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## Infectious Diseases

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INTRODUCTION

Although guinea pigs are sensitive and susceptible to the development of lesions from a wide range of viruses, bacteria, protozoa, and parasites, only a small number of organisms cause natural infection and only a portion of that group cause clinical disease. The intent of this chapter is to discuss naturally occurring diseases of guinea pigs, although some data from experimental infections may be covered as they relate to the pathogenesis of the disease.

The material is presented under the following headings: background, etiology, epizootiology/pathogenesis, pathology, diagnosis, prevention, and therapy. The diseases are discussed in an alphabetical order based on the taxonomic groups to which the organisms belong and are independent of the order of perceived importance of the various diseases.

In laboratory colonies, routine surveillance of guinea pigs is conducted monthly, quarterly, or yearly as required. The Federation of European Laboratory Animal Science Associations (FELASA) recommendations include monitoring for guinea pig adenovirus, guinea pig cytomegalovirus, Sendai virus, ectoparasites, endoparasites, E. cuniculi, and a variety of bacteria including Bordetella bronchiseptica, Chlamydia psittaci, Corynebacterium kutscheri, dermatophytes, Pasteurellaceae, Salmonella spp., Streptobacillus moniliformis, Streptococcus spp., Yersinia pseudotuberculosis, and Clostridium piliforme. Most laboratories also monitor for these additional viruses, simian virus-5 (SV5), pneumonia virus of mice (PVM), reovirus, lymphocytic choriomeningitis virus (LCMV), and parainfluenza virus-3 (PIV-3). These viruses are routinely monitored both to minimize the risk of transfERENCE to mouse and rat colonies (PVM, Reovirus, Sendai virus, LCMV) and to identify infections that are zoonotic (LCMV, PIV-3).

VIRAL INFECTIONS

The viral taxonomy used follows the recommendations of the VIIIth International Committee on Taxonomy of Viruses (Fauquet, 2005), but well-established common names for viruses are used when appropriate. Historically, PVM, parainfluenza viruses, cytomegalovirus, and reovirus have been commonly found in guinea pig colonies. From 1984 to 1988 serologic investigations of laboratory animal colonies originating from ten different European countries found seropositivity for four viral infections in guinea pig stocks; reovirus, PVM, Sendai virus, and SV5 (see Paramyxoviridae section for discussion of serological specificity of Sendai virus and SV5) (Kraft and Meyer, 1990). In a 2004 study guinea pigs reared conventionally were positive serologically for Sendai virus, PVM, and reovirus (Park et al., 2006).

DNA Viruses

Adenoviridae: guinea pig adenovirus (GPAdV)

BACKGROUND Virus-associated necrotizing bronchopneumonia in guinea pigs is a spontaneous multifactorial disease that has low morbidity, high mortality, and a worldwide distribution (Percy and Barthold, 2007). After the first description in Germany and experimental reproduction of the disease (Kunstyr et al., 1984; Naumann et al., 1981), sporadic spontaneous cases were reported from the United States, Australia, and Switzerland (Brennecke et al., 1983). A 10-year endemic “in-house” occurrence of adenovirus-associated disease was reported in a British pharmaceutical research facility. In all described spontaneous cases, some additional stress factors were involved (Pring-Akerblom et al., 1997).

ETIOLOGY GPAdV is a member of the Adenoviridae, genus Mastadenovirus that contains canine and bovine adenoviruses as well (Fauquet, 2005). A portion of the hexon gene was cloned and sequenced and found to be
similar to human adenovirus types 2 and 5 in structurally conserved areas, but different in areas associated with type-specific antigenicity (Feldman et al., 2001).

**EPIZOOTIOLOGY AND PATHOGENESIS** Adenoviral infections in guinea pigs may be more prevalent than are currently recognized as serological tests used to monitor guinea pig colonies use mouse antigens that may not robustly detect serologic responses in guinea pigs (Hankenson et al., 2010; Percy and Barthold, 2007). The virus and disease are reproducible in intranasally inoculated newborn guinea pigs, however, older animals are less susceptible to experimental disease (Kunstyr et al., 1984). The incubation period from experimental infection is 5–10 days.

**CLINICAL MANIFESTATIONS** GPAdV may cause inapparent infections (Crippa et al., 1997; Hankenson et al., 2010) or severe acute outbreaks with high mortality and low morbidity (Finnie et al., 1999; Naumann et al., 1981; Percy and Barthold, 2007). Dyspnea and tachypnea have been report as well as sudden death. Clinical disease occurs primarily in young animals.

**PATHOLOGY** Necropsy reveals well-demarcated areas of pulmonary consolidation in the cranial and ventral areas of the lungs (Eckhoff et al., 1998; Finnie et al., 1999; Percy and Barthold, 2007). Histologically, necrotizing bronchitis/bronchiolitis is evident with pronounced desquamation of the epithelium and predominantly mononuclear cell infiltration. Airway occlusion by necrotic epithelial cell debris, leukocytes, and fibrin is seen (see Figure 23.1). In infected epithelial cells of the bronchi, nuclei contain distinctive round to oval basophilic inclusions that are 7–15 μm in diameter. Electron microscopy of pneumatic lesions reveals classic intranuclear adenoviral arrays in epithelial cells. Typical lesions have been observed in the airways of non-symptomatic animals (Crippa et al., 1997; Hankenson et al., 2010).

**DIAGNOSIS** GPAdV infection can be detected by serology (ELISA, MFIA, or IFA) using antigen from mouse adenovirus (MAV) (Hankenson et al., 2010). Diagnostic labs use both MAV-1 (FL) and MAV-2 (K-87) strains, but unfortunately this method is not specific for GPAdV and infected animals may be only weakly positive using these reagents (Hankenson et al., 2010). Clinically ill animals can be diagnosed by PCR, immunohistochemistry, or characteristic lesions including intranuclear, basophilic inclusion bodies on electron microscopy (Finnie et al., 1999; Hankenson et al., 2010; Percy and Barthold, 2007; Pring-Akerblom et al., 1997).

**PREVENTION AND THERAPY** Animals with GPAdV are not appropriate for guinea pig pulmonary research projects. Rederivation of infected colonies with aseptic hysterectomy or embryo transfer should eliminate the virus. In addition, there could be a concern that natural infection with GPAdV would interfere with the use of adenovirus gene vectors. This was examined in a study of GPAdV naturally infected guinea pigs that were used as recipients of a human adenoviral vector carrying the gene for green fluorescent protein (Hankenson et al., 2010). In this model system, no difference in transfection-efficiency was seen in guinea pigs naturally infected with GPAdV or GPAdV-free.

**Herpesviridae**

Three members of the family Herpesviridae that specifically infect guinea pigs are catalogued in the Eighth Report of the International Committee on the Taxonomy of Viruses (Fauquet, 2005); *Caviid herpes virus 2* (commonly known as guinea pig cytomegalovirus and in some publications as caviid herpesvirus 1 (Staczek, 1990)), *Caviid herpes virus 1* (also known as guinea pig herpes-like virus or Hsiung-Kaplow herpesvirus, or in some publications as caviid herpesvirus 2 (Staczek, 1990)), and *Caviid herpes virus 3* (also known as guinea pig X virus) (Fauquet, 2005). In addition, *Equid herpes virus 1*, a virus of horses, has been shown to cause severe disease in guinea pigs in one outbreak in a zoo (Wohlsein et al., 2010). Of these viruses, guinea pig cytomegalovirus is the most commonly isolated herpes virus from guinea pigs and serological reactivity to this virus in colonies is not unusual. Guinea pig cytomegalovirus is used extensively in research as an animal model for human cytomegalovirus.

**Caviid Herpes Virus 2 (Commonly Referred To As Guinea Pig Cytomegalovirus (GPCMV))**

**BACKGROUND** GPCMV was the first herpes virus identified in guinea pigs and was originally detected by observing intranuclear inclusion bodies in the salivary...
glands (Jackson, 1920). Subsequently, virus isolation resulted in the identification of this important animal model of human cytomegalovirus infection (Cole and Kuttner, 1926).

