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Rodentia

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INTRODUCTION

The order Rodentia includes 29 families, 468 genera, and over 2052 species. Two separate systems exist to classify rodents (Carleton and Musser, 2005). The first classification scheme by J.F. Brandt (1855) is based on morphology of the jaw and skull together with masticatory muscle position and has three suborders: Sciuromorpha (squirrel-like); Myomorpha (mouse-like); and Hystricomorpha (porcupine-like). The second separates rodents into two suborders, Sciurognathi and Hysticognathi, based on the position of incisors and the angle of the jaw (Carleton and Musser, 2005). Molecular studies yield seven clades containing three phylogenetic lineages: squirrel-related (Sciuroidea and Gliridae); mouse-related (Anomaluomorpha, Castoridae, Geomyoidea, and Myodonta); and Ctenohystica. With diverse ecologic strategies, rodents are found naturally in a variety of habitats globally except Antarctica. The natural history and biology of members of this extensive order exhibit substantial variation. Nevertheless, similarities exist among rodents including dentition, anatomy, and disease susceptibility.

UNIQUE FEATURES

The unifying characteristic of all rodents is their dentition, which includes two pairs of continuously growing (elodont) incisors. Brachydonts have elodont incisors with brachydont molars; in Hystricomorphs, all of the teeth are elodont. Dentition is important when considering the diet and husbandry needs of these groups. Brachydonts, which include mice, rats, hamsters, and gerbils, need high calorie diets with low amounts of fiber, whereas the hystricomorphs (porcupine-like; guinea pigs, chinchillas, agoutis) are strictly herbivores and require ample abrasive roughage. Dental formulae vary but in general, rodents have four incisors, no canines, 1–2 premolars, and numerous (up to 12) molars.

As most rodents are omnivorous, their digestive system typically consists of a simple stomach (monogastric) and a variably adapted intestinal tract depending on the degree of hind gut fermentation (Stevens and Hume, 1998). Most practice coprophagy or cecotrophy to maintain normal microflora and absorb microbially derived amino acids and vitamins (e.g., B and K). As such, herbivorous, omnivorous, insectivorous, and carnivorous rodents have different gastric and large intestinal anatomy. Some rodents lack gall bladders (e.g., rats and pocket gophers). Rats and hamsters are unable to vomit due to a muscular sphincter at the esophageal-gastric junction. Members of Caviidae lack the enzyme L-gulonolactone oxidase, making vitamin C (ascorbic acid) a necessary dietary requirement for this group (see scurvy in section, Nutritional Diseases).

Rodents are typically small (as small as 10 g) and rotund with short legs, though the largest rodents are almost 70 kg (e.g., capybaras). Rodents are nocturnal and though some species hibernate (e.g., woodchucks) but most of the species do not. There are numerous specializations among rodents including cheek pouches (food transport), extremity and claw development (e.g., burrowing, jumping, climbing, flying), sensory organ variations (e.g., vibrissae and large ears or eyes), special integument and pelage (e.g., porcupine quills and chinchilla fur), and tail adaptations (e.g., prehensile, fat storage). Rodents have a strong sense of smell and a well-developed vomeronasal organ, which is important for reproduction and social behavior through the sensing of pheromones. Since rodents lack sweat glands, they are susceptible to overheating.

Reproductive anatomy varies though most female rodents ovulate spontaneously and are polyestrous. Like rabbits, chinchillas have two cervixes that communicate with individual uterine horns. Vaginas are imperforate prior to sexual maturing and during nonbreeding and/or postpartum intervals. Placentation is discoid and hemochorial. Mammary gland anatomy varies among species. The suborders

Sciuromyomata and Stricomyomata have altricial and precocial young, respectively. Some male rodents have testes within a scrotum, though the testes of porcupines, agoutis, chinchillas, cavies, and capybaras are located within the inguinal canal, which remains open in most male rodents. Male rodents also have well developed accessory sex glands and an os penis. Prairie dogs have perianal sacs similar to canids and felids, which are important for sexual communication. Male beavers have persistent paramesonephric ducts that resemble a uterus and are referred to as masculine uterus (Doboszynska and Zurowski, 1981; Meier et al., 1998).

South American rodents including guinea pigs and related species have unique pulmonary anatomy as do burrow-dwelling, subterranean mole-rats that live in low oxygen tension environments, for example, large and dilated, primitive bronchi and bronchioles (Ilgun et al., 2014; Widmer et al., 1997). Lung morphology of 40 different rodent species representing 11 families is well described (Wallau et al., 2000).

Common microscopic findings in rodents that may be misinterpreted as lesions include: multinucleated, karyomegalic, and cytomegalic hepatocytes are common in several rodent species and can increase with age (Fig. 20.1); hepatocellular intranuclear cytoplasmic invaginations (pseudoinclusions) (Fig. 20.1); eosinophilic cytoplasmic spherical inclusions in renal tubular epithelial cells and hepatocytes seen predominantly male mice, rats, and hamsters; splenic extramedullary hematopoiesis, which is very common in healthy rodents of all ages (Fig. 20.2); hemosiderin, lipofuscin, ceroid, and melanin (in dark or black coated animals) are commonly detected in various tissues, such as spleen, liver, kidney, and adrenal glands; cardiac muscle in the tunica of pulmonary veins in the lung is a normal finding in mice; male rodents may have refluxed seminal coagula in

the urinary bladder and urethra that is thought to occur *perimortem*; and adrenal X-zone vacuolation in female mice. Furthermore, there are evident sexual dimorphisms of some organs and glands, such as the cuboidal parietal epithelium of the glomeruli in male rodents.

Hematological reference ranges have been established for some common domestic, zoo-housed, and ubiquitous free-ranging species. In general, the lifespan of rodent erythrocytes is shorter than other mammals, thus, higher levels of circulating reticulocytes (1%–6%), seen as polychromasia and anisocytosis, is considered normal. Howell-Jolly bodies may also be present. In all age groups, lymphocytes are more numerous than neutrophils. In fact, lymphocytes are the predominant white blood cells in guinea pigs (45%–80%). In addition, guinea pigs and capybaras have Kurloff cells (Fig. 20.3), which are lymphocytes containing a single, large intracytoplasmic mucopolysaccharide inclusion body, known as a Kurloff body (Jara et al., 2005). Though the actual function of these cells is unknown, they are presumed to be natural killer cells. The number of Kurloff cells in females fluctuate with the reproductive cycle stage, thus they are considered to be estrogen-dependent. Pregnant females may have 2%–5% Kurloff cells in circulation while males typically have fewer. Guinea pigs have heterophils similar to rabbits. Rats, mice, and hamsters commonly have neutrophils with ring-form nuclei. Chinchillas and porcupines have well-defined and segmented neutrophil nuclei. Band neutrophils may be a normal finding in some species including New World porcupines, coypu, and agoutis.

Serum biochemical parameters have been compiled for some rodent species (Kurtz et al., 2017; Yarto-Jaramillo, 2015). Of note is that serum levels of alanine aminotransferase (ALT) are not sensitive biomarkers of liver health in guinea pigs and

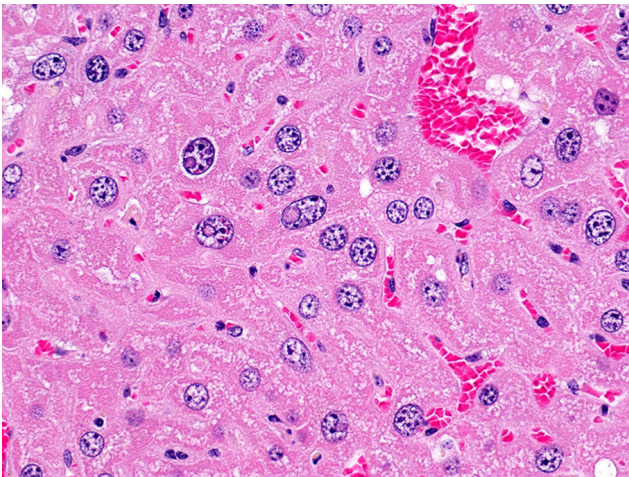


FIGURE 20.1 Normal liver in an aged mouse. Common findings include anisocytosis, anisokaryosis, and eosinophilic intranuclear pseudoinclusions of invaginated cytoplasm.

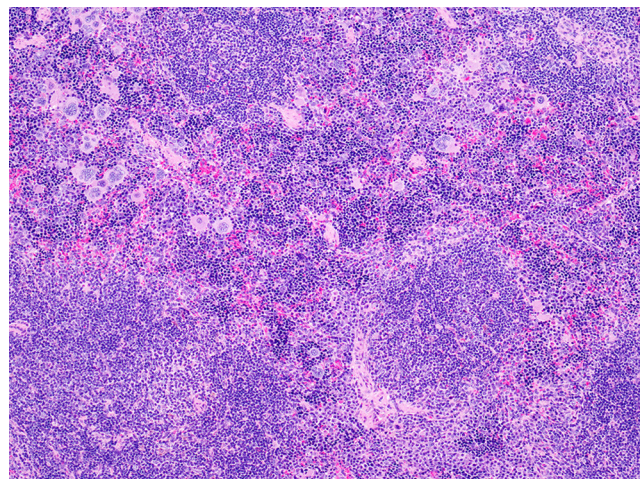


FIGURE 20.2 Splenic extramedullary hematopoiesis in an aged mouse. Within the red pulp are hematopoietic elements including erythroid and myeloid lineages. Note the large multinucleated megakaryocytes, which are readily visible at this magnification.

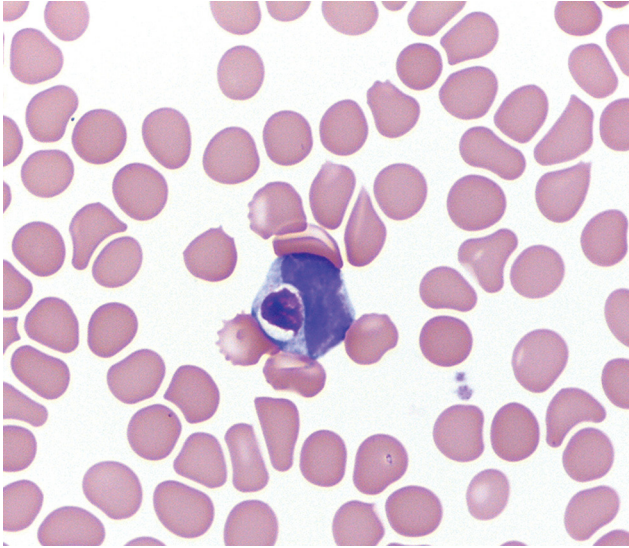


FIGURE 20.3 Normal Kurloff cell in a blood smear from a guinea pig. A Kurloff body is a mucopolysaccharide inclusion in the cytoplasm of lymphocytes. They are found in lymphocytes of guinea pigs and capybaras. In this image, it causes mild peripheralization of the nucleus. (Photo Courtesy of L. Black, University of Florida)

some other rodents as they normally have low hepatic levels of this enzyme. In contrast, gamma glutamyl transferase is present in the liver of all rodents and can be evaluated to determine the hepatic injury or disease. Hamsters and other desert species may have high levels of serum calcium. Rodents like mice and rats, and specifically those evolved in arid regions, have a profound ability to concentrate their urine, thus it is often turbid and contain calcium crystals.

The following list of diseases of rodents is not exhaustive but instead highlights the more common findings in species of which there is published literature or knowledge. A plethora of information exists regarding the anatomy, physiology, and diseases of rodents used as animal models in biomedical research (i.e., laboratory animals) and is a valuable resource when examining lesser-studied rodent species using a comparative approach (Barthold et al., 2016; Greaves, 2011; Suckow et al., 2012; Treuting and Dintzis, 2017). As many rodents are important prey species, diseased or dead rodents are exceedingly difficult to detect in nature using the passive surveillance techniques of traditional wildlife disease monitoring. Thus, less is known about the diseases and pathology of free-ranging rodents as compared to larger and charismatic mammals.

NON-INFECTIOUS DISEASES

Nutritional

One of the most well described nutritional diseases in rodents is **hypovitaminosis C** or **scurvy**. Guinea pigs and a number of other species including capybaras and humans,

lack the enzyme L-gulonolactone oxidase which is required for L-ascorbic acid (vitamin C) production therefore, these species require dietary vitamin C (Cueto et al., 2000). Vitamin C is necessary for the formation of collagen via hydroxylation of proline/lysine for cross linking of fibrillar collagen. Hypovitaminosis C results in decreased collagen fibril cross linking, leading to the increased fragility of blood vessels, cartilage, and osteoid. In affected individuals, gross and histologic lesions are characteristic and include capillary hemorrhage and lack of bone deposition and remodeling as a result of poorly formed and weak collagen. Other gross lesions include evidence of anemia (e.g., pallor, reactive bone marrow), periarticular hemorrhage, and swollen joints, specifically at the costochondral junctions (scurvitic lattice). Characteristic oral lesions include gingival swelling, erythema, hemorrhage, erosion, ulceration, and tooth loss. Histological examination is necessary to confirm and define bone lesions, which include: dilation of metaphyseal blood vessels, irregular columnization and hypertrophy of physeal cartilage, calcification of metaphyseal cartilage with reduced or absent osteoid, microfractures with surrounding and subperiosteal hemorrhage, medullary fibrosis, and decreased osteoclastic activity and remodeling. Tooth loss may result from a combination of abnormal odontoblasts, dentin resorption, pulp fibrosis, and a lack of/ abnormal alveolar bone remodeling.

