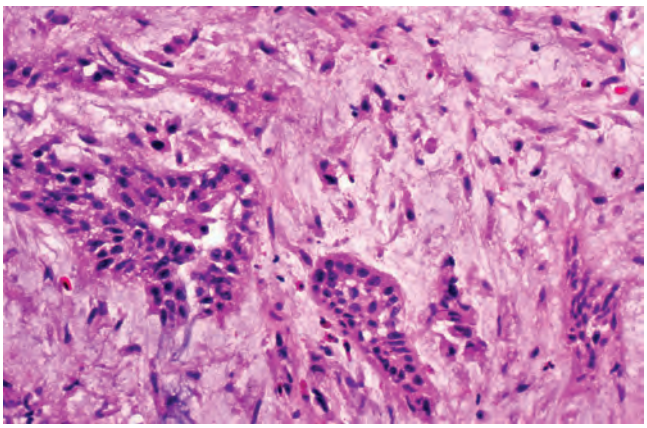

Figure 12.55 Histologic appearance of infiltrative ear canal carcinoma. Abundant stroma is seen.

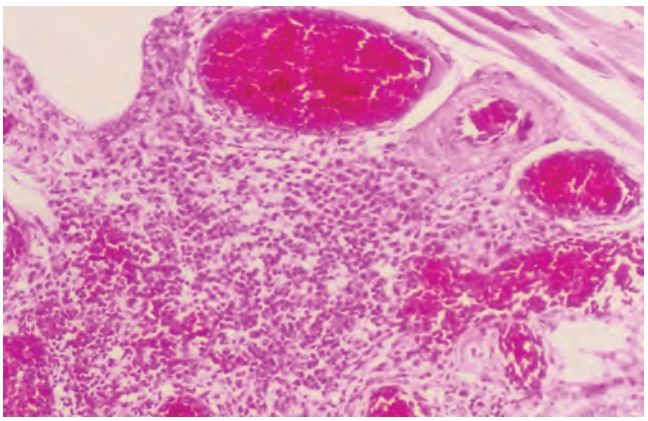

Figure 12.57 Nonsuppurative otitis interna due to paramyxovirus infection. A diffuse cellular infiltrate is seen.

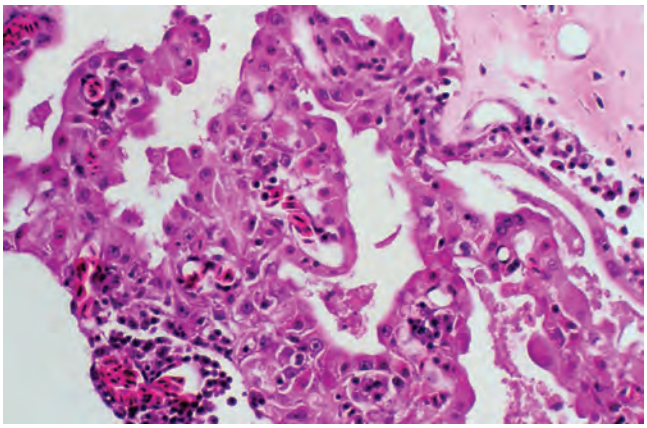

Figure 12.58 Swelling, necrosis, and distortion of hair cells of the crista basilaris due to paramyxovirus infection.

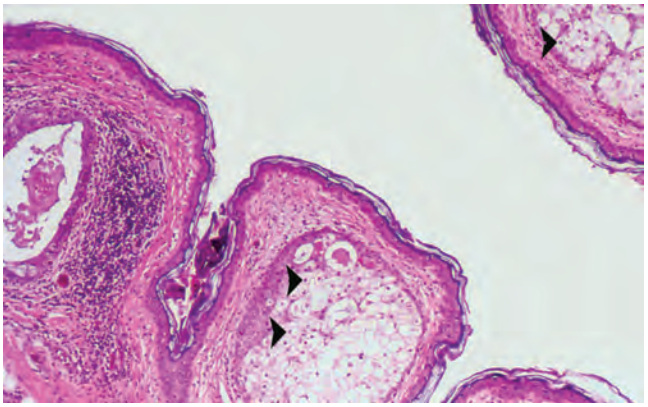

Figure 12.60 Poxvirus infection of the inner ear. Sensory epithelial cells are swollen with ballooning degeneration. Cytoplasmic inclusion bodies are small (arrowheads) and not seen in all affected cells.

Ototoxicity can be a problem in birds treated with aminoglycoside antibiotics. High doses lead to damage to the basilar papilla. At the cellular level, there are changes leading to loss of organelles and cell necrosis. There is a linear increase in the levels of intracellular calcium and reactive oxygen species associated with the antibiotic dose. After loss of hair cells, macrophages and microglia-like cells infiltrate the sensory epithelium. There may be associated sensory epithelial cell proliferation.

Acoustic trauma can lead to transitory or permanent loss of sensory epithelium. The amount of damage is related to the level of, and duration of, the sound.

Olfactory/taste organs

Normal structure

The avian olfactory organ arises as an area of thickened ectoderm on the ventrolateral surfaces of the head. The epithelial lining of the developing nasal passages becomes the olfactory epithelium (bipolar nerve cells). Each cell tapers to an olfactory nerve fiber, which joins others and grows toward the olfactory bulb of the brain. Axons of the receptor cells form the olfactory nerve—cranial nerve I—and terminate in the olfactory bulb. The olfactory receptors are in the nasal mucosa of the caudal nasal concha.

Taste receptors vary by species. Many species have no interest in sweet substances, with nectar feeders and many parrots as exceptions. Most birds will consume salt and have a range of tolerance for acidity and alkalinity. Birds vary in regard to tolerance to bitter substances.

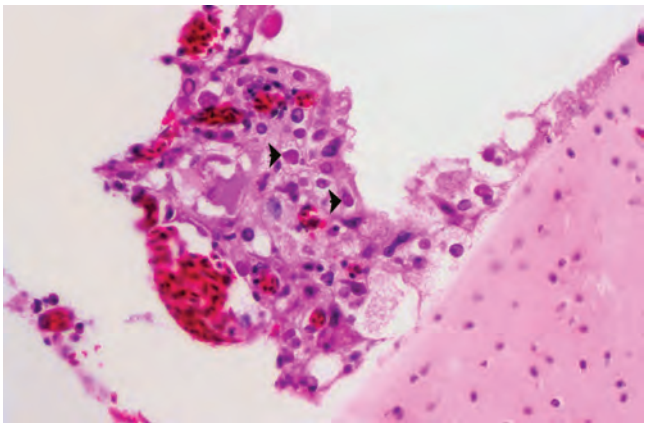

Figure 12.59 Intracytoplasmic inclusion bodies of paramyxovirus in damaged hair cells of the inner ear (arrowheads).

Disease

No specific avian disease syndromes are known that affect smell or taste, but there is no way to measure subjective changes. Lesions of the cranial nerves or brain could affect the senses of smell and taste. Infections, nerve degeneration, and neoplasia are all possible causes. Lesions of nasal or oral cavities may involve olfactory and taste organs.