ETIOLOGY GPCMV (species name Caviid herpes virus 2) is an unassigned species of the family of Herpesviridae, subfamily Betaherpesvirinae (Fauquet, 2005). Cytomegaloviruses are species-specific, large, enveloped, double-stranded, DNA viruses that cause diseases in animals and humans (Fox, 2002). The GPCMV genome has been sequenced, is 233 kb in length, and consists of highly conserved areas as well as unique open reading frames (ORFs) (Schleiss et al., 2008). When the sequenced glycoproteins of GPCMV were compared to other cytomegaloviruses, most were found to be more closely related to primate cytomegaloviruses (human, chimpanzee, and rhesus) than rodent cytomegaloviruses (rat and mouse).

EPIZOOTIOLOGY AND PATHOGENESIS GPCMV was once relatively common with 70–80% of guinea pigs of 6 months of age or older having typical salivary gland inclusion (Van Hoosier and Robinette, 1976). Current prevalence of GPCMV in laboratory animal colonies is lower with only six out of 15 institutions in Europe from 2000–2003 reporting positive antibody responses to GPCMV (Schoondermark-van de Ven et al., 2006). The incidence of natural infection in guinea pigs appears to be dependent on breeding conditions and husbandry (Staczek, 1990).

Transmission is transplacental and by contact with infected urine or saliva (Choi and Hsiung, 1978; Percy and Barthold, 2007). Transplacental infection occurs primarily during acute infection as once maternal neutralizing antibodies are present, transplacental infection of feti declines significantly (Choi and Hsiung, 1978). Transmission to neighboring guinea pigs in the same cage is less efficient than transmission via sexual contact with only six out of nine of the same sex pairs seroconverting in one study, while 100% of male/female pairs seroconverted (Choi and Hsiung, 1978).

The pathogenesis of GPCMV has been studied via experimental infection. The severity of the infection is dependent on the virus type, the strain of guinea pig, and the route of infection (Schleiss, 2002). Generally tissue culture-adapted strains produce milder infections than salivary gland-adapted strains. Outbred strains of guinea pigs, such as Hartley, are less susceptible to severe infection and excrete less virus in the urine than inbred strains such as strain 2 and JY-9 (Bia et al., 1979; Hsiung et al., 1980). Infection by mucosal routes usually results in less severe disease than intravenous, subcutaneous, or intraperitoneal inoculation.

Following experimental infection, two distinct phases of infection, acute and chronic, have been observed (Hsiung et al., 1980). In the acute phase, virus is consistently recovered from the blood and many other tissues including lung, spleen, and kidney during a 10-day period beginning at day 2 post-inoculation (Hsiung et al., 1978, 1980). Viral clearance from the blood and most tissues occurs by 10 days post-infection, but virus remains consistently detectable in the urine and salivary gland during the chronic phase of infection (Bia et al., 1979; Hsiung et al., 1980). Less consistently, virus is found in splenic macrophages, B lymphocytes, kidneys, spleen, pancreas, and cervix of infected animals during this chronic phase.

Pregnancy can lead to more severe disease and changes in viral load following experimental GPCMV infection (Choi and Hsiung, 1978; Griffith and Hsiung, 1980; Griffith et al., 1983). Pregnant guinea pigs may develop interstitial pneumonia, splenomegaly, and necrosis of the liver, kidney, thymus, pancreas, and bone marrow (Griffith et al., 1983). The mortality rate for pregnant animals during an acute viremic episode following experimental infection is significantly greater than for non-pregnant females.

Although the fetus is susceptible to GPCMV infection at any time throughout gestation, transplacental transmission occurs most readily during the acute phase of maternal infection. The frequency of stillbirths and viral infection in neonates is highest in animals infected late in gestation. In neonates, brain lesions are observed and virus can be recovered from the salivary glands and, to a lesser extent, from the brain, lungs, pancreas, and liver of the neonates. In some cases, lesions are detected in the salivary glands of offspring up to 14 weeks postpartum. Placental infection may be detected after maternal clearance of viremia and maintained despite the presence of significant levels of GPCMV neutralizing antibody. The site of infection is localized at the transitional zone between the capillarized labyrinth and the non-capillarized interlobrium of the placenta. Whenever infection of the fetus is demonstrated, the placenta is invariably infected; however, infected placentas may be associated with uninfected fetuses. The status of maternal immunity before pregnancy can favorably affect the outcome of maternal or fetal infections with virulent GPCMV strains (Staczek, 1990).

CLINICAL MANIFESTATIONS Natural infection with GPCMV causes a latent, persistent infection in the salivary gland generally without serious disease in animals in the vivarium (Staczek, 1990; Van Hoosier and Robinette, 1976). However, the death of a sow and fetuses (Motzel and Wagner, 1989) and disseminated infection, including pneumonia, in guinea pigs that were not being manipulated experimentally have been reported (Van Hoosier et al., 1985). Illness is more likely when associated with pre-existent immune suppression or pregnancy (Percy and Barthold, 2007).
The Guinea Pig Herpesvirus (GPHLV) is an unassigned species in the family Herpesviridae (Fauquet, 2005). It was originally isolated from leukocytes of strain 2 guinea pigs that were free of GPHLV and GPCMV (Bia et al., 1980). In one study of 112 Hartley and strain 2 guinea pigs tested serologically for GPVX, 38% were found to be positive.

**Clinical Manifestations and Pathology**

Inoculation of GPXV into Hartley guinea pigs caused viremia which persisted for at least 3 weeks (Bia et al., 1980). Virus could be recovered 5–6 months after inoculation suggesting a persistent infection. In this study, 50% of the animals died between 6 and 11 weeks post-inoculation. Hepatic necrosis was the only consistent lesion seen. GPXV is both morphologically and serologically distinct from GPCMV and GPHLV.

**Prevention and Therapy**

Natural disease from GPXV is unknown, but similar to GPHLV, this virus may be a complicating factor in research.

**Equid Herpesvirus 1 (EHV1)** (Also Known as Equine Herpes Virus 1 and Equine Abortion Virus)

**Background and Etiology**

EHV1 is an equine pathogen that causes a persistent infection in horses with a variety of clinical presentations including respiratory disease, abortion, neonatal death, and neurologic disease (Reed and Toribio, 2004). EHV1 is a species in the genus Varicellovirus of the Alphaherpesvirinae subfamily (Fauquet, 2005). Other members of this genus include...
the type species Human herpesvirus 3 (varicella-zoster virus or chickenpox) and Bovine herpesvirus 1 (infectious bovine rhinotracheitis virus).

**PATHOGENESIS AND CLINICAL MANIFESTATIONS**
One recent report describes infection with EHV1 resulting in hindlimb paralysis, ataxia, abortion, or stillbirth in 18 of 80 guinea pigs at a European zoo (Wohlsein et al., 2010). In this outbreak, Thomson gazelles (Equus thomsoni) kept in the same building as the guinea pigs were first affected and suffered a short course of fatal neurologic disease. The source of the virus was unclar, although a similar strain of virus was isolated 6 months earlier from affected black bears (Ursus americanus) and clinically unaffected onagers (Equus hemionus kulan). In the second outbreak, a similar strain of virus was also recovered from clinically unaffected zebra (Equus quagga boehmi) housed in the same building as the guinea pigs and gazelles.

**PATHOLOGY** Lympho-histiocytic meningoencephalitis was seen predominantly in the olfactory bulb and the frontal cortical regions of the brain with neuronal and glial necrosis, gliosis, and intranuclear inclusion bodies (Wohlsein et al., 2010). EHV1 antigen was demonstrated in the neurons, neuronal processes and glial cells by immunohistochemistry and encapsulated herpes viral particles of 120–150nm were detected by electron microscopy.