Like lagomorphs, some hindgut-fermenting rodents are susceptible to **gut stasis** and related diseases if they are not able to obtain enough fiber from the diet. **Obesity** can be common in rodent species if fed a high caloric diet and can predispose to diabetes mellitus, cardiac disease, pregnancy toxemia, and hepatic lipidosis in females.

Metabolic

Dystrophic mineralization occurs in guinea pigs, hamsters, and free-ranging rats (Rothenburger et al., 2015a). Mineralization most often affects the **myocardium** but can also occur in other tissues, such as the diaphragm, tongue, liver, kidney, lungs, cornea, and aorta (see section Congenital/Genetic). Though the pathogenesis is not fully elucidated, mitochondria appear to be preferentially mineralized based on ultrastructural studies. Gross lesions may include cardiomegaly with chalky to gritty white material and streaking within the myocardium of the atria and ventricles. Histologically, affected cardiac myocytes are degenerative and/or necrotic with rupture of the sarcolemma. Damaged myocytes will have variable and progressive mineralization until the entire myofiber is densely mineralized. Variably mature fibrosis surrounds individual and clusters of dead and mineralized myocytes. Satellite cells are frequently hypertrophic.

Pregnancy toxemia occurs in overweight, pregnant, and lactating female guinea pigs and hamsters. There are two forms in guinea pigs, a fasting type that results from

decreased carbohydrate intake and subsequent mobilization of fat stores and a circulatory type that occurs when the gravid uterus compresses the aorta and causes reduced blood flow to abdominal organs. Characteristic gross and histologic lesions include hepatic lipidosis and fat deposition in renal tubular epithelial cells. Similarly, hepatic lipidosis and associated metabolic effects occasionally affect overweight nongravid sows and boars.

Urolithiasis is common in guinea pigs, rats, and mice due to high urine pH and calcium concentrations. Obstructive urolithiasis has also been reported in captive male agoutis resulting in bilateral hydronephrosis, urinary bladder rupture, and peritonitis (Batista et al., 2010).

A number of other endocrine diseases have rarely been documented in various rodent species. They have typically been associated with hormone-producing neoplasms (adrenal, islet, thyroid, parathyroid, and pituitary tumors).

Toxic

Fluorosis is well studied in rats as they are used as models in toxicology studies. Guinea pigs and rabbits are also susceptible and fluorosis has occurred in free-ranging cotton rats in sites contaminated by petrochemical waste (Rafferty et al., 2000). Pathognomonic lesions occur in teeth and bones. Periosteal hyperostosis occurs first along the medial surface of the metatarsals, then progresses to affect the mandible, metacarpals, and ribs though all bones can be affected in severe, chronic disease. Bones are brittle and chalky-white. Pathological fractures are common but joints are typically spared. Although characteristic, enamel hypoplasia only occurs when fluorosis is present during tooth development. Tooth lesions include dull, dry, and chalky hypomineralized or hypoplastic enamel with pitting, grooves, and discoloration (due to oxidation); excessive attrition affects the incisors first. Irregular wear, malocclusion, and fractures may be present. Histologically, ameloblasts are small while osteoblasts are vacuolated and disorganized. There is abundant globular dentin and hypomineralization of the outer enamel layer. A differential for enamel hypoplasia in young Syrian hamsters is Hamster Parvovirus (HaPV); concurrent testicular hypoplasia, and cerebral malacia is present with this viral infection.

Cholecalciferol (Vitamin D) is used as a rodenticide. The deliberate poisoning of free-ranging rats and mice results in inadvertent toxicity of nontarget animals including other rodents, such as squirrels or carnivorous predators that consume affected carcasses. Multisystemic mineralization occurs prior to death in affected individuals. Unlike other rodents, naked mole-rats, beavers, and woodchucks do not require dietary vitamin D and toxicity can develop if they are fed rodent chow or diets supplemented with vitamin D. Lesions consistent with calcinosis cutis and circumscripta can develop in naked mole-rats fed such diets. Soft tissue

calcification is not limited to pressure points and can be found throughout the body in severe cases. Resolution occurs with correction of the diet (Delaney et al., 2013).

Anticoagulant rodenticides including warfarin and its derivatives are frequently used to control free-ranging mice and rat populations. These compounds antagonize vitamin K and thus inhibit production of vitamin K-dependent clotting factors (I, II, VII, IX, X). Gross lesions include multisystemic hemorrhage, particularly subcutaneous and periarticular hematomas. "Bait," some of which are brightly colored (e.g., teal-green), may be present within the intestines. Inadvertent consumption by nontarget wildlife may have fatal consequences.

Hindgut fermenting rodents are susceptible to similar **antibiotic-related toxicities** as rabbits (see Chapter 19). **Nephrotoxicosis** can be the result of exposure to numerous agents and has been extensively described in laboratory animals. For example, **Swainsonine toxicity** occurs following the ingestion of plants from the genus **Swainsona** and results in **acquired alpha-mannosidosis** in rats. Histologically, renal tubular epithelial cells are severely and diffusely vacuolated.

Congenital/Genetic

Dystrophic mineralization, also known as **dystrophic cardiac calcinosis** is considered as a genetic disease in inbred mouse strains, particularly in aged individuals (Eaton et al., 1978). Cardiac mineralization is detected grossly as pinpoint foci to larger irregular crusts composed of white, gritty material within and overlying the epicardium. Histologic lesions vary depending on severity and chronicity with degeneration and necrosis of individual myocytes to extensive regions of myocyte loss and replacement by deeply basophilic granular material. In severe cases, mineralization extends into the myocardium resulting in scar formation and can also be seen in the kidneys and lungs. The prevalence of this disease in wild mice from which these strains originated is unknown.

Diabetes mellitus (DM) in Chinese hamsters is a heritable, autosomal recessive disease (Green et al., 1963). Symptomology and lesions are similar to those found in humans and include hydropic degeneration and degranulation of pancreatic islet β -cells with secondary vascular lesions, such as arteriosclerosis and glomerulosclerosis. In addition, affected hamsters are predisposed to pancreatic adenocarcinomas. Serum levels of α -2 globulins are a useful indicator of risk for diabetes mellitus development in these populations.

Polycystic kidney disease has been diagnosed in captive populations of Brazilian agoutis (Müller et al., 2009). Most affected individuals have no clinical signs and are potentially related genetically. Grossly, affected agoutis have a range of bilateral renal changes including atrophy, roughened granular cortical surfaces, and multiple cysts.

Histologically, there is cystic dilatation of renal tubules and Bowman's capsules with mesangial and capsular thickening accompanied by mononuclear interstitial nephritis and fibrosis.

Age-Related/Degenerative

Many degenerative and age-related diseases are described in rodents used in toxicology studies (Barthold et al., 2016; Pettan-Brewer and Treuting, 2011). A significant disease confounding these studies is **chronic progressive nephropathy**, which is best described in rats though mice, naked mole-rats, and Australian rodents, particularly the stick-nest rat, are also affected (Delaney et al., 2016a). The exact pathogenesis is unknown; however genetic factors may play a role. Grossly, kidneys are bilaterally pale and either enlarged or shrunken with numerous pinpoint to large, 1 mm cortical microcysts creating a nodular surface. Histologically, renal tubules are markedly ectatic and tortuous and many contain brightly eosinophilic fluid (proteinosis) (Fig. 20.4). Tubules have a range of degeneration, necrosis, and regeneration with occasional tubular hyperplasia and adenoma formation (predominantly in rats). Glomeruli are variably affected by membranous and/or proliferative changes with thickened basement membranes, sclerosis, and obsolescence. Syneciae, dilated Bowman's capsules, and hypertrophied parietal epithelium are common. The interstitium is expanded by lymphoplasmacytic infiltrates with pigment-laden macrophages, mild hemorrhage, and edema. There is often substantial interstitial fibrosis and in severe cases, infarction. Diagnosis is based on histologic evaluation though in some species, clinical pathology may be preferentially used to determine renal function.

Cardiomyopathy is common in aged mice, rats and hamsters; it is particularly common in Syrian hamsters and is reported in woodchucks (Chanut et al., 2013; Rothenburger et al., 2015a; Roth and King, 1986). Lesion severity varies though it appears to increase with age and is more common in males. Though considered strain and thus possibly genetically related in laboratory rats, free-ranging rats develop similar disease (Rothenburger et al., 2015a). Grossly, there may be cardiomegaly but macroscopic changes are not always apparent. Histologically, myocardial lesions consist of multifocal and perivascular lymphoplasmacytic infiltrates accompanied by fibrosis, myocyte degeneration, and drop out (Fig. 20.5A,B). Trichrome, Movat pentachrome, or other stains that highlight the fibrosis are useful to evaluate severity and chronicity. Syrian hamsters develop cardiomyopathy associated spontaneous atrial thrombosis and subsequent coagulopathy that is often fatal (Fig. 20.6). Females appear to be affected earlier in the life than males.

Like other species, rodents are susceptible to skeletal degeneration and related diseases. Guinea pigs, specifically the Duncan-Hartley breed and Syrian hamsters, frequently

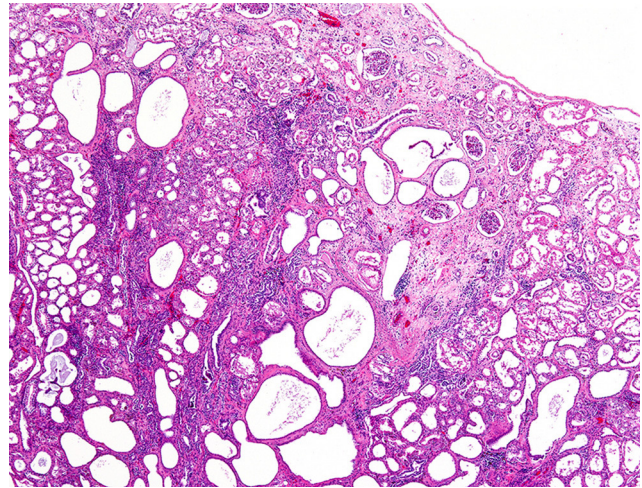


FIGURE 20.4 Chronic progressive nephropathy in a naked mole-rat. Renal tubules are variably ectatic, atrophied, degenerate, necrotic, and replaced by collagenous fibrous tissue. Within the interstitium are accumulations of mononuclear cells (primarily lymphocytes and fewer macrophages). There is also sclerosis of glomeruli and periglomerular fibrosis.

develop **degenerative joint disease**. Gross lesions include thickened joint capsules, variable osteophyte formation, roughened cartilage surfaces, eburnation, joint effusion, and synovial proliferation. Depending on which joints are affected and chronicity, crepitus may be present when joints are manipulated. Microscopic examination of joints reveals degeneration, necrosis, and ulceration of the articular cartilage with proliferation and fibrosis of the synovium and joint capsule, periarticular and periosteal bone formation, and remodeling. There may also be variable inflammation and hemorrhage within joint spaces.

Amyloidosis is typically seen in aged animals. Amyloid is an extracellular accumulation of insoluble protein. Excessive amyloid deposits can lead to tissue atrophy and dysfunction. Amyloidosis is most common in myomorphs (mice, rats, hamsters, gerbils) and appears in the kidneys, spleen, adrenals, and liver as well as the gastrointestinal lamina propria (mouse) (Fig. 20.7). There is a higher prevalence in females. Of note is the eosinophilic substance within the nasal planum of aged mice that was once thought to be amyloid, through histochemical and ultrastructural studies, has instead been shown to consist of collagen and complex carbohydrates produced by the nasal gland epithelial cells (Doi et al., 2007).

Hemosiderosis is the accumulation of iron within various tissues, most commonly the liver. It is described in numerous species including primates, birds, rhinoceros, hyraxes, and rodents. In one zoological institution, hemosiderosis was present in approximately 65% of adult naked mole rats (Delaney et al., 2013). Grossly, livers appear bronze. Iron accumulation appears histologically as zonal to diffuse hepatocellular accumulation of brown granular to

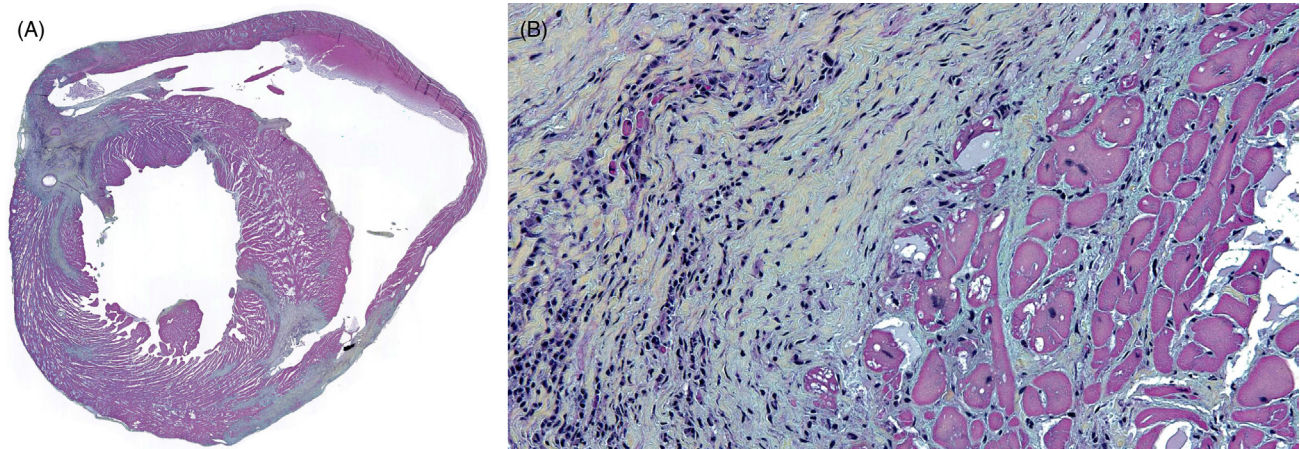


FIGURE 20.5 Cardiomyopathy in a free-ranging black rat. (A) There is multifocal disruption and replacement of the myocardium by fibrosis (blue-green staining), Movat pentachrome. (B) Cardiomyocyte degeneration is characterized by cell swelling, anisocytosis, and anisokaryosis and loss of cross striations. Cells are separated and surrounded by increased amounts of fibrosis (blue-green staining) and lymphoplasmacytic inflammation, Movat pentachrome.