Somatosensory receptors

Normal structure

These organs give information about the physical condition of the internal and external environment. They respond to mechanical, thermal, or chemical stimuli. Afferent nerves transmit impulses to the central nervous system. Peripheral structures include Herbst corpuscles that are probably mechanoreceptors. They occur in the integument, tendons, muscles, and joint capsules. They have a central area and perineural capsule and are variable in size and shape. Other structures are Grandry corpuscles that occur in ducks and are velocity sensitive, Ruffini nerve

endings that detect amplitude components in mechanical stimuli, muscle spindles, and tendon organs, and mechanoreceptors such as the bill-tip organ in parrots and other species, particularly those that use the beak for prehension. This organ comprises a dermal core and cornified epidermal covering.

Disease

Nothing specific is known. Any trauma, infectious disease, or tumor that damages one of the aforementioned structures could be the cause of a decrement in function. Inflammation of dermal receptors could cause sensation and lead to feather picking or self-trauma. The gross and histologic appearance depends on the particular disease process involved.

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13 Peritoneum and Mesenteries

Structure

The avian coelomic cavities are more complex than the peritoneal cavities of mammals. The best anatomic descriptions have been of the domestic fowl. In poultry, there are 16 cavities, eight of which are air sacs and eight pleuroperitoneal cavities. The caudal coelom is divided into five chambers or cavities: the intestinal, left and right ventral hepatic, and left and right dorsal hepatic peritoneal cavities. These chambers are separated by double-layered septa consisting of membranes formed by a thin band of fibrovascular stroma supporting a thin mesothelium with resident macrophages. Normally only a small amount of lubricating fluid is present. Passive diffusion of water and solutes of low molecular weight can occur between the peritoneal cavities and the subperitoneal vasculature. The remaining three cavities are present in mammals as well as in avian species. They are the pericardium and left and right pleural cavities.

The intestinal peritoneal cavity, which is midline and elongated, encloses the gonads and intestines that are suspended by the mesenteries. The abdominal air sacs also penetrate into this cavity. The cavity is formed by the left and right post-hepatic septa. The liver lobes protrude into the left and right ventral hepatic cavities. These are blind cavities along the lateroventral body wall. Nothing is suspended in these cavities. The left and right dorsal hepatic peritoneal cavities are smaller cavities in which project the craniodorsal left and right liver lobes. All these cavities are blind with the exception of the left dorsal hepatic peritoneal cavity that connects with the intestinal peritoneal cavity. The liver is essentially isolated from the rest of the viscera by the post-hepatic septum.

Because of the arrangement of the peritoneal partitions, disease conditions may be confined to specific cavities. Inflammation or neoplasms of the reproductive or intestinal tracts tend to remain confined to the intestinal peritoneal cavity. Acute pulmonary distress can occur if fluid accumulating within the intestinal peritoneal cavity gains access to the abdominal air sacs that penetrate into this cavity. Any mass effect that expands the intestinal peritoneal cavity can also result in increased respiratory effort that is clinically described as a "tail bob." Ascitic fluid may accumulate primarily in the ventral hepatic peritoneal cavities secondary to chronic liver disease. The inflammation and contents from ruptures or perforations of the proventriculus or ventriculus may remain confined to the left ventral hepatic peritoneal cavity.

The pericardial cavity is similar to that of mammals although the parietal pericardium is continuous with the peritoneal partitions of the coelom. In mammals, a diaphragm separates these cavities.

The pleural cavity has areas of fibrous strands connecting the parietal pleura to the visceral pleura, obliterating the potential space. In the fowl, there is an extensive region that has few delicate strands connecting the two pleura along the dorsolateral aspect of the lung. The lung can collapse inward if the pleural cavity is penetrated along the dorsolateral border.

Effusions

Effusions can accumulate within any of the cavities. Chronic hepatic disease can result in the formation of a transudate or modified transudate within the perihepatic cavities. Sustained portal hypertension secondary to hepatic fibrosis is suspected to be a common mechanism in pet birds. Hypoproteinemia due to reduced albumin synthesis may also contribute; however, severe hypoproteinemia alone rarely results in ascites, as most birds generally die before the fluid develops. The prominent accumulation of a modified transudate ascitic fluid in poultry is believed to be due to portal hypertension from right ventricular failure or right ventricular failure secondary to pulmonary hypertension.

Effusions into the peritoneal cavity are generally the result of inflammatory or malignant diseases. Exudative effusions are more cellular, with a specific gravity greater than 1.020 and total protein greater than 3.0 g/dl. Malignant effusions are not uncommonly associated with hemorrhage or evidence of hemorrhage (histiocytic erythrophagocytosis or cytoplasmic iron-pigment accumulation). Occasionally neoplastic cells may exfoliate into the fluid. Grossly effusions can vary from clear to cloudy and viscid, depending on the amount of the cellular and protein components.

A variety of inflammatory and toxic heart diseases can result in pericardial fluid accumulation. Hemopericardium has been associated with cardiac rupture due to myocardial infarction and

Pathology of Pet and Aviary Birds, Second Edition. Robert E. Schmidt, Drury R. Reavill and David N. Phalen.

dissecting aortic aneurysms, some associated with mycobacterial aoritis.

Inflammatory disease

Many of the inflammatory processes involving the pleural/peritoneum will generally result in the production of a protein-rich exudate with fibrin, desquamated mesothelial cells, and inflammatory cells. This is in contrast with air-sac inflammation that typically forms a dry purulent exudate.

Infectious disease

Viral disease

Avian viral serositis is an uncommon viral infection of neonatal and juvenile psittacines in which the causative agent is eastern equine encephalomyelitis (EEE) virus. In our experience this disease has been rarely diagnosed since it was first reported over 20 years ago. EEE virus is an alphavirus in the Togaviridae family that uses a mosquito vector. This infection results in a fibrinous epicarditis and the development of abundant coelomic effusion. The ascitic fluid is typically pale yellow with the specific gravity greater than 1.017 and a low cellularity (Fig. 13.1). The serositis involves all serosal surfaces and is characterized by a protein-rich exudate with proliferative and desquamated mesothelial cells, fibrin, and inflammatory cells (Fig. 13.2). Other common gross lesions include hepatomegaly and pulmonary edema/congestion.

The histologic lesions of avian viral serositis are similar to psittacine proventricular dilatation disease with perivascular lymphoplasmacytic accumulations and lymphocytic plasmacytic infiltrates in myenteric ganglia and nerves of crop, proventriculus, ventriculus, and duodenum. Lymphoplasmacytic infiltrates are also seen in the pericardial ganglia, cardiac conduction fibers, and as perivascular foci in brain and spinal cord. Avian viral serositis infection also leads to bursal lymphoid necrosis, hepatocellular necrosis, a heterophilic splenitis, and the prominent serositis.