**DIAGNOSIS** Differentiation from other members of the Herpesviridae is important for diagnosis. Immunohistochemistry, virus isolation, PCR, and DNA sequencing were used in this report to identify the virus involved (Wohlsein et al., 2010).

**PREVENTION AND THERAPY** EHV1 infection of guinea pigs is an example of the severe disease seen when members of the Alphaherpesvirinae infect unusual hosts similar to Human herpes virus 1 (herpes simplex virus) which has been shown to infect guinea pigs experimentally (Wohlsein et al., 2010) and has also been reported to cause naturally acquired clinical disease in rabbits (Weissenbock et al., 1997) and chinchillas (Wohlsein et al., 2002). Separation of species, control of fomites, and use of appropriate personal protective equipment can be used to prevent transmission of members of the Alphaherpesvirinae subfamily of viruses to aberrant hosts such as guinea pigs.

**Pox-Like Viruses**
There has been one report of pox-like virus particles obtained from tissue culture samples of fibrovascular proliferations involving the rear limb of half of a colony of guinea pigs (Hampton et al., 1968). Particles resembling pox viruses were observed by electron microscopy.

**RNA Viruses**

**Arenaviridae: Lymphocytic Choriomeningitis Virus (LCMV)**

**BACKGROUND** The first identified arenavirus, LCMV, was isolated in 1933 and shown to cause aseptic meningitis in humans and was named for its ability to cause lymphocytic choriomeningitis in mice and monkeys upon intracerebral injection (Amman et al., 2007; Charrel and de Lamballerie, 2010; Percy and Barthold, 2007; Van Hoosier and Robinette, 1976). LCMV is a rodent-borne zoonotic arenavirus endemic in housemice (Mus musculus) worldwide. Infection by LCMV in people is known to cause acute central nervous system disease and congenital malformations.

**ETIOLOGY** The viral genus Arenavirus includes 22 viral species, the type species is LCMV (Fauquet, 2005). Like other Arenaviruses, LCMV is a non-cytopathic, enveloped, single-stranded RNA virus.

**EPIZOOTIOLOGY AND PATHOGENESIS** LCMV is uncommon to rare in guinea pigs (Fox, 2002; Percy and Barthold, 2007). In May 2005, the Centers for Disease Control and Prevention reported a cluster of LCMV infections among four solid organ recipients in Rhode Island and Massachusetts who received organs from a single apparently asymptomatic donor (Centers for Disease Control and Prevention [CDC], 2005a). Recipients became gravely ill shortly after transplantation; three subsequently died. LCMV was identified as the etiologic agent. Viral sequences from the organ recipients were identical to those from a pet hamster acquired by the donor’s household 17 days before organ donation. Sequence and phylogenetic data provided strong support for the presence of the same LCMV lineage in hamsters and guinea pigs in the Rhode Island pet store and the Ohio distribution center (Amman et al., 2007; CDC, 2005b).

**CLINICAL MANIFESTATIONS** Clinical signs of LCMV are uncommon in the guinea pig, however meningoitis with hind limb paralysis has been reported (Van Hoosier and Robinette, 1976).

**PATHOLOGY** LCMV in guinea pigs results in lesions involving the brain including lymphocytic infiltrates in meninges, choroid plexus, and ependyma (Percy and Barthold, 2007). Lymphocytic infiltrates are also seen in the liver, adrenal, and lungs. Experimentally, neutrophilic destruction of the splenic red pulp, focal bone marrow necrosis, lymphopenia, and death occur following infection with the more virulent (WE) strain (Djavani et al., 1998).

**DIAGNOSIS** Diagnosis is typically by PCR, IFA, ELISA, or MFIA (Charrel and de Lamballerie, 2010; Fox,
2002; Percy and Barthold, 2007). Detection of viral antigen in tissue or section via immunohistochemistry is also feasible. Immunity to LCMV is primarily cellular, but virus-specific antibody is produced.

**Prevention and Therapy** Lymphocytic choriomeningitis is a zoonotic disease of concern with rodents kept as pets (Pickering et al., 2008). Human infection occurs most commonly through exposure to secretions or excretions of infected animals. In addition, LCMV can contaminate transplantable tumor or cultured cell lines from mouse, hamster, and guinea pig, and viral stocks (ILAR, 1991; Percy and Barthold, 2007). In mice, LCMV has been shown to limit tumor induction by polyomavirus, mouse mammary tumor virus, and transplantable guinea pig leukemia, delay tumor rejection, and alter sensitivity to endotoxins (ILAR, 1991). Natural infections would be expected to interfere with research studies involving enterohepatic, lymphoid, musculoskeletal, nervous, respiratory, and urinary systems.

**Coronavirus-Like Infection**

Coronavirus-like particles were found in the feces of young guinea pigs that developed wasting, anorexia, and diarrhea with low morbidity and mortality (Jaax et al., 1990). At necropsy, there were large amounts of mucoid material throughout the small intestine. Histologically, the primary lesion was acute to subacute necrotizing enteritis involving the distal ileum with blunting and fusion of the affected villi, necrosis and loss of enterocytes, and mucosal syncytial cells were evident. By electron microscopy, viral particles consistent with coronavirus were demonstrated in fecal matter from affected animals. Coronavirus shedding was also noted in the feces of clinically normal guinea pigs (Marshall and Douttree, 1996). The virus has not been isolated.

**Paramyxoviridae**

*Paramyxoviridae* is composed of pleomorphic, enveloped, linear, negative-sense single-stranded RNA viruses occurring worldwide in animals and humans, often associated with subclinical infections of the respiratory tract (Fauquet, 2005; Simmons et al., 2002). The family is split into two subfamilies, *Paramyxovirinae* and *Pneumovirinae* (Fauquet, 2005). In guinea pigs, three distinct members of the *Paramyxovirinae* have been described; *Human parainfluenza virus 3* (including *Human parainfluenza virus 3*, Cavian parainfluenza virus 3, and Guinea pig parainfluenza virus 3), *Sendai virus*, and Simian virus 5 (SV5). In addition, murine pneumonia virus, a member of the *Pneumovirinae*, has been described in guinea pigs.

**HUMAN PARAINFLUENZA VIRUS 3, CAVIAN PARAINFLUENZA VIRUS 3, GUINEA PIG PARAINFLUENZA VIRUS 3**

**Etiology** *Human parainfluenza virus 3* is a member of the genus Respirovirus, whose type species is *Sendai virus* (Fauquet, 2005). Sequence analysis of a Guinea-pig parainfluenza virus 3 isolated in 1998 from a colony of guinea pigs in Japan indicates that it has 95.6–97.9% nucleotide identity to *Human parainfluenza 3* virus and 71.0–79.6% to *Bovine parainfluenza virus 3* suggesting this virus was introduced into guinea pigs from a human with human parainfluenza virus 3 (Ohsawa et al., 1998). A novel paramyxovirus (cavian parainfluenza virus 3) was isolated in 2002 from a colony of guinea pigs (Simmons et al., 2002). This virus has 94% nucleotide identity to guinea-pig parainfluenza virus 3 and *Human parainfluenza virus 3* and 80% nucleotide identity to *Bovine parainfluenza virus 3*.

**Epidemiology and Pathogenesis** Seroconversion in endemic parainfluenza-3-positive breeding colony was studied in 2002 (Blomqvist et al., 2002) and indicated that pups become infected from 2 weeks to 8 weeks of age. The virus did not persist as sentinels exposed to 4–5-month-old seropositive animals did not seroconvert. Experimental infections indicate that seroconversion in naïve animals occurs approximately 10 days following infection (Graziano et al., 1989). In an infection study guinea pigs inoculated with cavian parainfluenza virus 3, *Sendai virus*, simian virus 5 (SV-5), murine pneumonia virus, or bovine parainfluenza virus developed no clinical signs of disease or lesions during the eight-week course of the study although they developed robust homologous or heterologous serologic responses to the majority of the antigens (Simmons et al., 2002). The serologic response, using an ELISA, of those inoculated with SV-5 was modest or equivocal. In addition, SV-5 ELISA resulted in the highest degree of non-specific reactivity among all of the paramyxovirus assays.