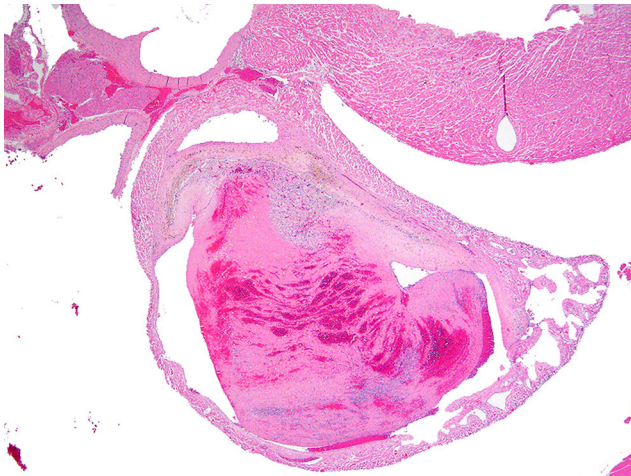


FIGURE 20.6 Atrial thrombosis in a Syrian hamster. The atrium is expanded by a large luminal thrombus that is regionally adherent to the endocardium. The thrombus is composed of laminated layers of fibrin, leukocytes, and erythrocytes, and intermixed hemosiderin-laden macrophages. (Photo Courtesy of J. Landolfi, University of Illinois Zoological Pathology Program)

globular pigment. Pigment is most intense in the periportal hepatocytes. The pigment stains positively with Prussian blue and is not refractile with polarized light.

Aged mice can develop **intrapulpal denticles**, which are dysplastic tooth-like growths arising in the pulp of incisors. These may result in abnormal wear and or breakage of the incisors contributing to periodontitis and decreased ability to effectively gnaw (Pettan-Brewer and Treuting, 2011).

Trauma

Despite their protective quills, porcupines are particularly susceptible to cutaneous trauma and tears due to an

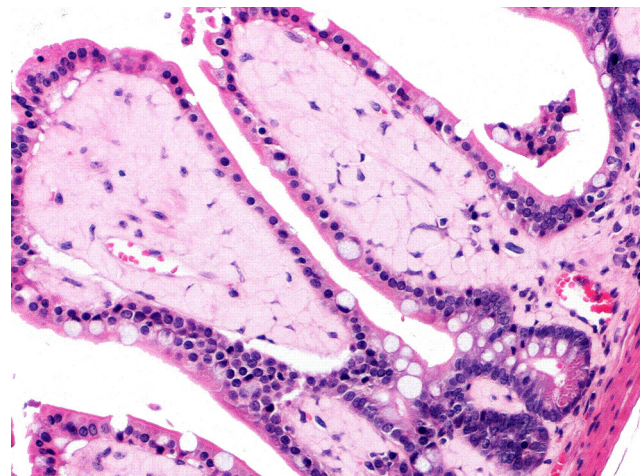


FIGURE 20.7 Intestinal amyloidosis in an aged mouse. The lamina propria is markedly expanded by homogenous, pale eosinophilic extracellular fibrillar material consistent with amyloid. There are few lymphocytes embedded within the amyloid. (Photo courtesy of C. Pettan-Brewer and P. Treuting, University of Washington)

exquisitely fragile integument. Secondary infections resulting in pyoderma and persistent ulceration may occur.

Inflammatory, Non-infectious

Stress dermatosis (or dermatitis) is a condition of several South American rodents including, the agouti, acouchis, and capybaras. This syndrome is seen in captive and free-ranging individuals in densely populated groups. It presents as alopecic skin lesions and lacerations along the lumbosacral spine. Stress is thought to increase skin fragility and overcrowding with intraspecific aggression contributes to lesion development. Sun exposure, pruritus, and self-mutilation result in large patches of alopecia with

erythema and excoriated skin with loss of the long hairs along the dorsum and tail. Microscopic lesions correlate to severity and chronicity and include variable epidermal degeneration, necrosis, erosion/ulceration, and associated dermatitis with hemorrhage and edema. Diagnosis is based on clinical history, demonstrated absence of a parasitic etiology in skin scrapings and histopathology.

Miscellaneous

Malocclusion is common especially in hysticomorphs, though it is also seen in brachydonts. It is a significant disease in captivity and may be related to genetics, nutrition and diet, and husbandry practices (Losco, 1995).

Ovarian cysts are common in rodents. **Cystic rete ovarii** are prevalent in female guinea pigs (Veiga-Parga et al., 2016) and can be distinguished from other ovarian cysts as they arise from the rete and compress adjacent ovarian tissue (Fig. 20.8). Other ovarian cystic structures reported in female rodents include: bursal cysts, epithelial cysts, follicular cysts, luteal cysts, and paraovarian cysts (Dixon et al., 2014).

The hemochorial placentation in rodents predisposes them to **trophoblast emboli**. This incidental lesion is best described in chinchillas and is not associated with clinical ramifications or gross lesions. Histologically, intravascular trophoblasts are present in the lung, uterus, spleen, liver, and other sites, such as the adrenal glands with no associated inflammation. Trophoblasts are large (>100 µm) with abundant amphophilic granular cytoplasm and large nuclei with prominent nucleoli.



FIGURE 20.8 Cystic rete ovarii in a guinea pig. The ovaries are bilaterally enlarged by multiple, intraovarian rete cysts. (Photo Courtesy of J. Landolfi, University of Illinois Zoological Pathology Program)

Neoplastic

Many neoplasms of inbred mice and rats appear to be strain related. Nevertheless, certain neoplasms occur more frequently among free-ranging and domesticated outbred rodents than in other mammalian orders. Several of them are described below. A list of other common neoplasms in rodent species is listed in the Supplemental Materials (Table e1).

Naked mole-rats are a popular zoo species and are heralded as animal models for cancer and aging due to their extreme longevity and purported cancer resistance. Rare cases of neoplasia have been reported in naked mole-rats and in the related Damaraland mole-rat, which is also long-lived and appears to be relatively resistant to cancer and age-related diseases (Delaney et al., 2016b; Sura et al., 2011; Taylor et al., 2016). Other subterranean rodents used as animal models for carcinogenesis research include some members of *Spalacidae* (mole-rats, blind mole-rats, zokors, and bamboo rats). There are currently no reported spontaneous tumors in this group; however, subcutaneous tumors (fibromas and fibrosarcomas) may be induced with application of carcinogenic compounds.

Odontoma, or more aptly named **odontogenic dysplasia**, is described in several rodent species (rats, mice, guinea pig, prairie dogs, degus, chinchilla, chipmunk, squirrels; Boy et al., 2006). Most odontomas are not true neoplasms and instead represent dysplastic changes resulting from chronic inflammation or trauma and associated regional tissue response. As there is no demonstrated metastatic potential or criteria for malignancy, these lesions are increasingly identified as hamartomas versus neoplasms (and also referred to as **pseudo-odontomas**). Nevertheless, these toothy masses are regionally destructive and almost exclusively affect the incisors. Grossly, odontogenic dysplasia presents as nodular swellings around the maxillary or mandibular incisors. Microscopically, these lesions are composed of disorganized and dysplastic proliferations of odontogenic epithelium, enamel matrix, and mineralized enamel, dentin, pulp, and cementum. In rodents, odontomas have been described as complex because they contain fully differentiated tooth elements but do not form the tooth-like structures grossly present in compound odontomas seen in other species (e.g., horse). Histologically, rodent odontomas are composed of well-differentiated odontogenic epithelium among an enamel organ with dental pulp mesenchyme and a variably mineralized enamel matrix.

INFECTIOUS DISEASES

Several important infectious and zoonotic diseases of rodents described are later with a focus on those that cause significant lesions in rodent species. Additional pathogens, including zoonotic pathogens that occur in rodent species are listed in the Supplemental Materials (Table e2). Several

references exist pertaining to rodent reservoirs of emerging and reemerging zoonotic pathogens (Han et al., 2015; Meerburg et al., 2009).

DNA Viruses

Poxviral diseases in rodents are caused by members of *Orthopoxviridae*, which includes **Mousepox** and **Cowpox** (OIE listed reportable zoonotic diseases). Several species of rodents serve as the reservoir for Cowpox virus, which results in cutaneous lesions in humans. In laboratory mice, Mousepox, more commonly known as **ectromelia**, is an important disease. This infection can be acutely fatal with minimal lesions. In the chronic form, gross lesions include crusting lesions of face, legs, and tail, conjunctivitis, an enlarged, swollen and friable liver and spleen, and in cases of recovery, splenic fibrosis. Necrosis of the kidney, thymus, and lymph nodes may also be grossly evident. The small intestine, urinary bladder, and vagina can have mucosal erosions and hemorrhage. Histologically, skin and mucosal lesions include epithelial ballooning degeneration, hyperplasia, and erosions with characteristic intraepithelial, intracytoplasmic inclusion bodies. Within the parenchymal organs, splenic and hepatocellular necrosis is typically coagulative and multifocal to coalescing. Diagnosis is based on characteristic lesions with viral inclusions. Electron microscopy, PCR, and virus isolation are useful for confirmation of the viral strain.

In 2003, an outbreak of **monkeypox** (*Orthopoxviridae*), a zoonotic virus, occurred in prairie dogs sold as companion animals in the United States (Gaurner et al., 2004). Fatal infections in infected prairie dogs were characterized by necrotizing bronchopneumonia, conjunctivitis, and glossal ulcers. Viruses and viral antigens were detected in multiple tissues and cell types via immunohistochemical staining, PCR, and electron microscopy. Infected humans developed fever and vascular rashes. Forty seven confirmed and probable cases of monkeypox were reported from six states. The prairie dogs contracted the virus following exposure to infected African rodents. Other rodents that also developed disease and died included: rope squirrels, tree squirrels, Gambian giant rats, brush-tailed porcupine, dormice, and striped mice.

Fibromas and **fibromatosis of gray squirrels** are potentially fatal conditions caused by **squirrel fibroma virus** (*Leporipoxviridae*). Disease is mainly reported in the eastern North America (Terrell et al., 2002) but also occurs in red squirrels and has been reported in a fox squirrel (Wilcoxon et al., 2015). Transmission is likely through biting arthropods (fleas, ticks, and mosquitoes). Gross and histologic lesions are similar to Shope fibromas in rabbits (both are *Leporipoxviruses*). Multifocal to coalescing tan, firm nodules may cover all parts of the body and begin as alopecic nodules with progression to plaque-like to pedunculated

masses (Fig. 20.9A). Systemic disease manifests as renomegaly and multiple pulmonary nodules (Kirschstein et al., 1958). Histologically, the skin nodules exhibit marked epidermal hyperplasia with ballooning degeneration of keratinocytes, spongiosis, and intracytoplasmic eosinophilic viral inclusions (Fig. 20.9B,C). Pulmonary nodules correlate histologically to adenomatous hyperplasia with similar viral inclusions. Other microscopic lesions may include atypical mesenchymal proliferation in the liver and seminal vesicles, and renal tubular epithelial hyperplasia with viral inclusions. Diagnosis is based on characteristic lesions and detection of virus by PCR or isolation.

Parapoxvirus is an important cause of disease in red squirrels in the United Kingdom and Ireland where it is a suspected factor in severe population declines (Bangari et al., 2009; Simpson et al., 2013; Tompkins et al., 2002). The causative agent is referred to as **Red squirrel parapoxvirus**. Grey squirrels are the likely maintenance hosts since a large percentage of healthy gray squirrels are positive for the virus and their range overlaps with that of red squirrels. Lesions in red squirrels include exudative dermatitis with crusting that is similar to other poxviral diseases. Viral inclusions can be detected histologically within the cytoplasm of infected cells. Electron microscopy and PCR are used to detect the virus.