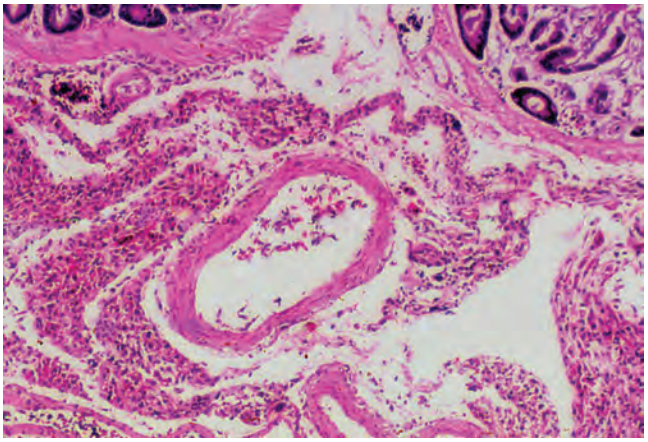

Figure 13.2 Serositis with proliferation of mesothelial cells and a mononuclear cell infiltrate.

Polyomavirus infections in both budgerigars and large psittacines can be associated with the development of hydropericardium and ascites. Viral damage to the vascular endothelium as well as hypoproteinemia associated with liver damage may lead to serositis, subcutaneous edema, and widespread ecchymotic and petechial hemorrhages (Fig. 13.3). The serositis and pericardial effusion are of low cellularity. A heterophilic serositis can suggest a secondary bacterial or fungal infection. The most consistent lesions of polyomavirus include hepatic necrosis, membranous glomerulopathy, variable karyomegaly of the liver and kidney, and large clear to basophilic intranuclear inclusion bodies of the splenic periarteriolar sheaths. Anasarca, including perihepatic and peritoneal effusions, is documented in macaw chicks that had survived the acute phase of a polyomavirus infection. These birds had low total proteins either secondary to renal protein loss or liver damage or both.

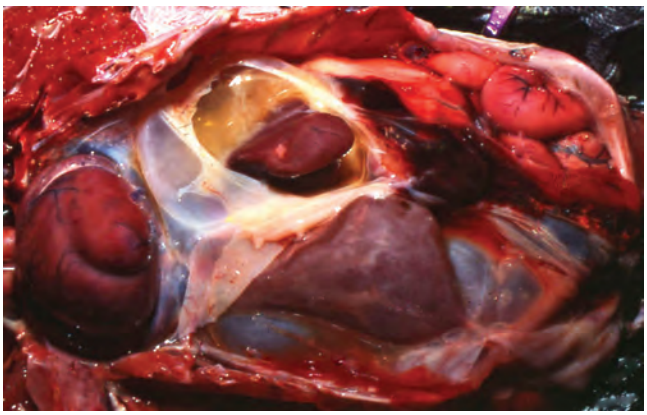

Figure 13.1 Peritoneal fluid and opaque serosal foci of a bird with probable avian serositis virus infection.

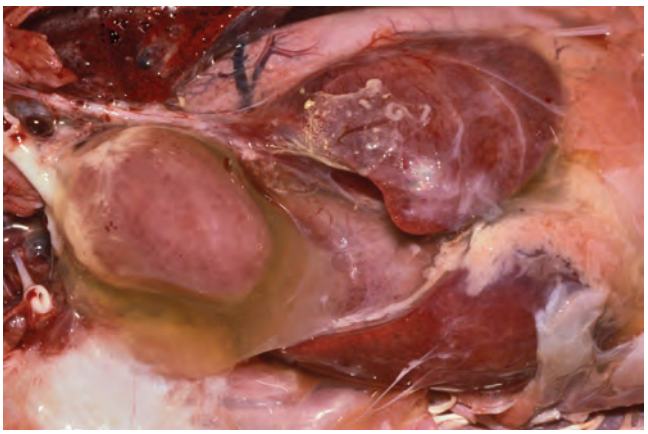

Figure 13.3 Severe serositis and pericardial effusion associated with polyomavirus infection.

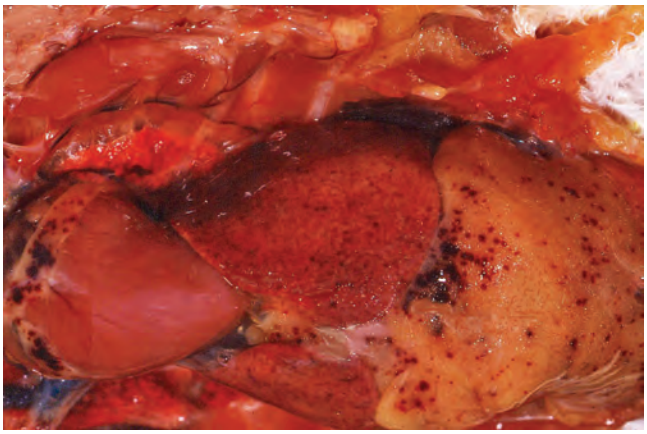

Figure 13.4 Mesenteric and serosal petechiae and ecchymoses due to herpesvirus (Pacheco's disease) infection.

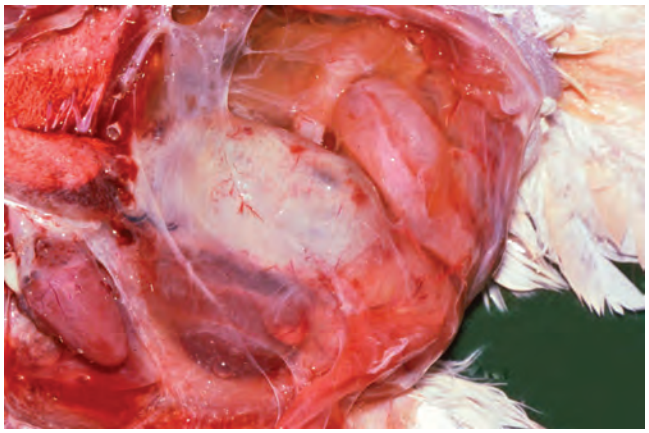

Figure 13.5 Bacterial peritonitis. The serosal surfaces are thickened, and there is fibrin and gelatinous fluid accumulation.

Psittacid herpesvirus-1 (Pacheco's disease virus) will produce multifocal serosal and mesenteric petechiation (Fig. 13.4). The hemorrhages may be secondary to the severe hepatic necrosis or viral proliferation in the endothelial cells of blood vessels. The defining lesions of Pacheco's disease virus are hepatic acute diffuse or multifocal necrosis with mixed inflammation, necrotic foci in periarterial lymphatic sheaths of the white pulp or in the red pulp of the spleen, syncytial cells, and eosinophilic intranuclear inclusions.

Uncommon lesions in systemic poxvirus infections of passerines have included air sacculitis, pneumonia, peritonitis, and heart and liver necrosis. The peritonitis is a proliferative lesion characterized by increased size and number of serosal cells, some of which contain cytoplasmic vacuoles and granular eosinophilic inclusions. The diagnosis of poxvirus rests on demonstration of the characteristic intracytoplasmic inclusion bodies generally in proliferative epithelium of the skin or mucosa.