**Clinical Manifestations and Pathology** In one study, no clinical signs or lesions were seen when guinea pigs were infected with Cavian parainfluenza virus 3 (Simmons et al., 2002). In a separate study, guinea pigs were shown to be susceptible to human parainfluenza virus 3, developing peribronchiolar and interstitial lesions (Clyde, 1980).

**Diagnosis** Identification of the virus via PCR and sequencing is ideal as cross-reactive serological results make interpretation of serology difficult (Simmons et al., 2002).

**Prevention and Therapy** It is apparent that *Human parainfluenza virus 3* can be transmitted to
guinea pigs and infection-control measures such as the use of face masks, gloves, and laminar flow hoods to prevent transmission in laboratory settings is prudent. It isn’t known whether human or cavian parainfluenza virus 3 can be transmitted to humans from guinea pigs.

**SENDAI VIRUS**

**Etiology** Sendai virus, also known as Murine parainfluenza virus, is the type species in the genus Respirovirus, which also contains the species Human parainfluenza virus 3, Bovine parainfluenza virus 3, and Human parainfluenza virus 1 (Fauquet, 2005).

**Epidemiology and Pathogenesis** Numerous studies have reported seropositivity to Sendai virus, including a publication in 1978 which describes seropositive reactions by HI or CF in seven out of 16 colonies tested over a 13-year period in the United States (Parker et al., 1978). In addition, there is one report of isolation of Sendai virus from guinea pigs associated with mice (Van Hoosier and Robinette, 1976), although no clinical signs were reported. More recently, five of 15 European guinea pig colonies were seropositive to either Sendai virus, Human parainfluenza virus 3, or both (Schoondermark-van de Ven et al., 2006). Inoculation of guinea pigs with Sendai virus in one report resulted in no clinical signs of disease or lesions (Simmons et al., 2002).

**Diagnosis** As with the other Paramyxoviridae, lack of specificity can result in false-positive results with routine serological testing (Simmons et al., 2002). In one study, Sendai ELISA-positive samples were seen in guinea pigs infected with Pneumonia virus of mice and Bovine parainfluenzavirus 3. Guineapigs were also positive by IFAT in the case of Bovine parainfluenza virus 3 infection.

**Prevention and Therapy** The importance of Sendai virus infections in guinea pigs is unclear. However, since it is a significant disease of mice housed in laboratory animal colonies, guinea pigs should be maintained free of Sendai virus. In addition, Sendai virus is used as a vector in research and natural infection or sero-reactivity may interfere with such uses (Baker, 1998).

**Simian Virus 5 (SV5)**

SV5 is a species of the genus Rubulavirus which also contains mumps virus and human parainfluenza virus 4 (Fauquet, 2005). SV5 was initially isolated from simian kidney cell cultures and has also been shown to infect guinea pig cells in vitro (Zakstelskaya et al., 1976). Serological reactivity to SV5 has been reported in guinea pig colonies (Kraft and Meyer, 1990). Seropositive guinea pigs show no clinical signs or lesions and inoculation with SV5 results in seroconversion, but not clinical signs of disease (Simmons et al., 2002). Infection of guinea pigs with Sendai virus, pneumonia virus of mice, or human parainfluenza virus 3 can result in positive SV5 ELISA results which were negative by indirect fluorescent antibody test, indicating low specificity of the SV5 ELISA (Simmons et al., 2002).

**Murine Pneumonia Virus** (Formerly Pneumonia Virus of Mice (PVM))

**Etiology** PVM is a member of the genus Pneumovirus, species Murine pneumonia virus (Fauquet, 2005). Other members of the genus Pneumovirus include the human and bovine respiratory syncytial viruses. The complete genomes of two strains of this virus were sequenced in 2005 (Thorpe and Easton, 2005). PVM is most often subclinical in immunocompetent mice although in immunodeficient mice, it can cause chronic wasting with cyanosis and dyspnea (Percy and Barthold, 2007).

**Clinical Manifestations and Diagnosis** Seropositive reactions to PVM have been seen historically in guinea pig colonies in animals without apparent disease (Van Hoosier and Robinette, 1976). Inoculation of guinea pigs with a strain of PVM that caused mortality in immunocompetent and immunodeficient mice resulted in no clinical signs, although the guinea pigs seroconverted within 11 days after inoculation (Griffith et al., 1997).

**Prevention and Therapy** Transmission of PVM from guinea pigs to mice, or vice versa, appears to be possible and similar in this regard to Sendai virus. In laboratory colonies, it is important to keep guinea pigs free of PVM in order to minimize potential transmission to mice.

**Picornaviridae (Poliovirus, Theiler’s Murine Encephalomyelitis Virus)**

It is unclear whether laboratory guinea pigs may harbor a poliovirus which, in 1911, was described as the cause of a disease called guinea pig lameness (Hansen et al., 1997; Van Hoosier and Robinette, 1976). A similar disease was described by Rohrer in 1958 (Van Hoosier and Robinette, 1976). In these investigations, sera from affected guinea pigs reacted positively to Theiler’s murine encephalomyelitis virus (TMEV) antigens. Clinical signs involved a flaccid paralysis and weight loss with an incubation period of 9–23 days, and a duration of 1–2 weeks. Affected animals had meningomyeloencephalitis. More recently, two pet shop guinea pigs were reported to suffer from rear limb paresis and generalized debilitation. The guinea pigs had extremely high titers against “poliovirus”, while healthy guinea pigs from the same pet shop were negative (Hansen et al., 1997). The diseased guinea pigs recovered...
fully after treatment with vitamin C in the drinking water. Further testing of other guinea pig colonies by the same authors demonstrated antibody responses to TMEV in 35 out of 152 laboratory guinea pig sera. Positive results were found in two out of six breeding centers, and in three out of three experimental units, all of which purchased guinea pigs from one of the seropositive breeding colonies. Guinea pig sera from some of the breeding units were also positive serologically for other infections; adenovirus, PVM, reovirus type 3, *Sendai virus*, SV5 and *Encephalitozoon cuniculi*. In experimental studies of susceptibility of laboratory animals to six strains of human poliovirus, newborn guinea pigs were the only species of laboratory animals in which multiplication of any of the viruses could not be detected (Koroleva et al., 1975).

**Reoviridae: Reovirus**

Naturally occurring antibodies to reovirus have been detected in laboratory guinea pig colonies by IFA, ELISA, and MFIA (Percy and Barthold, 2007; Van Hoosier and Robinette, 1976). No clinical signs or lesions have been described. Experimentally guinea pigs have been exposed to a reovirus associated with the SARS coronavirus (Liang et al., 2005).

**Retroviridae: Cavian Leukemia**

**BACKGROUND** Cavian leukemia was first described in 1954 by Congdon and Lorenz as being caused by a retrovirus, however herpes viral inclusions have also been seen in leukemic guinea pigs (Jungeblut and Opler, 1967; Opler, 1969; Percy and Barthold, 2007; Van Hoosier and Robinette, 1976). In experimental studies of susceptibility of laboratory animals to six strains of human poliovirus, newborn guinea pigs were the only species of laboratory animals in which multiplication of any of the viruses could not be detected (Koroleva et al., 1975).

**ETIOLOGY** Type C retrovirus particles have been seen in cases of cavian leukemia (Hsiung et al., 1980; Van Hoosier and Robinette, 1976). An endogenous guinea pig retrovirus was induced by bromodeoxyuridine (Michalides et al., 1975; Nayak, 1974). Molecular hybridization techniques were used to show that guinea pig virus nucleotide sequences are endogenous to both domestic (*Cavia porcellus*) and indigenous (*Cavia aperea*) guinea pigs, but cannot be detected in the DNA of other mammals tested (Dahlberg et al., 1980).