Woodchuck hepatitis virus (WHV; Hepadnaviridae) is a disease in captive and free-ranging animals (Roth et al., 1985). Although not zoonotic, this disease is a valuable animal model for viral hepatitis and hepatocarcinogenicity associated with hepatitis B in humans. It affects both sexes and is typically found in animals greater than 4 years of age. Activated T cells (CD8 +) cause cellular and DNA damage leading to persistent hepatitis. Simultaneously, viral DNA integrates into the host genome at loci containing oncogenes, creating the potential for carcinogenic transformation. Hepatocellular carcinomas are reported in 100% of experimentally infected woodchucks. Grossly, most carcinomas are solitary and involve one hepatic lobe. Histologically, neoplastic masses have differing growth patterns: trabecular, adenoid, or solid with and without cystic spaces, hemorrhage, and necrosis. An interesting feature of these tumors is the presence of atypical, bizarre, and giant neoplastic cells. Adenomas may be present and are considered a precursor to carcinomas. Mitotic index and cellular morphology are used to classify tumors as adenomas versus carcinomas. The remaining hepatic parenchyma often contains acute and/or chronic hepatitis with neutrophilic to mononuclear inflammation, variable hepatocellular degeneration, necrosis, fibrosis, and biliary changes. Electron microscopic identification of the virus is definitive. Beechey ground squirrels have a similar virus with variable hepatic lesions (Cullen and Marion, 1996).

Hamster polyomavirus (HaPyV), a papovavirus, causes cutaneous **trichoepitheliomas** in Syrian hamsters (Foster et al., 2002). The virus is transmitted via urine

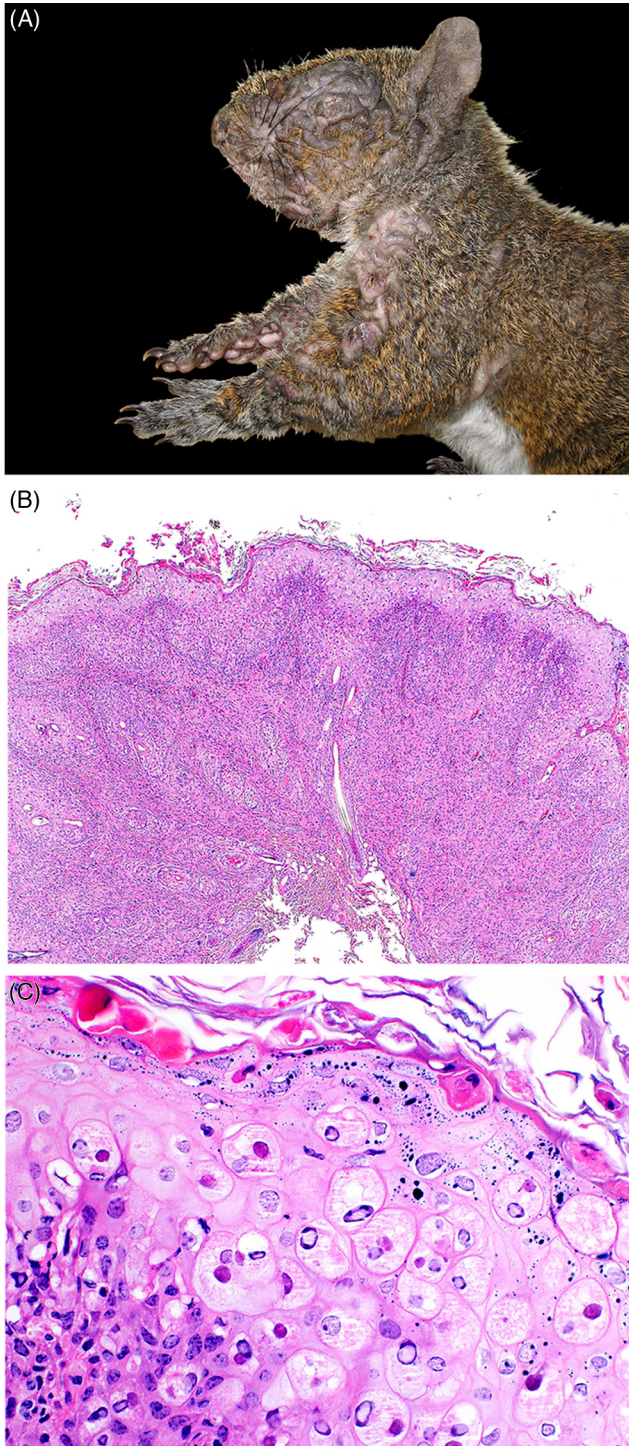


FIGURE 20.9 Fibromatosis in a free-ranging gray squirrel. (A) Multifocal, variably sized dermal plaque-like fibromas (coalescing areas of dermal thickening and alopecia) are present throughout the skin (B) The epidermis is severely thickened and there is dermal inflammation. (C) Numerous epithelial cells contain intracytoplasmic eosinophilic inclusions and are undergoing ballooning keratinocyte degeneration. Lymphocytic inflammation is present in the underlying dermis. (Part A: Photo Courtesy of J. Landolfi, University of Illinois Zoological Pathology Program; Part C: Courtesy of D. Campbell, Canadian Wildlife Health Cooperative Ontario-Nunavut)

and is highly contagious, with reported 50% morbidity in affected breeding colonies. Early lesions consist of wart-like growths and alopecic nodules of the face and perineum with progression to severe, multifocal to coalescing nodules throughout the body. Histologically, these characteristic skin tumors contain multiple islands of basilar to variably differentiated follicular epithelium and abrupt central keratinization with faded anuclear keratinocytes (ghost cells). Rudimentary hairs may be present and follicular rupture may be associated with inflammation.

Other polyomaviruses-associated neoplasms include other cutaneous tumors, lymphomas and salivary gland tumors. In virally induced lymphomas, affected tissues are effaced by diffuse sheets of neoplastic lymphocytes among scant stroma. Viral inclusions are not present. In a case of polyomavirus-induced, multicentric lymphoma in an 8-week old Syrian hamster, the virus was detected in tumor cells, renal tubular epithelial cells, and enterocytes via in situ PCR indicating some degree of tissue tropism (Simmons et al., 2001). Diagnosis is based on clinical history, gross and histologic lesions, and detection of the virus via PCR and/or electron microscopy.

RNA Viruses

Mouse hepatitis caused by **MHV** (*Coronaviridae*) is enzootic in some colonies of inbred laboratory mice (Barthold et al., 2016). Mouse hepatitis may also occur in nonlaboratory strains of mice in zoo settings. MHV causes polytropic and enterotropic disease syndromes, both of which occur following highly contagious viral infection by the oronasal route. Grossly, there is hepatomegaly, splenomegaly, lymphadenomegaly, and lymphadenopathy with jaundice and ascites. There may be gross evidence of intestinal (ileal and cecal) disease with thickened and necrotic mucosa. Within the liver, spleen, and lymph nodes, there are multiple coalescing and random white necrotic foci. Histologically, polytropic disease includes necrotizing hepatitis with syncytial cells within necrotic foci, and demyelination in CNS in immunodeficient mice. The enterotropic disease lesions are age-dependent and may include villous attenuation and syncytial cell formation with eosinophilic intracytoplasmic inclusion bodies in enterocytes, mesenteric lymph nodes, and endothelial cells; granulomatous serositis may also be present. Diagnosis is based on histologic features and immunohistochemical demonstration of viral antigens within lesions. Virus isolation, PCR, and serology are used to confirm infection and exposure, respectively.

Sendai virus infection (parainfluenza-1; Paramyxoviridae) is common in wild and pet rodents and is actively excluded from laboratory populations of mice, rats, and gerbils (Easterbrook et al., 2008). Disease manifestations occur quickly following the aerosol inhalation, direct contact, or in utero exposure. The virus targets respiratory epithelium

and type II pneumocytes, which may impair ciliary activity and predispose affected individuals to secondary *Mycoplasma pulmonis* and other bacterial infections. Gross lesions include dark purple discoloration, atelectasis, and consolidation of the cranioventral lung lobes and diffuse pulmonary edema. Splenomegaly and lymphadenomegaly are common and if infection occurs in a gravid female, fetal death may occur. Histologically, lesions include necrotizing rhinitis, laryngotracheitis, bronchitis, and bronchointerstitial pneumonia. In immunocompromised animals (e.g., athymic and SCID mice), intracytoplasmic and intranuclear inclusion bodies may be present. Diagnosis is based on supportive clinical history, histologic findings, and PCR detection of the virus.

Sialodacryoadenitis is a disease specific to rats and is caused by **sialodacryoadenitis virus (SDAV; Coronaviridae)**. The virus may be enzootic in some research colonies and in pet and free-ranging rats (Easterbrook et al., 2008). Virus is shed in nasal secretions and/or saliva. SDAV infects and replicates in the respiratory tract and spreads to salivary and lacrimal glands resulting in secondary lesions of the nasopharynx, respiratory tract, and eyes. Grossly, the parotid and submandibular salivary glands, Harderian glands, exorbital glands, and cervical lymph nodes are enlarged, pale, and edematous. The Harderian glands may exhibit brown pigmentation, which correlates to accumulations of porphyrin within acini. Histologically, there is acute necrotizing adenitis. In chronic cases, there is fibrosis and extensive squamous metaplasia of glandular tissue. There may be rhinitis, tracheitis, bronchitis, and bronchiolitis in severe and chronic cases. Histologic lesions are characteristic and supportive of the diagnosis.

Bacteria

Within this section are several zoonotic and notable non-zoonotic bacteria that infect rodents. Several others that are notable but not associated with disease in their rodent host are listed in the Supplemental Materials (Table e2).

Zoonotic Bacteria

Plague is an OIE-listed and WHO-reportable zoonotic disease that is important to consider when working with rodents. Fleas spread the causative agent, ***Yersinia pestis***, between hosts. Cats and other rodent-eating predators can also contract infection through ingestion and rarely via inhalation. Historically, plague has been implicated in the deaths of millions of humans, most notably in 14th century Europe during the Black Death. There are two main host types: enzootic reservoirs (voles and deer mice) and epizootic amplifiers (prairie dogs, rats, and squirrels). With close to 100% mortality, plague outbreaks in prairie dog colonies are a devastating and significant threat not only this species but to endangered black-footed ferrets,

who are susceptible to disease because prairie dogs are their primary food source (Cully et al., 2010). There are three disease forms: bubonic (lymphadenomegaly with abscessation); pneumonic (necrotizing pneumonia with fibrinous pleuritis); and septicemic (multifocal necrosis of liver, lung, spleen, kidney, eye, brain). Gross lesions include multifocal pulmonary hemorrhage (Fig. 20.10), hemorrhagic lymph nodes, erythema of axillary and inguinal skin, splenomegaly and localized hemorrhage and necrosis in the dermis and subcutis (suspected site of flea bite). Histologic lesions of bubonic disease include necrosuppurative lymphadenitis; in the pneumonic form, necrotizing pneumonia; and in the septicemic form, multifocal abscessation. All lesions contain Gram and Giemsa positive coccobacilli with characteristic bipolar morphology resembling a safety pin. Bacterial culture must be completed at a certified, biosecure laboratory; identification using immunohistochemistry or immunofluorescence is a beneficial diagnostic aid.

Yersiniosis (Pseudotuberculosis) is caused by *Y. pseudotuberculosis* and *Y. enterocolitica*. Rodents may serve as carriers of this zoonotic bacterial agent, though some species, including mice, voles, beavers, and muskrats may succumb to acutely fatal disease or develop more characteristic lesions and symptoms. Gross and histologic lesions include multifocal necrotizing hepatitis and splenitis and/or



FIGURE 20.10 Plague in a prairie dog. Multifocal pulmonary hemorrhage is consistent with *Yersinia pestis* infection. (Photo Courtesy of K. Fox, Colorado Parks and Wildlife)

fibrinonecrotizing and ulcerative enterocolitis (Fig. 20.11). Agoutis appear to be uniquely susceptible in zoo-settings (K. Terio, personal communication).

Tularemia caused by *Francisella tularensis* is an important zoonotic and OIE listed reportable disease that is maintained by wild rodents and lagomorphs. Disease occurs in many rodents including mice, beavers, and muskrats, while voles appear to be subclinical carriers and serve as a reservoir (Nelson et al., 2014; Rossow et al., 2014). Lesions of affected species are similar to those described in rabbits (see Chapter 19). Miliary to multifocal and coalescing hepatic necrosis with variable inflammation (depending on chronicity) characterize the disease (Fig. 20.12). Unlike yersiniosis and similar to listeriosis, bacteria are not readily detected but can be better visualized with special stains.

Listeriosis is a common zoonotic bacterium in rodent species. It can cause variable, yet similar lesions as for rabbits (see Chapter 19). The systemic form is most common. During an outbreak in bushy-tailed jirds, death occurred without clinical signs (Tappe et al., 1984).

Salmonellosis is reported in guinea pigs, rats, and mice, though any rodent species can be infected and develop disease. *Salmonella enterica* Enteritidis or Typhimurium are the most common zoonotic serovars. Guinea pigs become septicemic and often die acutely. Other rodents may develop gastrointestinal disease that includes diarrhea and abdominal pain prior to systemic spread. In hamsters, salmonellosis must be considered and ruled out in cases of “wet tail,” which is typically associated with infection by *Lawsonia intracellularis*. Gross lesions of salmonellosis include cyanosis of mucous membranes and polyserositis with splenomegaly. Hepatic, splenic, and lymph node

necrosis are typical, as are multifocal necrosis and button ulcers in the colon with segmental intestinal infarction. Histologic lesions correlate to gross findings and include small foci of hepatocellular necrosis containing necrotic cell debris and variable numbers of macrophages, lymphocytes, and fewer neutrophils (paratyphoid nodules) and Kupffer cell hyperplasia; granulomatous hepatitis, splenitis, and lymphadenitis; and fibrinonecrotic ileotyphlocolitis. Intestinal infarction can be attributed to vasculitis and thrombosis of the mesenteric or mesocolic vessels. Culture of the causative agent and histologic lesions confirm the diagnosis.