Highly pathogenic avian influenza (HPAI) can cause a fibrinous pericarditis and peritonitis. In chickens that survive Avian paramyxovirus-1 (APMV-1, Newcastle disease), there may be an increased risk of developing egg yolk peritonitis.

Bacterial disease

Bacterial peritonitis is an uncommon presentation in pet birds. Most cases of bacterial peritonitis are secondary to a gastroenteritis or perforation of the gastrointestinal tract (Fig. 13.5), although bacterial infections can also be present in cases of egg yolk peritonitis. Culture is necessary for an exact etiologic diagnosis. The lesions and inflammatory cells are generally dependent on the pathogenicity of the bacteria and the chronicity of the disease (Fig. 13.6). In acute to subacute lesions, there will be heterophilic infiltrates, edema, and fibrin deposition (Fig. 13.7). Microorganisms and occasionally foreign material may be present in the exudate cytologically or histologically.

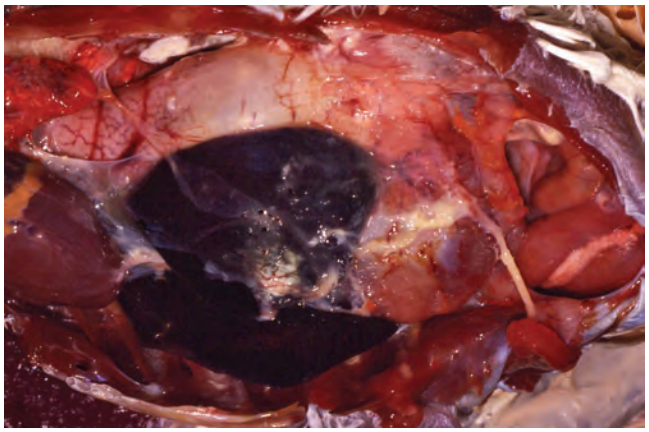

Figure 13.6 *Salmonella*-induced peritonitis. Note the fibrin and purulent material on the serosal surfaces and in the mesentery.

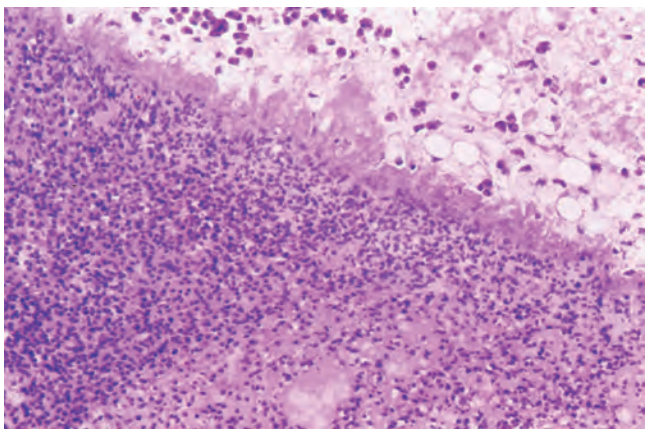

Figure 13.7 Bacterial peritonitis with large areas of necrosis, pleocellular inflammation, and fibrin deposition.

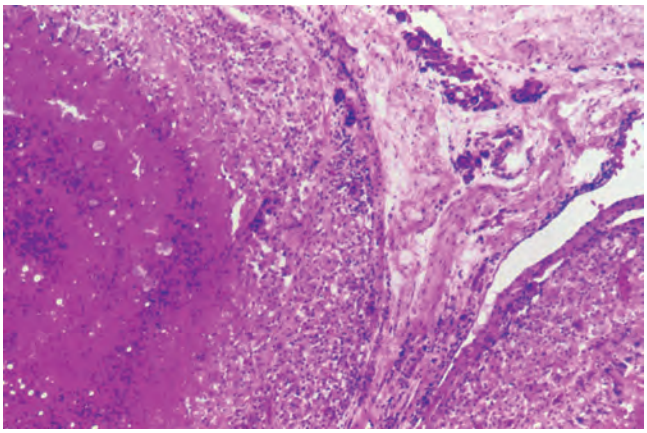

Figure 13.8 Chronic mycobacterial peritonitis with formation of large granulomas.

Figure 13.10 Chronic mycotic infection with peritonitis. Large amounts of thickened yellow-white exudate are present.

Mycobacterium is the most frequently reported isolate, although this most likely reflects the systemic nature of the infection and ease of recognizing the acid-fast positive bacteria (Fig. 13.8). The inflammation is typically granulomatous, with macrophages, multinucleated giant cells, and scattered nodules of lymphocytes and plasma cells. In chickens and pigeons, Serotypes of *Escherichia coli* cause serositis. In chickens this is usually peritonitis secondary to contamination/infection of the oviduct, and in pigeons it is usually part of systemic disease. The lesion is typically fibrinopurulent grossly and histologically.

Chlamydia psittaci

The acute lesions of *C. psittaci* are of a fibrinous peritoneal exudate, air sacculitis, hepatitis, pericarditis, myocarditis, bronchopneumonia, catarrhal enteritis, nephrosis, and splenitis. Fibrin exudation characterizes the peritoneal and epicardial lesions (Fig. 13.9). The single most consistent histologic lesion of this zoonotic disease is a systemic histiocytic inflammation.

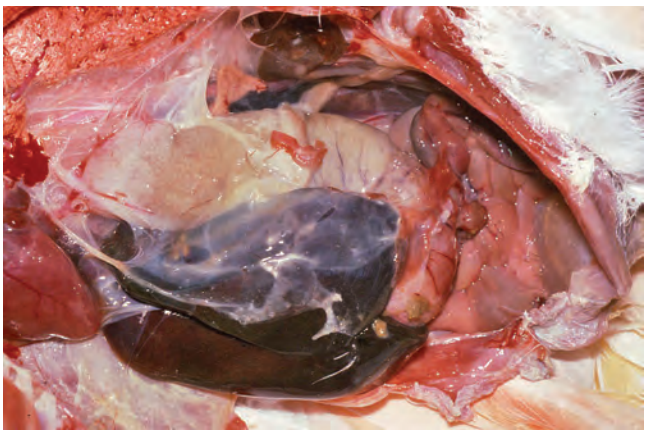

Figure 13.9 Tenacious, slightly opaque, peritoneal exudate seen in *Chlamydia* infection.

Fungal disease

Fungal peritonitis usually represents an extension of a fungal air sacculitis or pneumonia or, less likely, a gastrointestinal perforation and a mixed infection with bacteria. With an acute infection, the mesentery, pericardium, or serosa will be thickened with edema, scattered heterophils, and fibrin deposition. The more chronic lesions contain large amounts of yellow-white caseous exudate (Fig. 13.10). Histologically they are pyogranulomatous to granulomatous lesions with a thick proliferation of epithelioid macrophages, degenerate heterophils, multinucleated giant cells, smaller numbers of lymphocytes and plasma cells, and mats of fungal hyphae. Mycetomas may form with central cores of necrosis (Fig. 13.11).