In 1982, a transplantable leukemia (KSL) of unknown etiology, that had the characteristics of a B cell tumor, was found in a female Sewall-Wright strain 2 guinea pig. KSL leukemia was also shown to be distinct from another guinea pig lymphatic leukemia (L2C) with respect to cell morphology, antigenicity, and in vivo growth rate (Key et al., 1983). A C-type virus was reported in the urine of diabetic guinea pigs (Lee et al., 1978).

**CLINICAL MANIFESTATIONS** Clinical signs of cavian leukemia include lethargy, pale mucous membranes, secondary infections, peripheral lymph node enlargement, and death (Van Hoosier and Robinette, 1976). Leukocyte counts may vary from 25,000–250,000, with the preponderance of cells being lymphoblastic. Peripheral lymphadenopathy is generally evident.

**PATHOLOGY** Enlarged lymph nodes in the cervical, axillary, mediastinal, retroperitoneal, and inguinal areas are seen in cavian leukemia with splenomegaly and hepatomegaly (Van Hoosier and Robinette, 1976). There is a moderate infiltration of leukemic cells in all organs including the spleen, liver, bone marrow, lung, thymus, gastrointestinal associated lymphoid tissue (GALT), heart, eyes, and adrenals (Opler, 1969).

**TREATMENT AND CONTROL** There is no described treatment.

**Rhabdoviridae: Rabies**

Rabies has been reported in a pet guinea pig associated with a bite from a raccoon (Eidson et al., 2005).

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**BACTERIAL INFECTIONS**

**Gram-Positive Organisms**

**Clostridia**

Most clostridia are large, spore-forming, Gram-positive, anaerobic rods. The one exception is *C. piliforme* which is Gram negative and is discussed in the section covering Gram-negative organisms below. Two species of clostridia are discussed here, *C. difficile* and *C. perfringens*.

**Clostridium difficile** (Antibiotic-Associated Typhilitis)

**BACKGROUND** Severe profuse diarrhea, associated with *Clostridium difficile* in guinea pigs treated with antibiotics, is an important and preventable disease process.

**ETIOLOGY** *Clostridium difficile* is most commonly associated with antibiotic-induced typhilitis in guinea pigs, although other organisms including *Escherichia coli*, *Clostridium perfringens*, *C. sordelli*, *C. histolyticum*, and *Bacillus pumilis* have been implicated in different studies (Booth et al., 1989; Brophy and Knoop, 1982; Knoop, 1979; Lowe et al., 1980; Rehg and Pakes, 1981, 1982; Rehg et al., 1980; 1982). *C. difficile* is a common anaerobic, spore-forming, fecal-borne, Gram-positive, rod-shaped organism that generally produces both an enterotoxin (toxin A) and a cytoxin (toxin B) that are crucial in the pathogenesis of disease (Greenwood, 2007).

**EPIZOOTIOLOGY AND PATHOGENESIS** Normal guinea pigs may carry low resident populations of *C. difficile* in the intestines and toxins can be identified...
in normal cecal contents (Boot et al., 1989). In one study, *C. difficile* was recovered by culture in one out of eight normal guinea pigs and 18 out of 34 guinea pigs with typhilitis. Oral or parenteral antibiotic administration, including penicillin, ampicillin, streptomycin, clindamycin, lincomycin, spiramycin, aureomycin, erythromycin, and bacitracin, have all been implicated in causing antibiotic-associated typhilitis by permitting an overgrowth of primarily Gram-negative organisms including toxin-producing *Clostridium* such as *C. difficile* (Young et al., 1987). The enteric flora of guinea pigs is primarily Gram-positive and those antibiotics that target Gram-positive organisms preferentially are of greatest risk to cause this disease (Farrar and Kent, 1965). One study demonstrated that in the 24–48 hours post-administration of penicillin, there was a significant increase in Gram-negative anaerobic and aerobic (coliforms predominantly) bacteria bringing the levels of coliform bacteria from less than 100 organisms per gram to 10^5–10^6 organisms per gram. This shift in the normal gut flora allows bacteria such as *C. difficile*, which is generally nearly undetectable, to predominate (Farrar and Kent, 1965; Fox, 2002; Percy and Barthold, 2007). Other Gram-negative organisms, *E. coli* in particular, and other *Clostridium* spp. also can contribute to disease.

*Clostridium difficile* (toxin)-associated typhilitis has also been diagnosed in guinea pigs not treated with antibiotics that had been rederived by caesarian section and were exposed to mice as a source of anaerobic flora (Boot et al., 1989). Two years after rederivation, an outbreak of typhilitis was investigated. Young guinea pigs 2–4 weeks old and a few adults were affected. *Clostridium difficile* was isolated from half of the animals tested and the cytotoxin was identified in cecal contents from 95% of the affected animals. Co-infection with *C. perfringens* and *Encephalitozoon cuniculi* was present. The authors speculate that the anaerobic flora that the animals were exposed to was not sufficient to protect guinea pigs from *C. difficile* infection. This same flora has been shown to be unsuitable for rats and rabbits.

**CLINICAL MANIFESTATIONS** Generally, affected guinea pigs have weight loss, rough hair coats, anorexia, dehydration, decreased activity, and hypothermia beginning 24–48 hours after antibiotic administration (Farrar and Kent, 1965; Fox, 2002; Knoop, 1979; Wasson et al., 2000). Some animals have no stool, while others have diarrhea and acute death has been reported.

**PATHOLOGY** At necropsy, the cecum is often gas-filled and dilated with hemorrhage evident in the cecal mucosa. Histopathologically, there is usually hyperplasia of the ileal mucosa as well as ulceration, edema, and degeneration of the cecal epithelium with leukocytic infiltration.

**DIAGNOSIS** *C. difficile* can be isolated from cecal contents via anaerobic culture (Boot et al., 1989; Greenwood, 2007). Detection of toxin in cecal contents, tissue, or feces via an enzyme immunoassay, cytotoxin activity in cell culture, serum neutralization assay, or PCR are considered the gold standard, however, false positives and false negatives are not uncommon (Greenwood, 2007; Houser et al., 2010; Songer, 1996).

**PREVENTION AND THERAPY** Antibiotic-associated diarrhea is usually treated symptomatically. In humans, administration of metronidazole or vancomycin is standard (Greenwood, 2007; Rupnik et al., 2009; Songer, 1996). Anecdotal information suggests that administration of yogurt or other *Lactobacillus*-containing products in conjunction with antimicrobial agents will prevent or minimize the effects of antibiotic-associated enteritis. A recent study attempted to induce antibiotic-associated enteritis by a single subcutaneous injection of clindamycin (Wasson et al., 2000). *C. difficile* and other enteric pathogens were not isolated, however, several guinea pigs that received clindamycin developed enteritis. In affected animals, administration of antibiotics with the oral *Lactobacillus* preparation did not result in any clinical improvement over those animals receiving antibiotics alone.

Certain PCR ribotypes of *C. difficile* are found in both human and animal populations, suggesting that this can be a zoonotic disease, although most of these studies are concerned with *C. difficile* found in food animals rather than guinea pigs (Rupnik et al., 2009).

**CLOSTRIDIUM PERFRINGENS (ENTEROTOXEMIA)**

*Clostridium perfringens* is a ubiquitous Gram-positive anaerobic spore-forming bacterium that is the primary cause of enterotoxemia in domestic animals. *C. perfringens* strains produce a variety of toxins, as many as 17 exotoxins, although four major toxins are associated with typing of the bacteria; alpha, beta, epsilon, and iota. Infections typically occur via contaminated food, water, bedding, or soil and primarily affect sheep, pigs, and cattle.