Mycobacteriosis is a zoonotic disease that is rarely reported in rodents, though some species may serve as reservoirs. There are reports of mycobacteriosis (*Mycobacterium microti*) in British voles and wood mice (Cavanagh et al., 2002), hamsters, and Korean and Richardson’s ground squirrels in Spain.

Chlamydomphila caviae and less frequently *C. psittaci* cause disease in guinea pigs, primarily juveniles. Conjunctivitis, bronchitis, and pneumonia may occur and result in debilitation and death. Histologically, there is heterophilic keratoconjunctivitis and uveitis. Pneumonia has a cranioventral pattern and is heterophilic. Some animals may be asymptomatic. Diagnosis is achieved through cytology of ocular discharge and/or PCR of affected tissues. Immunohistochemistry of tissue sections is also available.

Nonzoonotic Bacteria

Bordetella bronchiseptica causes **bordetellosis (epizootic pneumonia)**, a common respiratory disease in guinea

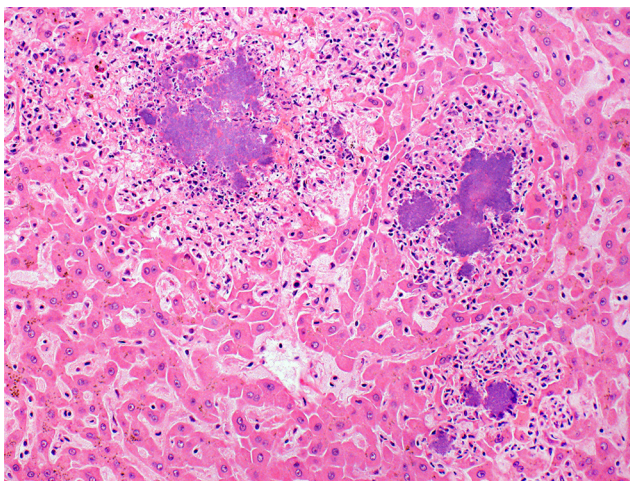


FIGURE 20.11 Yersiniosis in the liver of a free-ranging North American beaver. Bacterial infection causes multifocal, random, necrosis throughout the hepatic parenchyma. Large, central colonies of the causative agent, *Yersinia pseudotuberculosis* are surrounded by mild neutrophilic inflammation and necrotic cell debris. (Photo Courtesy of D. Campbell, Canadian Wildlife Health Cooperative Ontario-Nunavut)

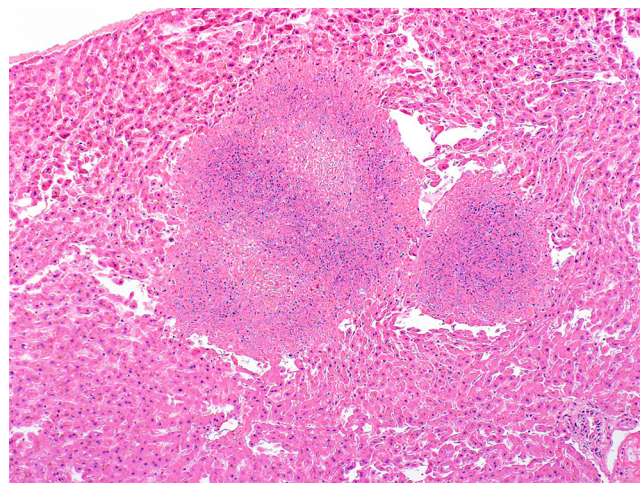


FIGURE 20.12 Tularemia in the liver of a free-ranging North American beaver. Large, multifocal random areas of coagulative necrosis are present throughout the hepatic parenchyma. Note the relative lack of inflammation. Unlike Yersiniosis, bacterial colonies are not readily detected with routine hematoxylin and eosin staining. (Photo Courtesy of D. Campbell, Canadian Wildlife Health Cooperative Ontario-Nunavut)

pigs though is also reported in free-ranging squirrel populations (Simpson et al., 2013). Similar disease can occur in other rodents, particularly in the context of immunosuppression or coinfection. Grossly, there is cranioventral pneumonia with multifocal to coalescing, discrete, reddish-gray consolidated regions affecting multiple lobes, and pleuritis. Mucopurulent exudate may be present in the nares, nasal passages, trachea, and tympanic bullae. There is often crusting conjunctivitis. Females may have metritis and pyosalpinx. Histologically, lung lesions consist of necrotizing and heterophilic bronchopneumonia with obliteration of the airways. Diagnosis is confirmed with bacterial culture or PCR. Other predisposing pathogens (e.g., adenovirus, *Mycoplasma* spp.) must be ruled out.

Ciliated associated respiratory (CAR) bacillus is an unclassified bacterium that colonizes the ciliated epithelium of the respiratory tract of rats, mice, rabbits, and a variety of other species. This agent acts synergistically with other respiratory pathogens including *Mycoplasma pulmonis*, Sendai virus, coronavirus, *Streptococcus pneumoniae*, *Corynebacterium kutscheri*, *Bordetella bronchiseptica*, *Klebsiella pneumoniae*, or *Pasteurella* spp. Lesions include suppurative to mucopurulent bronchopneumonia, perivascular and bronchiolar lymphoid hyperplasia, rhinitis and lymphoplasmacytic tracheitis in free-ranging, pet and laboratory rats (Baker, 1998; Rothenburger et al., 2015b). Coinfection of CAR bacillus and mycoplasmas has been reported in rats and spinifex hopping mice with pneumonia (Mackie et al., 2001).

Murine respiratory mycoplasmosis is caused by *Mycoplasma pulmonis* (Baker, 1998). Gross lesions include catarrhal exudate in the upper respiratory tract with cranioventral bronchopneumonia and mucopurulent exudate in airways with atelectasis. Histologic lesions include peribronchial lymphoid cuffing with BALT hyperplasia; neutrophilic bronchopneumonia; type II pneumocyte hyperplasia of alveolar epithelium; and emphysema; bronchiectasis is a characteristic finding. Histology alone cannot differentiate *M. pulmonis* and CAR bacillus respiratory infections (Rothenburger et al., 2015b). Other lesions associated with *M. pulmonis* include endometritis, salpingitis, and perioophoritis. Diagnosis is based on histologic features, culture or PCR detection, and ELISA.

Pasteurellosis caused by *P. multocida* affects young and immunocompromised rodents, most frequently following direct transmission from the dam. Strain virulence and species determine lesions, which in general, are similar to those reported in other species, including rabbits (see Chapter 19). Prairie dogs develop upper respiratory disease and pneumonia, while conjunctivitis is more common in rats and mice. Hamsters have variable susceptibility.

Cervical lymphadenitis, a disease classically described in guinea pigs, is caused by *Streptococcus equi* subsp.

zoepidemicus. Infection is associated with coarse foods that cause traumatic lesions of the oral mucosa; bite wounds may serve as another route of entry. Grossly, the cervical and submandibular lymph nodes are markedly enlarged and contain thick purulent yellow-white to red-gray exudate. Lymph nodes in severely affected and chronic cases may rupture. Histologically, affected lymph nodes are effaced by heterophilic lymphadenitis with central necrosis and peripheral fibrosis. Thoracic lesions include fibrinous pleural adhesions, fibrinosuppurative bronchopneumonia, pleuritis, and pericarditis. Chains of Gram-positive cocci are present within lesions. Diagnosis is based on gross and histologic lesions and culture of causative agent.

Tyzzers' Disease, caused by *Clostridium piliforme*, is a potentially fatal disease of many rodent species. It has been reported in captive gerbils, hamsters, and spinifex hopping mice (Stannard et al., 2017). Infection results in a triad of gross lesions including icterus and hepatomegaly with military gray foci, congestion, and edema of the intestine, and lymphadenomegaly with edema and hemorrhage. Sudden death without clinical disease or lesions is possible in peracute cases. Histologically, multifocal random to coalescing hepatic necrosis is surrounded by hemorrhage, heterophils, and macrophages (Fig. 20.13A). At the necrotic margins, hepatocytes may accumulate characteristic criss-crossed bundles of faintly staining bacilli that are best visualized with silver stains (Fig. 20.13B).

Proliferative ileitis (wet tail) due to *Lawsonia intracellularis* is most commonly reported in hamsters. Similar to this infection in other species, there is segmental thickening of ileum with serosal nodules. Histologically, there is marked crypt hyperplasia and herniation and villous elongation, hyperplasia, and fusion with variable necrosis and hemorrhage. Silver stains and PCR are useful to confirm infection.

Fungi

A diverse array of *Pneumocystis* spp. are carried without clinical signs by a variety of wild rodents; these organisms are thought to be highly host-specific. *Pneumocystis* spp. are found within alveoli and alveolar macrophages and appear as small, eosinophilic round organisms with a small central body. In severe cases, organisms within alveolar spaces and alveolar macrophages can obliterate alveoli; in some cases they can be associated with interstitial pneumonia (Fig. 20.14A,B). This fungus can cause significant opportunistic infections in immunocompromised individuals.

Cryptococcosis (*Cryptococcus neoformans*) can be a significant pathogen in some rodent species. For example, approximately 20% of slender-tailed cloud rats at one zoological institution died with or as a result of cryptococcal pneumonia over a 15-year period (Berliner et al., 2007). These large, arboreal rodents were likely infected by

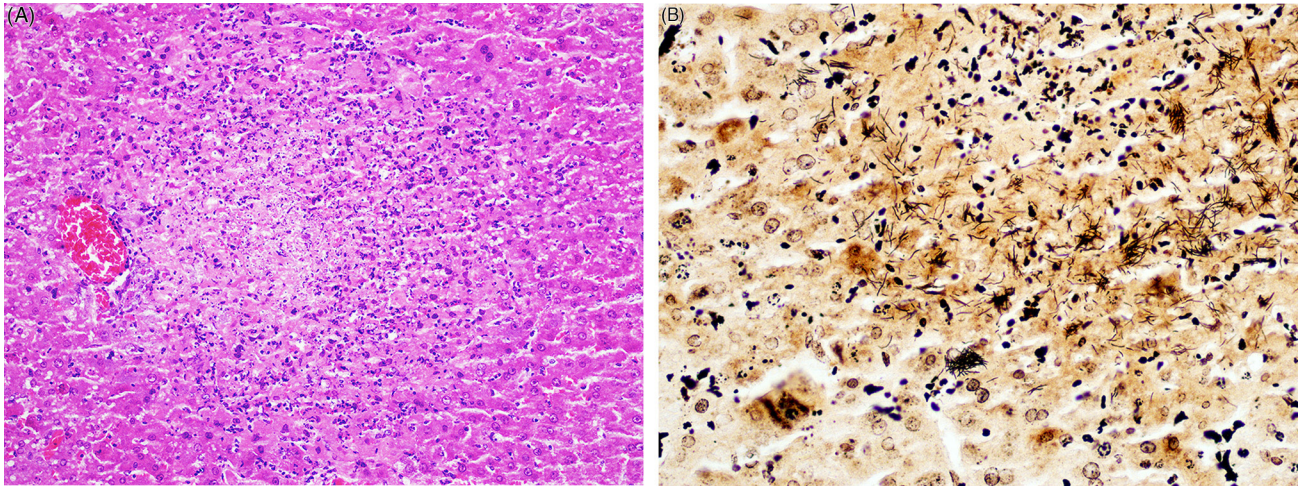


FIGURE 20.13 Tyzzer's disease (*Clostridium piliforme*) in the liver of a gerbil. (A) There is multifocal to coalescing necrosis of hepatic parenchyma with low numbers of faintly basophilic bacilli. (B) Multiple individual and clusters of filamentous *Clostridium piliforme* stain brown-black. Steiner's silver stain. (Photo Courtesy of J. Landolfi, University of Illinois Zoological Pathology Program)

contaminated substrates and may be a highly susceptible species, similar to some species of nonhuman primates and felids. Lesions included none or mild to severe, chronic granulomatous pneumonia with or without necrosis and regional lymphadenitis. Disseminated disease can produce subcutaneous nodules (cryptococcoma) and meningoencephalitis. Microscopically, characteristic fungal yeasts with narrow-based budding are present in cytologic preparations and histologic sections. GMS staining can enhance detection of fungal yeasts, which are 5–20 μm diameter with a distinct, thick (5–10 μm), nonstaining mucopolysaccharide capsule, the latter of which is best visualized using the PAS reaction and mucin stains. Culture can confirm infection (Fig. 20.15)

Adiaspiromycosis is a systemic fungal disease reported in several captive and free-ranging rodent species. It is caused by the saprophytic fungi *Chrysosporium parum* and *C. crescens*. Once inhaled, these fungi cause pulmonary granulomas with fungal spherules and conidia. Additional diagnostic tests may be useful, including immunodiffusion and complement fixation. These fungi are zoonotic.

Other systemic mycoses of rodents include infections caused by the endemic (and zoonotic) fungi *Blastomyces dermatitides* and *Histoplasma capsulatum*. Reported cases include juvenile mice and chinchillas. Immunity to fungal pathogens appears limited in mice.