Protozoal disease

A serous and fibrinous serositis has been associated with *Toxoplasma gondii* infection of canaries (*Serinus canaria*) and other

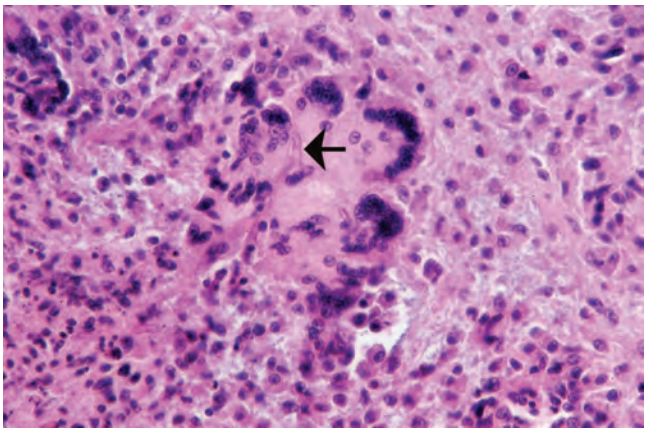

Figure 13.11 Typical serosal mycetoma with a necrotic core surrounded by an inflammatory reaction. A fragment of a fungal organism is present (arrow).

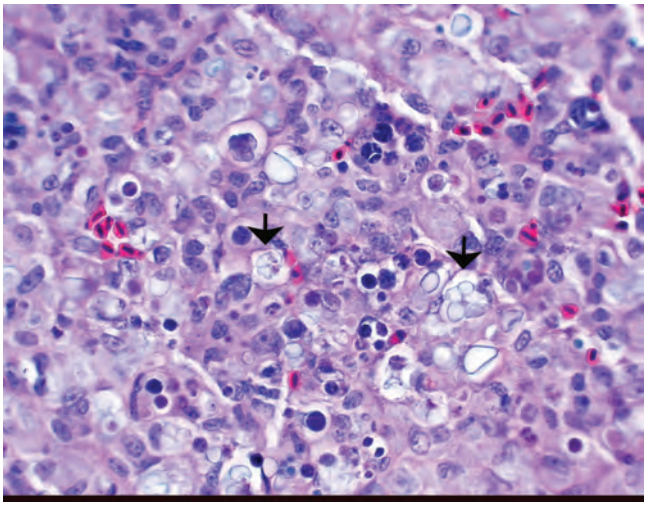

Figure 13.12 Granulomatous peritonitis due to algae. Numerous organisms are present (arrows).

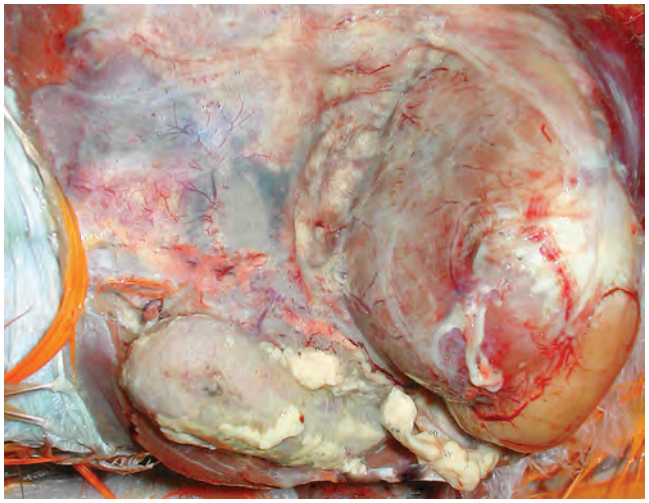

Figure 13.13 Severe egg yolk peritonitis with deposition of yolk material, fibrin, and adhesions of visceral organs.

small passerine cage birds. Disseminated massive hemorrhage and pulmonary necrosis with intra- and extracellular organisms, a heterophilic interstitial pneumonia, acute hepatitis, splenitis, nephritis, and necrotic nonsuppurative myocarditis characterize the acute phase (see the relevant chapters). Birds surviving the initial infection may develop ocular atrophy. *Toxoplasma gondii* cysts can be found in the brain and eye, with a nonsuppurative chorioretinitis and meningoencephalitis.

Other agents

Opportunistic infection by algae has been reported in a variety of mammals, and we have seen a case in a conure manifested by a peritoneal mass. As with mammals, this probably was the result of a transmural infection of the intestine. Grossly the lesion is not specific, and histologically there is a granulomatous reaction with the organisms present (Fig. 13.12).

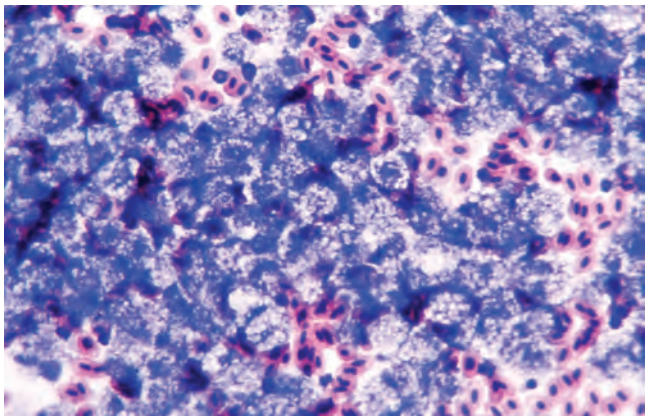

Figure 13.14 Cytology of fluid from a bird with egg yolk peritonitis. Numerous lipid-containing macrophages are present.

Noninfectious diseases

Egg yolk peritonitis

The peritonitis associated with the presence of egg yolk material can range in severity from nonclinical to life threatening. The yolk material (proteins and fats), which in small amounts can be gradually resorbed, generally elicits a mild histiocytic response along the serosa of the intestines and oviduct. Large amounts of yolk material and the presence of bacteria can result in severe adhesions between the loops of intestines and variable organ dysfunction (Fig. 13.13).

Acute egg yolk peritonitis can lead to coelomic fluid that has a high fat content and/or globules of proteinaceous material (Figs. 13.14 and 13.15). Histologically the lesion is characterized by large amounts of slightly refractile amphophilic to basophilic, variably sized protein globules deposited on the serosal surfaces

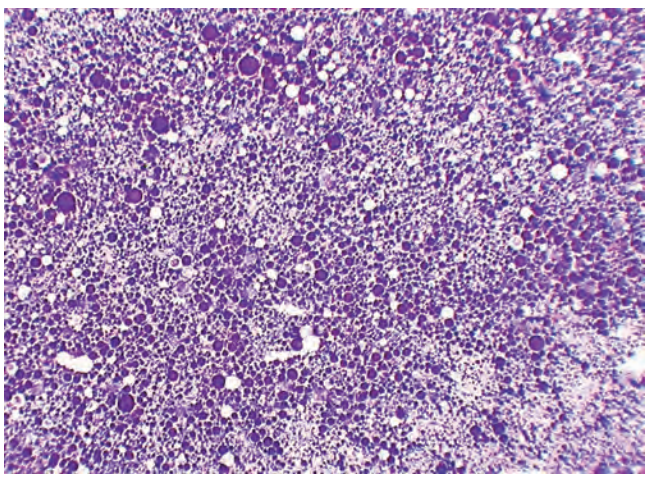

Figure 13.15 Protein globules seen on a cytology preparation from a bird with egg yolk peritonitis. Compare with Figure 13.17.