Confirmed *C. perfringens* infections have been reported in germ-free guinea pigs in 1970 and, more recently, in a conventionally housed guinea pig (Feldman et al., 1997; Madden et al., 1970; Songer, 1996). Clinical signs seen in the conventionally housed guinea pig were lethargy and anorexia. At necropsy, there were fibrinous adhesions involving the small intestine and liver (Feldman et al., 1997). The ileum and cecum had ecchymotic hemorrhages. Histopathology revealed acute, multifocal, severe, necrotizing, ulcerative typhilitis and ileitis as well as focal, severe, necrotizing, centriflobular vascular thrombosis of the liver with infarction and coagulative necrosis of the adjacent hepatocytes. PCR was used
to identify the toxins of *C. perfringens* both in the intestine and the liver.

**Corynebacterium**

**ETIOLOGY** *Corynebacterium* spp., members of the family *Corynebacteriaceae*, are Gram-positive, non-spore-forming, non-motile, aerobic, pleomorphic rods with coc-ccoid or club-shaped appearance that are catalase-positive and non-acid-fast (Boone et al., 2001; Greenwood, 2007).

**PATHOGENESIS, CLINICAL MANIFESTATIONS, AND PATHOLOGY** *Corynebacterium* spp. can cause disease in guinea pigs, but are also part of the normal flora. Specifically, they are commonly isolated from guinea pig conjunctiva. In one study, 27 out of 30 clinically normal pet guinea pigs grew *Corynebacterium* spp. from conjunctival cultures (Coster et al., 2008).

Spontaneous disease of guinea pigs associated with corynebacterial infections has rarely been reported, but have involved numerous different species of *Corynebacterium*. In one report, *Corynebacterium pyogenes* was isolated from a guinea pig with septicemia (Ganaway, 1976). Further research with that agent demonstrated it was pathogenic when administered IP to other guinea pigs, but not if it was given orally or intranasally. In another report, *C. kutscheri* was isolated from the lung of a guinea pig during an epizootic of group C, beta-hemolytic strep-tococcal disease. Further research with this isolate was similar to *C. pyogenes*, in that intraperitoneal administration resulted in disease while intranasal administration did not. The organism was also given intravenously in this case and was rapidly fatal. In a retrospective study of urinary bladder calculi in guinea pigs, it was reported that *Corynebacterium renale* was the most common isolate from urine and bladder samples (Hawkins et al., 2009). Of the 44 cases submitted for bacterial culture, 77% were negative. The most common pure culture isolate was *C. renale*, which was also commonly found in mixed infections with *Staphylococcus* and *Streptococcus* spp.

**DIAGNOSIS** Diagnosis is made by recovering the organism using aerobic culture conditions, generally on blood agar plates with standard biochemical tests to differentiate corynebacterium from other species (Greenwood, 2007). PCR and sequencing has been used for further identification (Greenwood, 2007; Hawkins et al., 2009).

**PREVENTION AND THERAPY** Many *Corynebacterium* spp. have significant resistance to a number of antibiotics and this may be true of some organisms in guinea pigs as well (Greenwood, 2007). In the study isolating *C. renale* from the urine and bladder wall, many of those animals were already on antibiotics when those isolates were obtained (Hawkins et al., 2009). In addition, the *Corynebacterium* spp. recovered from the normal conjunctiva of guinea pigs, demonstrated some bacterial resistance with six out of nine isolates resistant to oxy-tetracycline, four out of nine resistant to polymyxin B, two out of nine resistant to bacitracin, and one out of nine resistant to erythromycin, gentamicin, amikacin, and ciprofloxacin (Coster et al., 2008).

**Mycobacterium tuberculosis**

Guinea pigs are highly susceptible to *M. tuberculosis*. Natural infection has rarely been reported in the literature, but in those cases, the sources of the infections were believed to be from contact with human cases (Van Hoosier and Robinette, 1976).

**Staphylococcus aureus**

**BACKGROUND** Markham and Markham (1966) studied the prevalence of staphylococcal organisms in various animal species. A 42% incidence of coagulase-positive *Staphylococcus* was noted in the nasal passages of guinea pigs. This was the greatest incidence of staphylococcal infection of any species tested, including humans. All of the guinea pigs cultured appeared clinically normal.

**ETIOLOGY** The *Staphylococcus* genus, members of the *Staphylococcaceae* family, are common inhabitants of the skin, oral cavity, respiratory system, and intestine, and cause supplicative lesions and septicemia in all species (Songer and Post, 2005). These Gram-positive cocci are coagulase-positive, catalase-positive, oxidase-negative, non-spore-forming and facultative anaerobic organisms (Harkness and Wagner, 1995; Songer and Post, 2005). In guinea pigs, *Staphylococcus aureus* has been isolated from cases of ulcerative pododermatitis and exfoliative dermatitis (Percy and Barthold, 2007).

**PATHOGENESIS** Despite the existence of species-specific serotypes and biotypes, human *Staphylococcus aureus* phage types have been recovered from animals, and human–animal contact is one means of transmission of *S. aureus* (Harkness and Wagner, 1995). Additionally, direct contact with an infected animal or contaminated surface, as well as spread via aerosol can result in the dissemination of infection.

Ulcerative pododermatitis, or dermatitis of the foot-pad, is also known as “bumblefoot”. Trauma to the footpad from fighting, a sharp cage edge, or abrasive flooring creates a site of entry for bacteria (Harkness and Wagner, 1995). Obese guinea pigs, as well as any other natural or experimental cause that results in a sedentary lifestyle, can predispose an animal to bumblefoot, since perfusion is decreased and the pressure on the feet is increased (Brown and Donnelly, 2008; Harkness and Wagner, 1995).
Exfoliative, or acute staphylococcal, dermatitis has also been associated with *S. aureus* in guinea pigs. Strain 13 guinea pigs are reported with this condition more frequently than other strains, and mortality rates due to this condition are higher in young animals, especially if born to an affected dam that is too painful to nurse (Ishihara, 1980; Percy and Barthold, 2007).

**CLINICAL MANIFESTATIONS** Swollen, erythemic paws and lameness are noted with bumblefoot (Brown and Donnelly, 2008). Paws will often have erosions or ulcerations on the palmar or plantar surfaces. Osteoarthritis or osteomyelitis may result, and animals that develop such sequel have a poorer prognosis. Alopecia and erythema of the ventral abdomen, leading to cracking and scabbing of the epidermis, are often observed with exfoliative dermatitis (Fox, 2002; Ishihara, 1980; Percy and Barthold, 2007). In addition to its association with ulcerative pododermatitis and exfoliative dermatitis, pneumonia, mastitis, conjunctivitis, cheilitis, and osteoarthritis have been attributed to *S. aureus* infection in guinea pigs (Fox, 2002). Systemic amyloidosis can develop secondary to chronic *S. aureus* infection (Brown and Donnelly, 2008; Fox, 2002; Percy and Barthold, 2007).

**PATHOLOGY** Hypertrophy of the stratum corneum with a minimal inflammatory response is noted histologically in cases of dermatitis associated with *S. aureus* (Percy and Barthold, 2007). Diffuse cellulitis is the primary lesion associated with ulcerative pododermatitis (Brown and Donnelly, 2008). In cases that progress to amyloidosis, amyloid may be noted in the liver, spleen, adrenal glands, and pancreatic islets (Ganaway, 1976).

**DIAGNOSIS** Stained impression smears of lesions can demonstrate clumps of Gram-positive cocci (Harkness and Wagner, 1995). *S. aureus* can often be cultured directly from affected tissues and from the upper respiratory tract and pharynx of affected animals (Percy and Barthold, 2007). Blood agar or selective mediums, such as mannitol salt or Staph 110 agar, can be used for primary culture (Soner and Post, 2005). *S. aureus* colonies often present with a golden pigmentation.