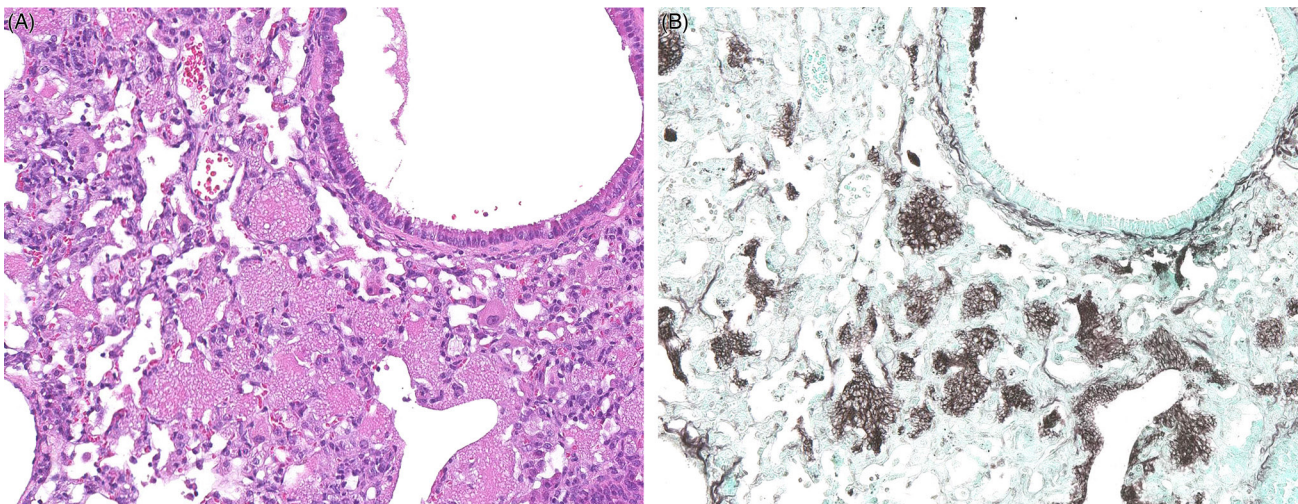


FIGURE 20.14 *Pneumocystis* spp. in the lungs of an immunocompromised mouse. (A) Alveoli are filled with lightly eosinophilic material that appears foamy to honeycomb and is associated with chronic pneumonitis. (B) Silver stains are useful to highlight intralesional and intracellular pneumocystis cysts. GMS (Reprinted with permission from Treuting et al., Vet Pathol, 49:44–63, 2012).

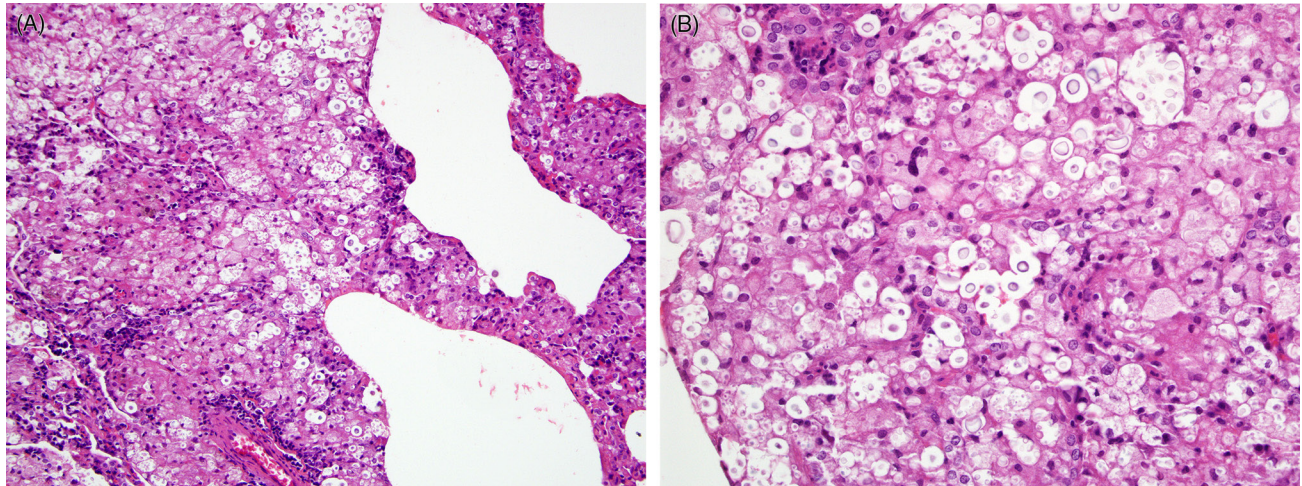


FIGURE 20.15 Cryptococcosis in the lungs of a slender-tailed cloud rat. (A) The interstitium is moderately to markedly expanded and distorted by myriad fungal yeasts and associated histiocytic to granulomatous inflammation. Aggregates of lymphoplasmacytic inflammation can be seen but are typically infrequent. (B) Yeast vary in size, have narrow-based budding, and are surrounded by a thick mucopolysaccharide capsule that does not stain with hematoxylin and eosin and appears as a clear halo. (Photos Courtesy of D. McAloose, Wildlife Conservation Society)

Dermatophytosis is a cutaneous fungal disease that can be found in any rodent species and is similar to that of other mammalian species. Causative agents include *Trichophyton mentagrophytes*, *Microsporum canis*, *M. gypseum*, and *Epidermophyton*. Of note, these fungi are zoonotic and can cause skin lesions in other animals. Additionally, *Sporothrix schneckii* associated cutaneous disease is reported in several rodent species and can be zoonotic. Dermatitis lesions vary from suppurative and necrotizing to granulomatous and fibrosing depending on chronicity. PAS-positive yeast are present within macrophages. Character-

istic organisms on cytologic preparations of skin scrapes prepared with potassium hydroxide support the diagnosis.

Metazoa

Capillaria hepatica (synonym **Calodium hepaticum**) affects a broad host range worldwide, including rodents and humans. It is a ubiquitous parasite of globally invasive Norway and black rat populations (Rothenburger et al., 2014). Gross lesions consist of multifocal to coalescing, tortuous, white tracks in the liver parenchyma (Fig. 20.16A). Histologically,

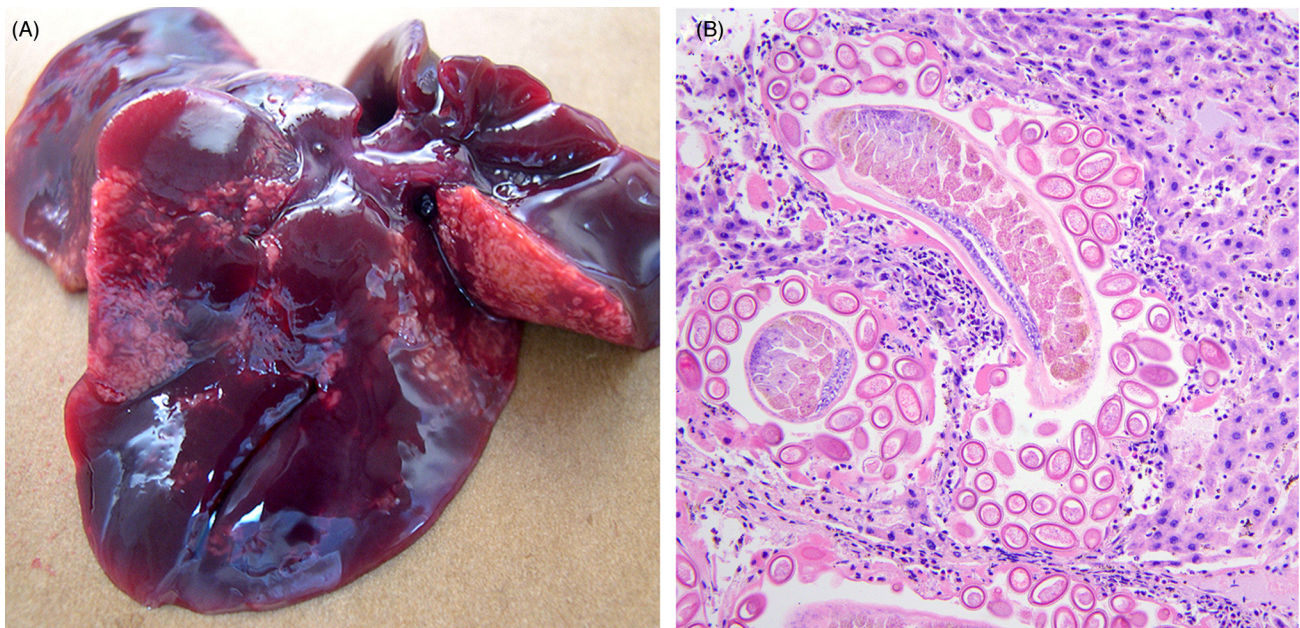


FIGURE 20.16 *Capillaria hepatica* in the liver of a free-ranging Norway rat. (A) Multiple liver lobes contain locally extensive tortuous, white nematode tracks. (B) Adult nematodes and eggs replace the liver parenchyma. The eggs are characteristically bioperculate. Inflammation is lymphoplasmacytic to granulomatous and may be associated with fibrosis in chronic infections.

varying combinations of lymphoplasmocytic and granulomatous inflammatory infiltrates, fibrosis, and bioperculate eggs and occasionally adult parasites replace hepatic parenchyma (Fig. 20.16B). Cross sections of viable or mineralized capillarid nematodes may be present. Eggs are only released from the liver following carcass decomposition or ingestion by a predator/cannibalistic conspecific. Therefore, diagnosis is based on the presence of the nematode and/or eggs in the liver and not fecal parasitology.

Many species of free-ranging rodents are susceptible to fatal visceral larval migrans associated with the raccoon nematode *Baylisascaris procyonis* (Fig. 20.17). Significant clinical disease is often related to parasite migration in the brain, where they may be accompanied by low numbers of eosinophils, gliosis, spheroids, and rarefaction or necrosis of the neuropil.

Ectoparasites

Rodents, particularly squirrels are prone to **Notoedric mange** (Anholt et al., 2014; Cornish et al., 2001; Stephenson et al., 2013). Mites burrow into the stratum corneum inducing marked hyperkeratosis, which results in patchy alopecia, and crusting and thickening of the skin (lichenification), which can appear yellow to gray. Gross lesions are predominantly found on the ears, nose, tail, external genitalia, inguinal and perianal regions, and feet though they can cover the entire body in severe cases. Peripheral lymphadenopathy may also be seen. Skin scrapings and fecal floats are beneficial to best examine mite features and presence of eggs, respectively. Histologically, there is marked

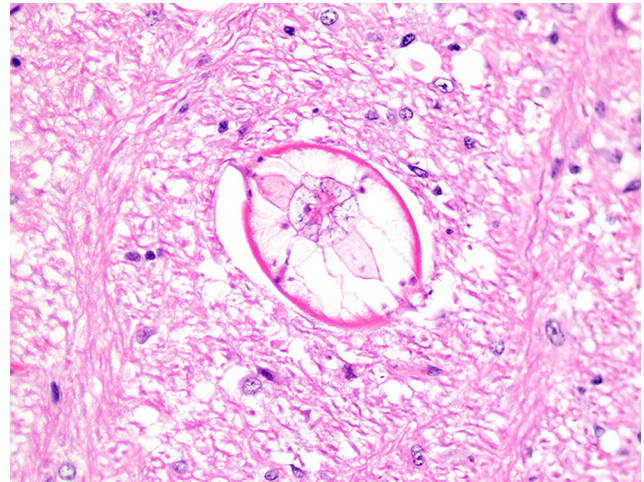


FIGURE 20.17 Visceral larval migrans due to *Baylisascaris procyonis* in the brain of a free-ranging groundhog. The larval nematode parasites contain prominent lateral alae and lateral cords, a thick cuticle, and coelomyarian musculature. (Photo Courtesy of J. Landolfi, *Of Mice and Microflora Considerations for Genetically Engineered Mice*. P. M. Treuting, C. B. Clifford, R. S. Sellers, C. F. Brayton. First Published December 14, 2011)

epidermal hyperplasia with parakeratotic hyperkeratosis forming caps over tunnels containing mites with superficial, perivascular eosinophilic dermatitis (Fig. 20.18A,B). Secondary bacterial infections are common. Additional notable parasites of rodents are listed in the Supplemental Materials (Table e3).