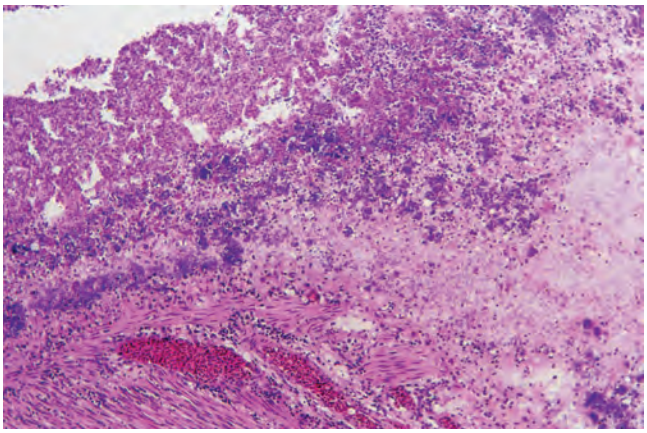

Figure 13.16 Severe yolk peritonitis. Individual globules can be seen within the exudate.

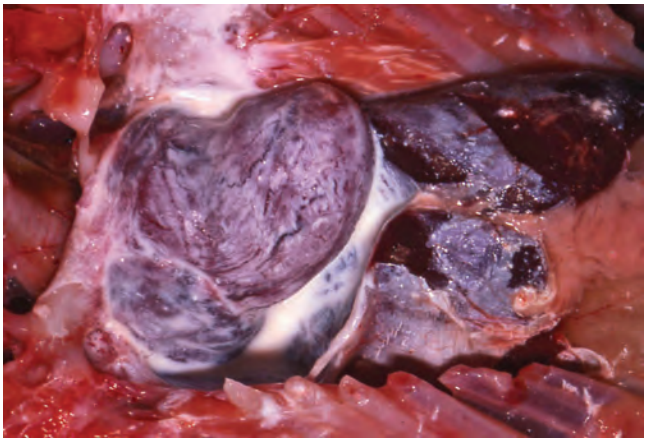

Figure 13.18 Visceral/serosal urate deposition. The reaction must be differentiated from infection.

(Fig. 13.16). There may be some hemorrhage as well as mild heterophilic inflammation (Fig. 13.17). Egg yolk peritonitis may occur from trauma, salpingitis, rupture of the oviduct, neoplasia, ovarian cystic hyperplasia, and ectopic ovulation due to reverse peristalsis of the oviduct. Most birds with egg yolk peritonitis present in respiratory distress with a distended, fluid-filled abdomen.

Egg yolk peritonitis is very common in laying hens particularly backyard chickens. These birds will often present with a massive peritoneal effusion. In other instances the peritoneum will be filled with egg yolk and little fluid. Many of these birds will have tumors of the oviduct.

Visceral gout

Visceral gout is the deposition of urates on serosal surfaces. The common sites are the epicardium, pericardium, and serosal surfaces of the proventriculus/ventriculus and liver. Grossly these deposits are gray-white and of variable shape (Fig. 13.18). Fluid from the coelomic cavity may contain numerous urate crystals as well as erythrocytes and variable numbers of inflammatory cells (Fig. 13.19). Histologically many cases are peracute, although there may be heterophilic infiltrates subtending the deposits. These heterophils are generally degenerative or necrotic and are associated with edema and mild hemorrhage/congestion. The urates appear as faint basophilic feathery material on the serosa. Formalin fixation will dissolve most of the crystals, but a negative image can be recognized in most cases with obvious gross lesions (Fig. 13.20). Severe renal lesions are typically associated with visceral gout.

Hemorrhage

Trauma, neoplastic rupture, and toxic exposure (anticoagulant rodenticides) can result in hemorrhage into the coelomic cavities (Fig. 13.21). The amount and duration of the hemorrhage will determine the lesions. In all but peracute lesions, there will be an influx of macrophages that exhibit erythrophagocytosis

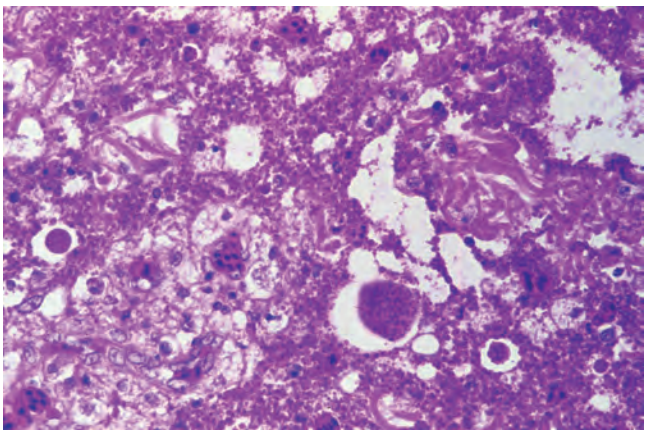

Figure 13.17 Detail of exudate in yolk peritonitis. Basophilic globules of varying sizes characterize the reaction.

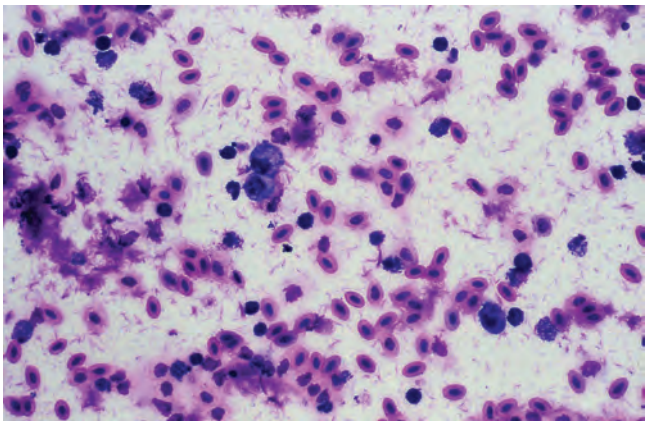

Figure 13.19 Cytology of peritoneal fluid from a bird with visceral gout. Numerous urate crystals are seen.