**PREVENTION AND THERAPY** Prevention of ulcerative pododermatitis and exfoliative dermatitis is easier than treatment. Preventing cutaneous wounds by providing sturdy, smooth flooring to guinea pigs, offering non-abrasive feedstuff, and preventing obesity are highly effective in minimizing infection with *S. aureus*. Pododermatitis and exfoliative dermatitis are not usually conditions conducive to lesion drainage and surgical removal (Brown and Donnelly, 2008). Lesions can be cleaned, but the possibility of causing greater trauma to the affected area must be considered. Also, disinfectants that dry out the skin or agents that are cytotoxic to fibroblasts and reduce white blood cell viability and phagocytic efficiency, such as povidone-iodine or chlorhexidine, should be avoided. Long-term antibiotic treatment is necessary, and enrofloxacin or ciprofloxacin administered twice a day for 2–6 months has been reported in the treatment of ulcerative pododermatitis. Use of an analgesic agent, especially a non-steroidal anti-inflammatory drug such as meloxicam, is also recommended. Low-level laser therapy, or phototherapy, has been reported as successful in treating bumblefoot by accelerating angiogenesis and stimulating vasodilatation, although such therapy can only be used after the infection is first controlled.

**Streptococcus**

Two strains of *Streptococcus* cause disease in guinea pigs. *Streptococcus pneumoniae* can lead to severe pneumonia and *Streptococcus equi* subsp. *zooepidemicus* is associated with the development of chronic lymphadenitis (Wagner et al., 1976). Infections due to *S. equi* subsp. *zooepidemicus* are more prevalent in guinea pigs than are pneumococcal infections. Members of the *Streptococcus* genus are part of the *Streptococcaceae* family and consist of Gram-positive, catalase-negative, facultative anaerobic bacteria that are non-spore-forming and non-motile (Soner and Post, 2005).

**STREPTOCOCCUS PNEUMONIAE**

**BACKGROUND** *Streptococcus pneumoniae* was first recognized in guinea pigs in Europe in the late 1800s (Wagner et al., 1976). Homberger et al. (1945) are credited with the first report of this organism in guinea pigs in the United States; the animals were from a colony in Massachusetts and presented with signs of respiratory infection.

**ETIOLOGY** *Streptococcus pneumoniae* is an oval- to lancet-shaped, encapsulated coccus that presents in pairs (diplococcus) or short chains (Fox, 2002; Percy and Barthold, 2007). *S. pneumoniae* is an α-hemolytic streptococcus that ferments trehalose and is optochin-sensitive (Harkness and Wagner, 1995; Keyhani and Naghshineh, 1974; Songer and Post, 2005). Additionally, it is not categorized according to one of the Lancefield groupings (Soner and Post, 2005). Serovars of pneumococci are differentiated according to their capsular polysaccharide content, and serovars 4 and 19 are the two most often recovered from guinea pigs (Fox, 2002; Percy and Barthold, 2007).

**EPIZOOTIOLOGY AND PATHOGENESIS** Asymptomatic guinea pigs can carry pneumococci in the upper respiratory passages; the carrier rate for laboratory colonies can be as high as 50–55% (Fox, 2002; Percy and Barthold, 2007). While...
pneumonia epidemics due to \textit{S. pneumoniae} seldom occur in well-managed facilities, stressors which may predispose to infection include poor husbandry, pregnancy, sudden or prolonged changes in temperature, poor ventilation, shipping, inadequate nutrition, concurrent infections, and experimental procedures (Nakagawa et al., 1986; Percy and Barthold, 2007). Transmission of \textit{S. pneumoniae} is by aerosol or via direct contact with abraded skin or oral mucosa (Fox, 2002; Percy and Barthold, 2007; Wagner et al., 1976). Infection can also be passed at the time of parturition by an infected dam. Abortions and stillbirths can accompany a high mortality rate during an epizootic outbreak in a guinea pig colony (Percy and Barthold, 2007).

**CLINICAL MANIFESTATIONS** In 1974, a spontaneous epizootic of respiratory infection involving 2400 guinea pigs was caused by \textit{S. pneumoniae} type 19 (Keyhani and Naghshineh, 1974). During this outbreak, 450 guinea pigs died within 33 days of infection, and a short course of listlessness and failure to thrive were the only noted clinical signs prior to death. In less acute cases of \textit{S. pneumoniae}, guinea pigs display depression and lethargy, anorexia, and have ruffled fur. They may have a wet nose, nasal or ocular discharge (rhinitis, conjunctivitis), sneezing, coughing, dyspnea, or torticollis (head tilt due to otitis media) (Fox, 2002; Wagner et al., 1976). Wagner, Owens, Kusewitt, and Corley reported that otitis media occurred in 177 of 1373 guinea pigs necropsied during a 6-year period in the 1970s (Wagner et al., 1976). \textit{Streptococcus pneumoniae} was noted in 20\% of these cases, and was the most common bacteria isolated. Gupta et al. (1970), reported mastitis caused by \textit{S. pneumoniae} in two guinea pigs.

**PATHOLOGY** Acute bronchopneumonia is most often associated with \textit{S. pneumoniae} infections. Fibrinous exudate, a polymorphonuclear cell infiltrate and thrombosis of the pulmonary vessels may be observed in the lung (Fox, 2002; Keyhani and Naghshineh, 1974; Percy and Barthold, 2007). Other pyogenic processes noted in infected animals include pericarditis, peritonitis, otitis media, arthritis, endometritis, and suppurative meningitis (Fox, 2002; Percy and Barthold, 2007). Additionally, splenitis, fibrinopurulent meningitis, metritis, and lymphadenitis with focal hepatic and ovarian abscessation have been reported (Percy and Barthold, 2007). Pneumococci are readily demonstrated on impression smears and in stained tissue sections (Wagner et al., 1976).

**DIAGNOSIS** Culture of nasal washings is an ante-mortem means of diagnosing \textit{S. pneumoniae} (Homburger et al., 1945), as is culture of the nasal passages (Harkness and Wagner, 1995). Post-mortem, direct smears and culture of inflammatory exudates can be performed. \textit{S. pneumoniae} is a fastidious bacterium that grows best when incubated under 5–10\% CO\textsubscript{2} on blood agar or enrichment media (Fox, 2002; Percy and Barthold, 2007). Serological diagnosis via ELISA has been reported (Matsubara et al., 1988).

**PREVENTION AND THERAPY** Antibiotic treatment of a clinical animal usually results in reversion to a sub-clinical carrier state, so elimination of clinical animals is recommended whenever possible (Fox, 2002). Chloramphenicol, trimethoprim-sulfa combinations, and tetracycline have been used during epizootic outbreaks (Harkness and Wagner, 1995; Homburger et al., 1945; Keyhani and Naghshineh, 1974). Prevention should focus on good husbandry, adequate diet, early isolation of streptococcal carrier animals, and reduction of environmental stressors.

The same \textit{S. pneumoniae} serovars commonly detected in guinea pigs have been isolated from humans (Songer and Post, 2005). \textit{S. pneumoniae} can lead to respiratory and neurological disease in humans, especially in older and immune-compromised individuals. To date, interspecies transmission of \textit{S. pneumoniae} has not been reported (Harkness and Wagner, 1995; Percy and Barthold, 2007).

**STREPTOCOCCUS EQUI SUBSP. ZOOEPIDEMICUS**

**BACKGROUND** Charles Boxmeyer (1907) described his findings of epizootic lymphadenitis in over 3000 guinea pigs in 1907. Cunningham (1929) reported on 20 guinea pigs from a colony of 150 that had “lumps,” and from which “the same unusual type of mucoid hemolytic streptococcus was isolated”. Cunningham noted a 3:1 female to male ratio among the animals with chronic lymphadenitis.