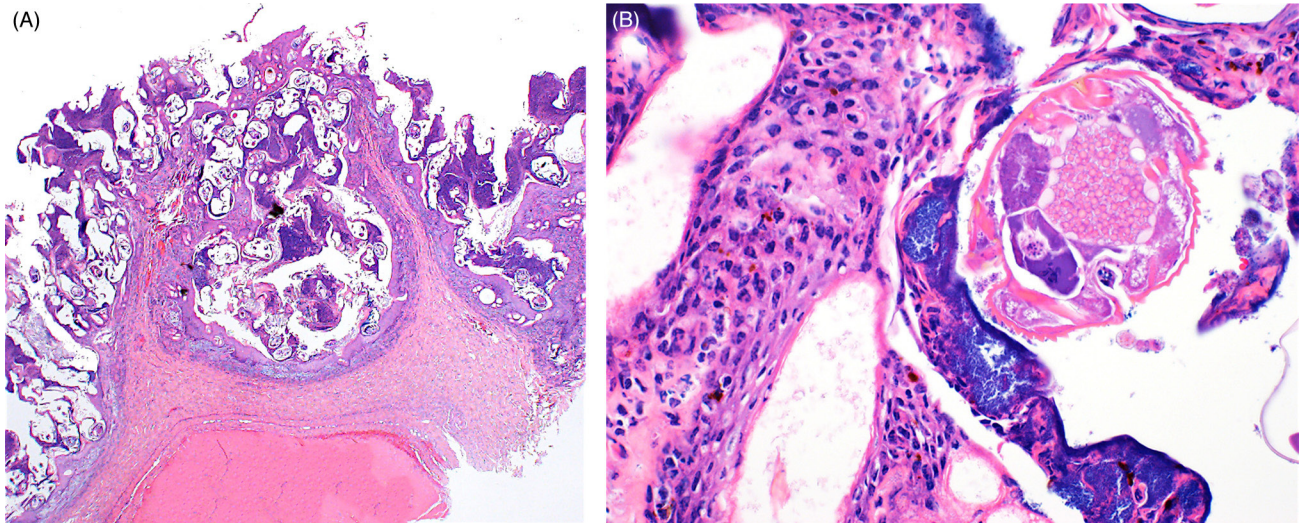


FIGURE 20.18 Notoedric mange in a free-ranging grey squirrel. (A) Severe hyperkeratosis and epidermal hyperplasia contain multiple large mite tunnels. (B) Cross section of a *Notoedres centrifera* mite adjacent to colonies of coccoid bacteria, parakeratotic hyperkeratosis, and neutrophilic cellular debris. (Photos Courtesy of D. Campbell, Canadian Wildlife Health Cooperative Ontario-Nunavut)

E-SLIDES

- 20.e1 Chronic progressive nephropathy (CPN), naked mole-rat, kidney.** In the kidney, there is marked ectasia of tubules and Bowman's spaces forming numerous microcysts seen at low magnification. Some ectatic tubules contain luminal proteinaceous material and there is multifocal tubular degeneration, necrosis, and regeneration. Interstitium has areas of mixed inflammation, fibrosis and edema. Glomeruli have segmental to global membranous change and multifocal sclerosis. (see Fig. 20.4). Hepatic hemosiderosis is seen in sections of the liver. eSlide: [VM05054](#)
- 20.e2 Chronic progressive nephropathy (CPN), naked mole-rat, kidney.** In the kidney, there is marked ectasia of tubules and Bowman's spaces forming numerous microcysts seen at low magnification. Some ectatic tubules contain luminal proteinaceous material and there is multifocal tubular degeneration, necrosis, and regeneration. Interstitium has areas of mixed inflammation, fibrosis and edema. Glomeruli have segmental to global membranous change and multifocal sclerosis. (see Fig. 20.4). Hepatic hemosiderosis is seen in sections of the liver. eSlide: [VM05053](#)
- 20.e3 Chronic progressive nephropathy (CPN), naked mole-rat, kidney.** There is mild to moderate ectasia of tubules and Bowman's spaces forming numerous microcysts seen at low magnification. Some ectatic tubules contain luminal proteinaceous material and there is multifocal tubular degeneration, necrosis, and regeneration. Interstitium has areas of mixed inflammation, fibrosis and edema. Glomeruli have segmental to global membranous change and multifocal sclerosis. (see Fig. 20.4). eSlide: [VM05057](#)
- 20.e4 Hepatic hemosiderosis, naked mole-rat, liver.** Prussian blue staining highlights bright blue granular intracytoplasmic (iron) pigments throughout the liver. The kidney has changes consistent with chronic progressive nephropathy. eSlide: [VM05058](#)
- 20.e5 Yersiniosis, beaver, liver and diaphragm.** Yersiniosis in the liver and diaphragm of a free-ranging North American beaver. Bacterial infection causes multifocal random necrosis throughout the hepatic parenchyma. Large, central colonies of the causative agent, *Yersinia pseudotuberculosis* are surrounded by mild neutrophilic inflammation. (see Fig. 20.11). eSlide: [VM04954](#)
- 20.e6 Tularemia, beaver, liver and spleen.** Tularemia in the liver and spleen of a free-ranging North American beaver. Large, multifocal random areas of coagulative necrosis are present throughout the hepatic and splenic parenchyma. Note the relative lack of inflammation. Unlike Yersiniosis, bacterial colonies are not readily detected with routine hematoxylin and eosin staining. (see Fig. 20.12). eSlide: [VM04952](#)
- 20.e7 Pneumocystis murina pneumonia, mouse, lung.** Multifocally, alveoli are partially to completely filled with large macrophages containing small round yeasts. (see Fig. 20.14). eSlide: [VM05178](#)
- 20.e8 Pneumocystis murina pneumonia, mouse, lung, GMS.** Gomori methenamine silver (GMS) staining highlights the intrahistiocytic yeasts within the alveoli. (see Fig. 20.14). eSlide: [VM05275](#)
- 20.e9 Pulmonary cryptococcosis, slender-tailed cloud rat, lung.** The interstitium and air spaces are moderately to markedly expanded and distorted by myriad fungal yeasts that are associated with histiocytic to granulomatous inflammation. Aggregates of lymphoplasmacytic inflammation are present but infrequent. (see Fig. 20.15). eSlide: [VM05089](#)
- 20.e10 Pulmonary cryptococcosis, slender-tailed cloud rat, lung. GMS.** Intralesional yeasts are highlighted gray/blue with silver staining. GMS (see Fig. 20.15). eSlide: [VM05096](#)
- 20.e11 Pulmonary cryptococcosis, slender-tailed cloud rat, lung. Mucicarmine.** Mucicarmine staining highlights the thick mucopolysaccharide capsule of the cryptococcal yeast and stains it bright pink. Mucicarmine (see Fig. 20.15). eSlide: [VM05097](#)
- 20.e12 Capillaria hepatica (Calodium hepaticum), Norway rat, liver.** *Capillaria hepatica* in the liver of a free-ranging Norway rat. Adult nematodes and eggs invade and efface the liver parenchyma. There are examples of viable and degenerative adults. The eggs are characteristically bioperculate with a thick shell. Inflammation is lymphoplasmacytic to granulomatous and is associated with fibrosis indicating chronic infection. In some areas, there is multifocal mineralization adjacent to eggs. (see Fig. 20.16). eSlide: [VM04956](#)
- 20.e13 Baylisascaris visceral larval migrans, groundhog, brain.** Multifocally, multiple sections of larval nematodes with prominent lateral alae and lateral cords, a thick cuticle, and coelomyarian musculature, features consistent with larval ascarids, are present in the brain. Inflammation, including eosinophils, gliosis, and spheroids and rarefaction of the neuropil due to parasite migration, are multifocal and occasionally associated with intralesional nematodes. (see Fig. 20.17). eSlide: [VM04961](#)

E- ONLY CONTENTS

TABLE e1 Rodent Neoplasia

System	Species Affected	Neoplasia Type	References
Cardiovascular			
	Rats	Endocardial schwannoma	Berridge (2016)
	Guinea pig	Myocardial rhabdomyoma	Barthold (2016)
Endocrine			
	Rats	Adrenocortical adenoma	Strandberg (1983)
	Rats	C cell carcinoma	Boorman (1996)
	Rats	Pituitary adenoma	Benitz (1965), Barthold (2016)
Glands			
	Mice, Rats	Mammary adenocarcinoma	Rudman (2012); Krinke (1994), Krinke (1996)
	Mice, Rats	Mammary fibroadenoma	Rudman (2012); Krinke (1994), Krinke (1996)
	Gray squirrel	Mammary (mixed malignant)	Williams (1989)
	Mice, Rats	Zymbal gland adenoma/carcinoma	Rudman (2012); Krinke (1994), Krinke (1996)
	Mice, Rats	Preputial/Clitoral adenoma/carcinoma	Rudman (2012), Barthold (2016), Krinke (1994), Krinke (1996)
Female reproductive			
	Mice, Rats	Ovarian adenocarcinoma	Dixon (2014), Krinke (1994), Krinke (1996)
	Mice	Teratoma	Dixon (2014), Barthold (2016)
	Mice, Rats	Uterine decidual reaction/deciduoma	Dixon (2014)
	Woodchuck, mice, rats	Uterine leiomyoma	Foley (1993), Dixon (2014)
	Mice, Rats	Uterine leiomyosarcoma	Dixon (2014)
Male reproductive			
	Woodchuck	Adenoma of the rete testis	Foley (1993)
	Rat, woodchuck	Interstitial cells tumors	Foley (1993), Barthold (2016), Creasy (2012)
	Woodchuck	Sertoli cell tumors	Foley (1993)
	Woodchuck	Seminoma	Foley (1993)
	Woodchuck, mice	Teratoma	Foley (1993), Barthold (2016), Creasy (2012)
Hepatobiliary			
	Rat	Foci of cellular alteration	Thoolen (2010)
	Woodchuck, rat, mice	Hepatocellular adenoma	Roth (1991), Thoolen (2010), Krinke (1994), Krinke (1996)
	Woodchuck, rat, mice	Hepatocellular carcinoma	Roth (1985), Thoolen (2010), Krinke (1994), Krinke (1996)
Hemolymphatic			
	Mice, Rats	Histiocytic sarcoma	Krinke (1994), Krinke (1996), Kogan (2002), Barthold (2016)
	Guinea pig, rat	Lymphocytic leukemia	Yarto-Jaramillo (2011), Barthold (2016)
	Guinea pig, hamster, mice, woodchuck, rat	Lymphoma	Nagy (2002), Simmons (2001), Yarto-Jaramillo (2011), Kogan (2002), Barthold (2016)
	Woodchuck, mice, rats	Myeloproliferative disease	Roth (1991), Kogan (2002), Barthold (2016)

TABLE e1 Rodent Neoplasia (Cont.)

System	Species Affected	Neoplasia Type	References
Gastrointestinal			
	Black-tailed prairie dogs	Odontoma	Phalen (2000)
	Tree squirrels	Elodontoma	Boy (2006)
	Red squirrels	Gastric spindle cell tumor	Simpson (2013)
	Muskrat, free-ranging rats	Gastric squamous papillomas	Cosgrove (1968), Rothenburger (2014)
	Woodchuck	Oral leiomyosarcoma	Kang (2005)
Integument			
	Red backed vole	Adnexal carcinoma	Williams (1989)
	Gerbils, guinea pigs	Aural polyps	Benitz (1965)
	Gerbils	Ear canal fibropapilloma	Benitz (1965)
	Gerbils	Cholesteatomas	Benitz (1965)
	Gray, red, and fox squirrels	Fibroma	Bangari (2009)
	Beechey ground squirrel, rats, mice	Harderian gland carcinoma	Ranck (2008), Barthold (2016), Krinke (1994), Krinke (1996)
	Ground squirrel	Integumentary gland adenocarcinoma	Carminato (2012)
	Damaraland mole rat	Melanomas	Sura (2011)
	Yellow cheeked vole	Sebacious gland adenoma	Williams (1989)
	Capybara, tundra vole, arctic ground squirrel, woodchuck	Squamous cell carcinoma	Hamanno (2014), Takahisa (2014), Anderson (1990)
	Beaver, insular vole, porcupine	Squamous papilloma	Williams (1989)
	Hamsters, red squirrels	Trichoepithelioma	Foster (2002), Simpson (2013)
	Guinea pig	Trichofolliculoma	Barthold (2016)
Musculoskeletal, Adipose, Connective tissue			
	Damaraland mole rat	Fibrosarcoma	Sura (2011)
	Rat	Hibernomas	Brunner (2009)
	Woodchuck	Lipoma	Anderson (1990)
		Liposarcoma	
	Mice, Rats	Mesenchymal tumors	Greaves (2013)
	Rat, woodchuck	Mesothelioma	Barthold (2016), Creasy (2012), Kang (2004)
	Beaver	Rhabdomyoma	Williams (1989)
	Red backed vole	Rhabdomyosarcoma	Williams (1989)
	Tundra vole	Osteoma	Williams (1989)
Respiratory			
	Guinea pig	Alveogenic carcinoma	Yarto-Jaramillo (2015)
	Guinea pig	Bronchogenic carcinoma	Yarto-Jaramillo (2015)
	Guinea pig	Papillary adenoma	Yarto-Jaramillo (2015)
	Gray squirrels	Pulmonary adenomatosis	Kirschstein (1958)
	Red squirrels, mice	Pulmonary carcinoma	Simpson (2013), Barthold (2016), Renne (2009)
	Mice, Rats	Pulmonary adenoma	Barthold (2016), Renne (2009)
Urinary			
	Red and Gray squirrels, mice, rats	Renal adenoma	Simpson (2013), Williams (1989), Frazier (2012)
	Mice, Rats	Renal carcinoma	Frazier (2012)

(Continued)

TABLE e1 Rodent Neoplasia (Cont.)