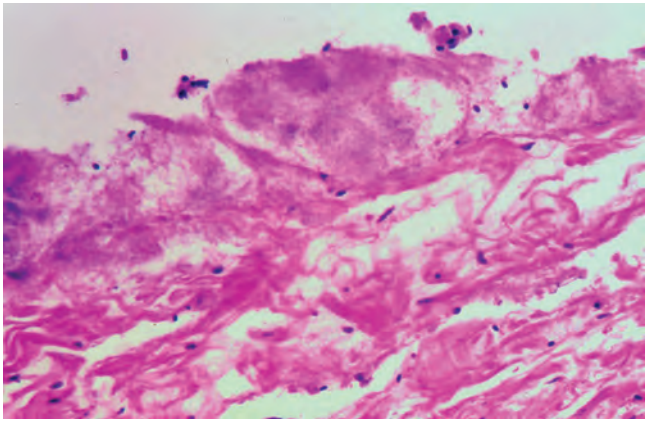

Figure 13.20 Detail of serosal crystalline urate deposition.

and cytoplasmic hemosiderin pigment accumulation. Perihepatic trauma is particularly common in wild birds that have been struck by motor vehicles.

Avocado toxin

Although the toxic principle is unknown, a number of psittacines, passerines, and ratites have died after ingesting avocado fruit. The majority of cases have few gross or histologic lesions. Hydropericardium due to myocardial damage is recognized in some cases. The fluid is described as clear and light tan, with a low specific gravity (less than 1.014). Degeneration and necrosis of myocytes, a marked infiltration of heterophils, and rare early fibroplasia characterize the cardiac lesions. Other lesions include mild nephrosis and pulmonary congestion, edema, and hemorrhage.

Neoplastic disease

The tumors described of the pleural/peritoneum may be primary or of systemic and local metastases. These include

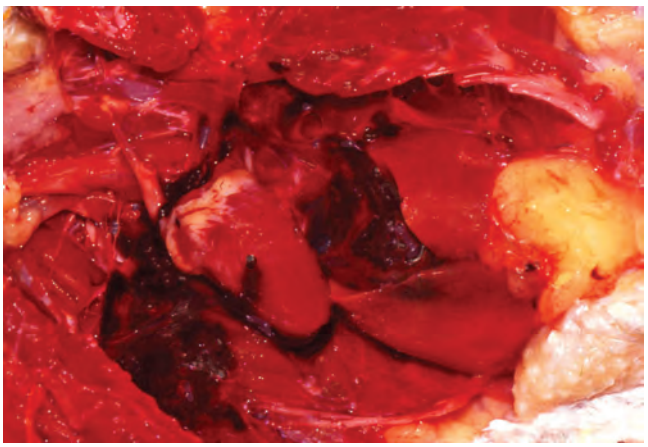

Figure 13.21 Marked hemorrhage within the peritoneal cavity.

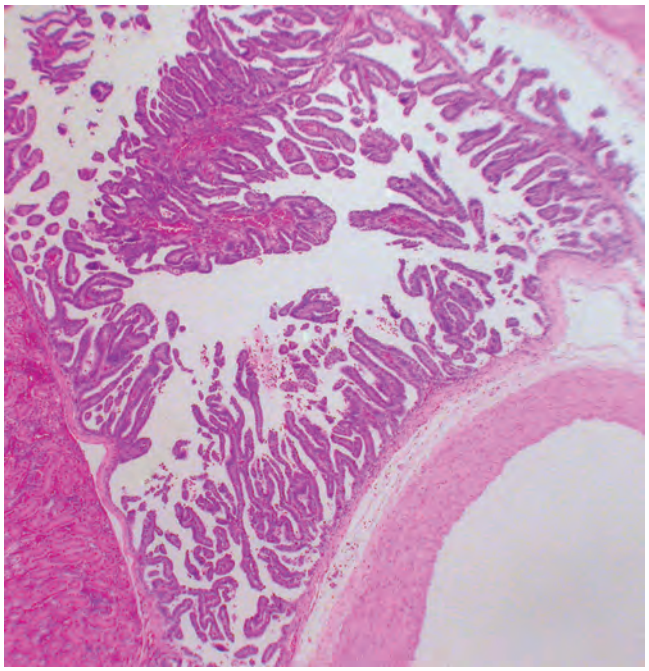

Figure 13.22 Mesothelioma arising from serous membranes in the coelomic cavity. The papillary appearance is typical.

mesothelioma, malignant melanoma, lymphosarcoma, lymphangioma, fibrosarcoma, ovarian/oviductal carcinomas, pancreatic carcinomas, and gastric carcinomas.

Mesotheliomas are primary tumors arising anywhere in the coelomic cavity. Grossly there is often coelomic fluid, and affected serous membranes are gray-white, opaque, and thickened. Microscopically these tumors comprise papillary structures covered by cuboidal mesothelial cells (Figs. 13.22 and 13.23). These tumors have been reported in chickens as well as

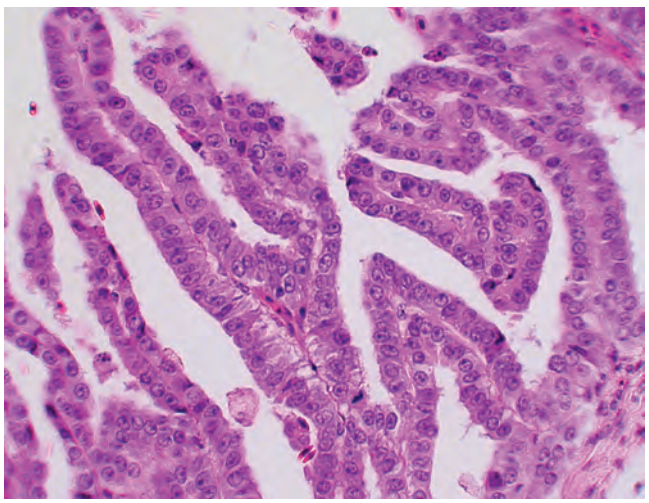

Figure 13.23 Higher magnification of Figure 13.22 to illustrate the cellular morphology.

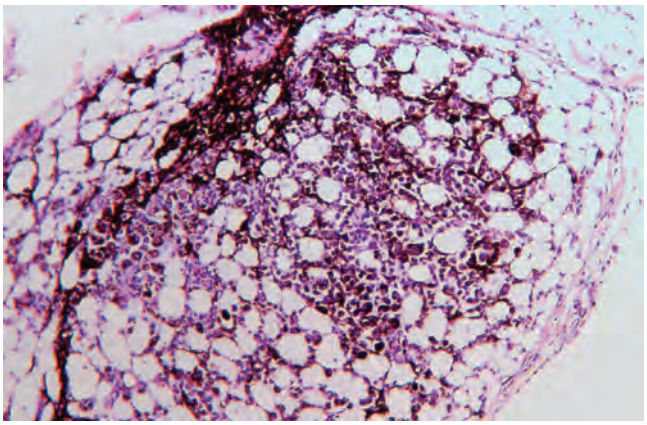

Figure 13.24 Early malignant melanoma in the mesentery.