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TABLE e2 Summary of Zoonotic Pathogens and Associated Diseases of Rodents*

	Etiology	Disease Name	Known Host	Disease in Host (if any)	Other Species infected	Disease in non-host species	Disease in Humans	Transmission Route	References
Bacteria									
	<i>Bartonella</i> spp.	Bartonellosis	Many rodent species	None	Dogs, cats	None, endocarditis, myocarditis	Lymphadenopathy, neuroretinitis, endocarditis, myocarditis, acute febrile illness, anemia and chronic fatigue	Fleas, ticks, lice, flies, contact with infected blood	Gutiérrez (2015)
	<i>Francisella tularensis</i>	Tularemia	Beavers, muskrat, rabbits	NA	Mice, squirrels, hares, many mammal susceptible	Sudden death, necrotizing hepatitis and splenitis	Febrile illness, lymphadenitis, pneumonia, sepsis	Direct contact with infected animals, ticks, flies, contaminated water	Wobeser (2007), Wobeser (2009), Mörner (1992)
	<i>Leptospira</i> spp.	Leptospirosis	Rats, many rodent species	None, interstitial nephritis	Guinea pigs, hamsters	Sudden death, vasculitis, hemorrhage	Fever, icterus, pulmonary hemorrhage	Contact with urine-contaminated water	Adler (2010)
	<i>Listeria monocytogenes</i>	Listeriosis	Rats, mice, many rodent species	None	Cattle, sheep, rabbits, hares	Abortion, septicemia, encephalitis	Abortion, septicemia, encephalitis	Fecal-oral	Low (1997)
	<i>Rickettsia akari</i>	Rickettsialpox	House mice and rats	None	Other rodents, dogs	NA	Febrile illness, lymphadenopathy, papulovesicular rash	Biting mites	Meerburg (2009)
	<i>Rickettsia typhi</i>	Murine/Endemic typhus	Rats	None	House mice, cats, dogs, opossums, skunks	NA	Febrile illness, rash	Fleas, other ectoparasites	Meerburg (2009)
	<i>Streptobacillus moniliformis</i> and <i>S. minus</i>	Rat bite fever	Norway and black rats	Infected bite wounds, abscesses	NA	NA	Rash, arthritis, variably severe febrile illness, death	Rodent bites (also in urine and blood)	Meerburg (2009)
	<i>Yersinia enterocolitica</i>	Yersiniosis (syn. Pseudotuberculosis)	Many rodent species	Necrotizing hepatitis, splenitis, enterocolitis	Mice, voles, beavers, muskrats, agoutis, hares	Necrotizing hepatitis, splenitis, enterocolitis	Enterocolitis, fever	Fecal-oral via contaminated food and water	Mair (1973), Gasper (2009)
	<i>Yersinia pestis</i>	Plague	Voles, deer mice, prairie dogs, rats, squirrels	Bubonic, pneumonic, septicemic	Cats	Bubonic, pneumonic, septicemic	Bubonic, pneumonic, septicemic	Fleas, contact with infected animals, inhalation	Gage (2005), Wobeser (2009)
	<i>Yersinia pseudotuberculosis</i>	Yersiniosis (syn. Pseudotuberculosis)	Many rodent species	Necrotizing hepatitis, splenitis, enterocolitis	Mice, voles, beavers, muskrats, agoutis, hares	Necrotizing hepatitis, splenitis, enterocolitis	Enterocolitis, fever	Fecal-oral via contaminated food and water	Mair (1973), Gasper (2009)

(Continued)

TABLE e2 Summary of Zoonotic Pathogens and Associated Diseases of Rodents (*Cont.*)

	Etiology	Disease Name	Known Host	Disease in Host (if any)	Other Species infected	Disease in non-host species	Disease in Humans	Transmission Route	References
Viruses									
	<i>Orthopoxviridae</i>	Pox (Mousepox, Cowpox)	Mice and other rodents	Ectromelia (mice): acute mortality, chronic (crusting dermatosis of face, legs and tail; conjunctivitis, organ and lymph node necrosis)	Many rodent species susceptible	Cutaneous lesions	Cutaneous lesions	Direct contact	Meerburg (2009)
	<i>Orthopoxviridae</i>	Monkeypox	Monkeys, Gambian giant rat, squirrels	Cutaneous lesions	Prairie dogs	Necrotizing bronchopneumonia, conjunctivitis, and tongue ulcers	Fever, vascular rash	Direct contact	Meerburg (2009)
	<i>Arenaviridae</i>	Hemorrhagic fever	Many rodent species (coevolution with host), Mice, hamsters, guinea pigs and muskrats	None, may include conjunctivitis, ascites, splenomegaly, and hepatic lipidosis with multicentric vasculitis and perivascular lymphocytic infiltrates	None	None	Fever, malaise, headache, vomiting, diarrhea, mucosal hemorrhage	Contact with excretions or contaminated materials, inhalation	Meerburg (2009)
	<i>Arenaviridae</i>	Lassa fever	Multimammate rat	None	None	None	Fever, malaise, headache, vomiting, diarrhea, mucosal hemorrhage	Contact with excretions or contaminated materials, inhalation	Meerburg (2009)
	<i>Arenaviridae</i>	Lymphocytic choriomeningitis	House mice	None	None	None	Meningitis, encephalitis, fetal defects (intrauterine infection)	Contact with excretions or contaminated materials, inhalation	Meerburg (2009)

	<i>Bunyaviridae</i>	Hantavirus cardiopulmonary syndrome	Deer mice, cotton rats, rice rats, whitefooted mice	None	None	None	Pneumonia, pulmonary edema, death	Contact with excretions or contaminated materials, inhalation, bites (rare)	Meerburg (2009)
	<i>Bunyaviridae</i>	Hemorrhagic fever with renal syndrome	Norway and black rats, field mice, voles	None	None	None	Fever, multisystemic vascular leakage, renal failure	Contact with excretions or contaminated materials, inhalation, bites (rare)	Meerburg (2009)
	<i>Flaviviridae</i>	Omsk hemorrhagic fever	Muskrats (Siberia)	Fatal encephalitis (muskrat)	Watervoles, Norway rats, mice, some bird species	None	Fever, hemorrhage without encephalitis	Direct contact with infected muskrats, Ticks (Dermacentor & Ixodes)	Meerburg (2009)

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*This list includes the zoonotic pathogens carried by rodents that cause disease in wild animals and those deemed most relevant to wildlife and zoo animal specialists; therefore it is not an exhaustive list. Readers are directed to Meerburg (2009) and Han (2015) for more information.

TABLE e3 Summary of Parasites and Associated Diseases of Rodents

	Etiology	Location in Host	Associated Disease (if any)	Species Affected	References
Metazoan					
	<i>Baylisascaris procy-lonis</i>	Multiple systems	Granulomatous and eosinophilic inflammation from larval migrans	All	Bauer (2013)
	<i>Capillaria hepatica</i> (syn. <i>Calodium hepaticum</i>)	Liver	Multifocal granulomatous hepatitis with fibrosis	All	Rothenburger (2014a), Simpson (2013)
	<i>Cysticercus fasciolaris</i>	Liver	Parasitic cysts	Mice and rats	Morrissey (1996)
	<i>Cysticercus mustelae</i>	Liver	Parasitic cysts	Squirrels	Langham (1990)
	<i>Cysticercus serialis</i> (syn. <i>Muticeps serialis</i>)	Subcutaneous tissues, abdomen, liver, spleen, thorax	Parasitic cysts	Chinchilla	Morrissey (1996)
	<i>Echinococcus cruzi</i> (syn. <i>oligarthus</i>)	Subcutaneous tissues, abdomen, liver, spleen, thorax	Parasitic cysts	Agouti	Rausch (1984), Zimmerman (2009)
	<i>Echinococcus granulosus</i>	Liver	Parasitic cysts	Ground squirrels (<i>Spermophilus dauricus/alashanicus</i>)	Yang (2009)
	<i>Echinococcus multilocularis</i>	Liver, other organs	Parasitic cysts	All	Janovsky (2002), Campbell-Palmer (2015), Miller (2016)
	<i>Echinococcus vogeli</i>	Liver, other organs	Parasitic cysts	Agoutis, spiny rats	Gardner (1988)
	<i>Eucoleus</i> sp.	Esophagus, stomach	Hyperplasia, hyperkeratosis, inflammation	Rats	Rothenburger (2014b)
	<i>Gongylonema neoplasticum</i>	Stomach	Hyperplasia, hyperkeratosis, inflammation	Rats	Hitchcock (1952)
	<i>Hymenolepis</i> sp.	Intestines	Diarrhea, enteritis	Chinchilla, mice, rats, hamsters	Morrissey (1996)
	<i>Obeliscooides cuniculi</i>	Stomach	None	Woodchuck	Measures (1983)
	<i>Synhimantus</i> sp.	Stomach	Squamous papillomas	Muskrats	Cosgrove (1967)
	<i>Syphacia</i> sp.	Cecum	None	Mice, rats, hamsters	Morrissey (1996)
	<i>Taenia crassiceps cysticercosis</i>	Subcutaneous tissues, abdomen, liver, spleen, thorax	Parasitic cysts	Woodchuck, squirrel	Klein (2011)
	<i>Trichosomoides crassicauda</i>	Urinary bladder, renal pelvis	Mild inflammation, predisposes to calculi formation	Rats	Morrissey (1996)
Protozoan					
	<i>Babesia</i> sp.	Blood	None	Agouti, porcupine, spiny rat	de Thoisy (2000)
	<i>Besnoitia</i> sp.	Bone, inner ear, scleral conjunctiva, subcutaneous tissues, mesentery, large intestines, pancreas	Range from one to acute, fatal infections	Kangaroo rat, hamsters, mice, rats	Ernst (1968)
	<i>Cryptosporidium</i> sp.	Intestine	Diarrhea, enteritis	Chinchilla, guinea pig, hamster, rat, mice	Morrissey (1996)
	<i>Eimeria</i> sp.	Intestine	Diarrhea, enteritis	Guinea pig, rat, mice	Morrissey (1996)

TABLE e3 Summary of Parasites and Associated Diseases of Rodents (Cont.)

	Etiology	Location in Host	Associated Disease (if any)	Species Affected	References
	<i>Encephalitozoon cuniculi</i>	Brain, kidney, liver, heart, lung, spleen	Multisystemic inflammation & necrosis	All	Hinney (2016)
	<i>Frenkelia</i>	Brain	None, lymphoid hyperplasia, lymphocytic meningoencephalitis	All	Geisel (1979), Kennedy (1986)
	<i>Giardia sp.</i>	Intestine	Diarrhea, enteritis	Hamster, mice, rat	Morrissey (1996)
	<i>Hepatozoon sp.</i>	Mutliple organs, blood	None	Squirrel, porcupine	Simpson (2013), de Thoisy (2000)
	<i>Klossiella sp.</i>	Kidney	Interstitial nephritis and fibrosis	Guinea pigs, mice	Pearce (1961), Morrissey (1996)
	<i>Leishmania lainsoni</i>	Skin	None	Agouti	Silveira (1991)
	<i>Pneumocystis carinii</i>	Lungs	Interstitial pneumonia, perivascular lymphoid cuffs	All	Henderson (2012)
	<i>Syphacia</i> spp.	Cecum and colon	None to rectal prolapse, intussusception, enteritis	Mice and rats	Baker (1998)
	<i>Spironucleus muris</i>	Intestine	None to fatal enteritis	Mice and rats	Baker (1998)
	<i>Toxoplasma gondii</i>	Brain, liver, spleen, lung, skeletal muscle, heart	None to multisystemic inflammation & necrosis	all	Bangari (2007), Forzan (2004), Simpson (2013)
	Trypanosomatidae	Blood	None to thrombocytosis, ascites, immunodepression, lymphoid & erythroid hyperplasia	agouti, porcupine, spiny rat, Norway rats, mice	Albright (1991), de Thoisy (2000)
Ectoparasite					
	<i>Chirodiscoides caviae</i>	Skin	None	Guinea pigs	Morrissey (1996)
	<i>Demodex</i>	Skin	Alopecia, dermatitis, pruritis	Gerbil, hamster	Morrissey (1996)
	<i>Gliricola porcelli</i>	Skin	Alopecia, crusting dermatitis, pruritis	Guinea pigs	Morrissey (1996)
	<i>Gyropus ovalis</i>	Skin	Alopecia, crusting dermatitis, pruritis	Guinea pigs	Morrissey (1996)
	<i>Myobia musculi</i>	Skin	Alopecia, pruritis, self-mutilation	Mice	Baker (1998)
	<i>Mycoptes musculinis</i>	Skin	Alopecia, pruritis, self-mutilation	Mice	Morrissey (1996)
	<i>Notoedres</i> sp.	Skin	Alopecia, crusting dermatitis	Hamster, grey squirrel, rats	Anholt (2014), Cornish (2001), Morrissey (1996), Stephenson (2013)
	<i>Ornithonyssus bacoti</i>	Skin	Anemia	Rats	Morrissey (1996)
	<i>Polyplax serrata</i>	Skin	Anemia, pruritis, dermatitis	Mice	Morrissey (1996)
	<i>Polyplax spinulosa</i>	Skin	Anemia, pruritis	Rats	Morrissey (1996)
	<i>Psoregates simplex</i>	Skin	Follicular nodules	Mice	Morrissey (1996)
	<i>Radfordia affinis</i>	Skin	Alopecia, pruritis, self-mutilation	Mice	Baker (1998)

(Continued)

TABLE e3 Summary of Parasites and Associated Diseases of Rodents (Cont.)

	Etiology	Location in Host	Associated Disease (if any)	Species Affected	References
	<i>Radfordia ensifera</i>	Skin	Anemia, pruritis, dermatitis	Rats	Morrissey (1996)
	<i>Trixacarus caviae</i>	Skin	Alopecia, crusting dermatitis	Guinea pigs	Morrissey (1996)

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