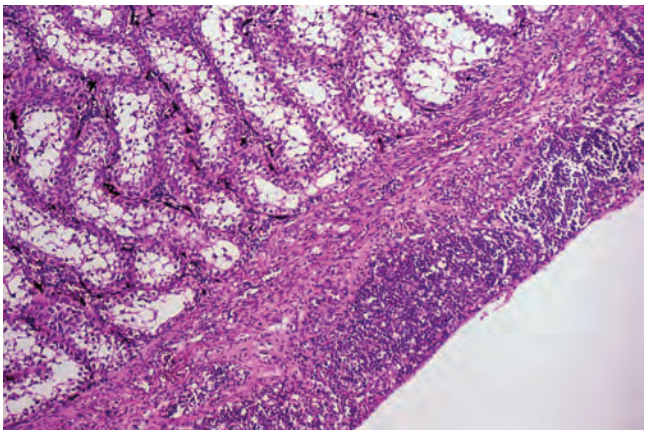

Figure 13.26 Histologic appearance of serosal lymphosarcoma. Neoplastic cells are infiltrating the testicular capsule and smooth muscle.

other birds, and we have seen cases in psittacine birds. Differential diagnoses include other neoplastic processes and chronic peritonitis. Malignant melanomas may be pigmented, and histologically the cells are pleomorphic and identified by the pigment present (Fig. 13.24), or by histochemistry if amelanotic.

Lymphosarcoma (malignant lymphoma) is a common neoplasm of psittacines and passerines. To date, there has been no evidence of a viral link to the tumor formation in pet birds. This neoplasia develops in primary and secondary lymphoid tissues and spreads to other tissues. Diffuse to nodular involvement is characteristic. The liver is most commonly involved, followed by involvement of the spleen and kidneys. These organs will appear enlarged and pale. Serosal infiltration of neoplastic lymphoid cells leads to thickening and opacity of the involved organs (Fig. 13.25). The neoplastic lymphocytes typically have scant to moderate amounts of amphophilic to eosinophilic cytoplasm and a central nucleus with a reticulated to coarse chromatin (Fig. 13.26).

Lymphangiomas may arise in the mesenteries. They are grossly not specific but may contain fluid-filled spaces. Histologically they comprise endothelial-lined spaces that may be empty or contain proteinaceous material (Fig. 13.27). Fibrosarcomas have been seen in the coelomic cavity. They are grossly not specific (Fig. 13.28), and histologically typical.

Both oviductal and ovarian tumors can implant widely throughout the coelomic cavity (Chapter 6). Carcinomas of the oviduct can appear as columnar epithelial cells forming tubular structures closely resembling cells of normal glands except for their orientation or as nodules composed of cuboidal cells that form definitive tubules to solid sheets. The cells are large and basophilic, with vesicular nuclei and numerous mitotic figures.

Pancreatic adenocarcinomas are rare tumors that may implant on the serosal surfaces and metastasize to the liver or lung. Grossly the typical lesion is of a diffusely enlarged, white, nodular, and firm pancreas. They are most common in the cockatiel and may completely envelope the intestines. Histologically the tumors comprise irregular glandular and tubular structures embedded in variable amounts of fibrous connective tissue stroma. The cells are tightly packed columnar cells with

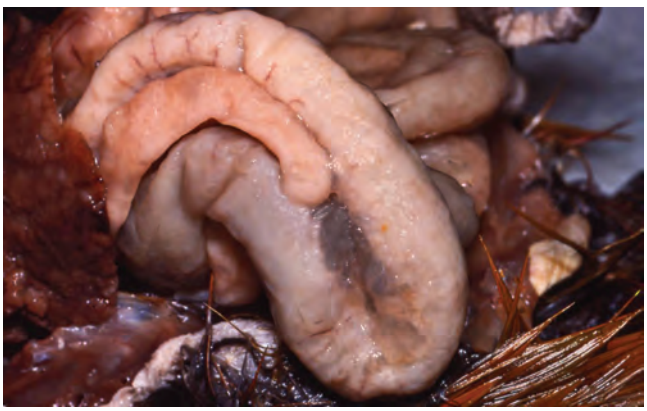

Figure 13.25 Serosal lymphosarcoma. Markedly thickened and opaque intestinal serosa is seen.

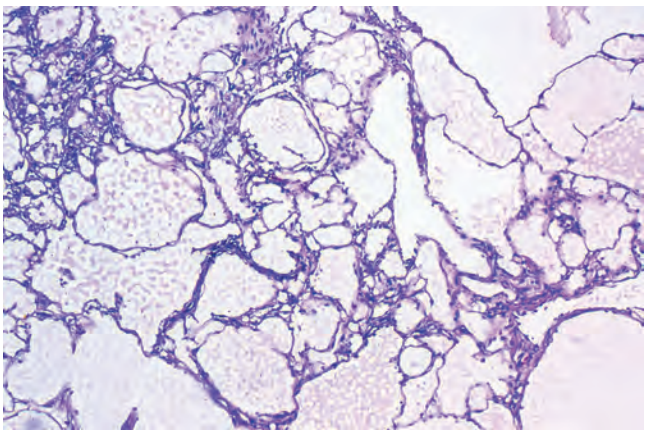

Figure 13.27 Lymphangioma composed of numerous endothelial-lined spaces many of which contain proteinaceous fluid.

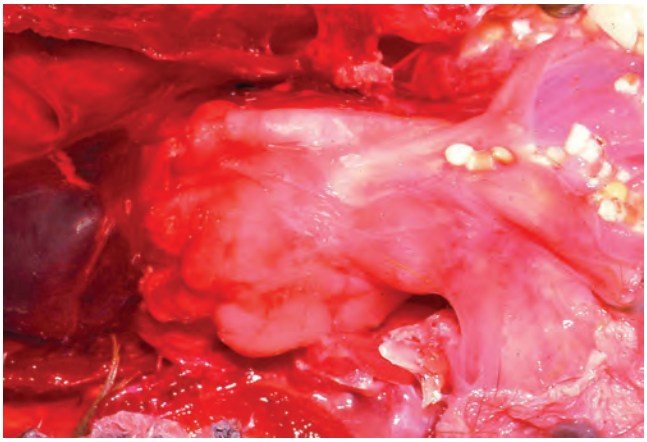

Figure 13.28 Nonspecific mass in the coelomic cavity that was diagnosed as a fibrosarcoma histologically. The gross appearance of any expansile sarcoma would be similar.

large vesicular nuclei, prominent nucleoli, and scant apical cytoplasm.

Primary, malignant gastric neoplasms are seen in psittacine birds (Chapter 3), and carcinomas/adenocarcinomas of the proventriculus are more frequently reported than those of the ventriculus. Gastric tumors may appear grossly as a thickening at the junction of proventriculus and ventriculus that presents as a flat or slightly raised subserosal or serosal lesion. Late in the disease, there may be implants or extension to the serosa of ventriculus, intestine, pancreas, and lungs.

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