**ETIOLOGY** \textit{Streptococcus equi} subsp. \textit{zooepidemicus} is a Lancefield group C streptococcus that is beta-hemolytic, encapsulated, and ferments sorbitol (Percy and Barthold, 2007; Songer and Post, 2005). \textit{S. equi} subsp. \textit{zooepidemicus} has a high degree of DNA homology with \textit{S. equi} subsp. \textit{equi}. \textit{S. equi} subsp. \textit{zooepidemicus} has been recovered from human infections, while \textit{S. equi} subsp. \textit{equi} has not (Songer and Post, 2005).

**EPIZOOTIOLOGY AND PATHOGENESIS** Guinea pigs can carry \textit{S. equi} subsp. \textit{zooepidemicus} asymptptomatically in the nasopharynx and conjunctiva (Percy and Barthold, 2007), but compared to \textit{S. pneumoniae}, clinical disease is more often noted in guinea pigs infected with \textit{S. equi} subsp. \textit{zooepidemicus}. As noted by Cunningham, females are indeed more susceptible to disease than males (Cunningham, 1929; Fox, 2002; Percy and Barthold, 2007). Strain 2 guinea pigs also appear to be more sensitive than other strains (Fox, 2002; Percy and Barthold, 2007;
While the cervical lymph nodes are the most common point of entry for infection is via the conjunctiva or nasal mucosa (Harkness and Wagner, 1995). Cervical lymphadenitis is commonly noted in guinea pigs when nasal mucosa does not need to be abraded in order for entry of the bacterium. The female genital tract can be infected during farrowing (Percy and Barthold, 2007). After initial entrance, the organism travels to the draining lymph node and replicates (Harkness and Wagner, 1995). Cervical lymphadenitis is colloquially referred to as “lumps,” due to the pyogenic nature of the bacteria and its propensity to travel and replicate in the lymph nodes (Fox, 2002; Percy and Barthold, 2007). While the cervical lymph nodes are the most common site of S. equi subsp. zooepidemicus replication and abscessation, any lymph node, and practically any organ, can be affected (Harkness and Wagner, 1995). A common presentation for infection with this organism is an animal that appears in good condition except for a swelling in the neck at the position of the cervical lymph node (Fox, 2002). The swelling is often soft to firm, pus-filled, non-fluctuant and freely movable (Percy and Barthold, 2007). Cunningham’s (1929) observations were that “in some cases, one or two nodes were greatly enlarged; in others, as in one animal with cervical node involvement, several plum-sized encapsulated abscesses formed a collar across the front and side of the neck”. Depending on what additional organs are affected, torticollis (if middle ear involvement), dyspnea and cyanosis or nasal and ocular discharge (if respiratory involvement), or hematuria and hemoglobinuria (if septic) may be noted (Fox, 2002; Harkness and Wagner, 1995). Abortions, stillbirths and unexpected deaths are possible (Fox, 2002). During epizootic outbreaks, septicaemia, acute pneumonia, and high mortality can occur (Harkness and Wagner, 1995).

**PATHOLOGY** The most common finding at necropsy is that of an abscessed, encapsulated cervical lymph node (Fox, 2002). The node architecture is often destroyed by central necrosis and peripheral fibrosis, and a thick pustular exudate is present (Cunningham, 1929; Fox, 2002; Percy and Barthold, 2007). Smears of the exudate reveal numerous Gram-positive cocci in short chains (Cunningham, 1929). A generalized lymphadenitis may be noted, as may retroorbital abscessation, otitis media, pneumonia, pleuritis, pericarditis, or hepatitis (Cunningham, 1929; Fox, 2002; Percy and Barthold, 2007).

**DIAGNOSIS** *S. equi* subsp. *zooepidemicus* can be cultured from affected tissues or heart blood (Harkness and Wagner, 1995; Percy and Barthold, 2007; Quesenberry and Carpenter, 2004; Wagner et al., 1976). Culture requires blood agar, on which after 24 hours, a clear zone of hemolysis is observed (Harkness and Wagner, 1995).

**PREVENTION AND THERAPY** Trimming of teeth, elimination of sharp edges to feeders, and feeding non-abrasive feed may assist in prevention of *S. equi* subsp. *zooepidemicus* infection (Fox, 2002). Infected animals should be isolated from the colony. Surgical removal of abscess contents and capsule can be done with creation of drainage and lavage. Antibiotic therapy is required. In epizootic cases, depopulation of affected animals and disinfection of the environment is advised. Enzootic disease represents significant potential for research complications. Disease-free replacement stock should be obtained and is available from commercial vendors. Vaccines are typically type-specific and do not provide reliable protection (Fox, 2002; Mayora et al., 1978).

**Gram-Negative Organisms**

**Actinobacillus**

*Actinobacillus lignieresii* and *Actinobacillus equuli* have been noted in laboratory guinea pigs (Songer and Post, 2005). The genus *Actinobacillus* is a member of the *Pasteurellaceae* family (Boone et al., 2001). These organisms are pleomorphic Gram-negative rods that on Gram stain, can have a “Morse code” appearance (Songer and Post, 2005).

*Actinobacillus lignieresii* and *Actinobacillus equuli* were cultured from 36 guinea pigs, rats and mice during a 6-month period at the University of Missouri Research Animal Diagnostic and Investigative Laboratory (Lentsch and Wagner, 1980). Organisms grew on blood agar inoculated with swabs from the posterior nasopharynx, conjunctiva, and middle ear. Conjunctivitis was noted in one animal and otitis media was noted in six.

**Bordetella**

**BACKGROUND** Tartakowsky is credited with one of the first accounts of *Bordetella* infection in guinea pigs in the late 1880s (McCartney and Olitsky, 1923; Smith, 1913). Woolfrey and Moody (1991) in their review of this organism stated “Ferry, using the name *Bacillus bronchisepticus*; McGowan, using the term *Bacillus bronchicanis*; and Torrey and Rahe, using Ferry’s epithet, independently observed the association of a small gram-negative coccobacillus with outbreaks of “canine distemper” and respiratory tract illness in laboratory animals such as the cat, rabbit, and guinea pig”. In the early 1970s, *B. bronchiseptica* was still considered to be the primary cause of acute pneumonia in guinea pigs and while it is not often
noted in modern laboratory facilities, it continues to be a major cause of respiratory disease in pet guinea pigs and this species is thought to be quite susceptible to infection (Percy and Barthold, 2007; Rigby, 1976).

**ETIOLOGY** *Bordetella bronchiseptica* is a short, Gram-negative rod or cocccobacillus, that is aerobic, motile, and non-spore-forming (Fox, 2002; Percy and Barthold, 2007). *B. bronchiseptica* is oxidase, catalase, and urease positive, as well as positive for citrate utilization and nitrate reduction (Songer and Post, 2005; Woolfrey and Moody, 1991). *B. bronchiseptica* is considered a commensal organism in the guinea pig, as well as many other mammalian species, including humans (Fox, 2002; Percy and Barthold, 2007; Woolfrey and Moody, 1991). The *Bordetella* genus is a member of the Alcaligenaceae family (Songer and Post, 2005).

**EPIZOOTIOLOGY AND PATHOGENESIS** *B. bronchiseptica* is carried by guinea pigs in the nasal cavity and trachea, and up to 20% of non-clinical animals in a colony can be carriers (Ganaway, 1976). Stressful events, such as transport or pregnancy, may trigger an acute fatal pneumonia in carriers or animals with previously inapparent infections. Transmission of *B. bronchiseptica* is via aerosol spread, direct contact, direct contact with respiratory secretions of infected animals, or fomites (Fox, 2002; Ganaway, 1976). *B. bronchiseptica* adheres to ciliated respiratory epithelium and causes ciliary paralysis (Fox, 2002). Pathogenic *B. bronchiseptica* produce adhesion and cytolytic toxins that lead to an inflammatory response, antiphagocytic activity, and dermonecrosis. While not explicitly described in the guinea pig, the impairment in mucociliary clearance caused by the binding of *Bordetella* is known to reduce the clearance of additional respiratory pathogens in other animal species. The incubation period is 5–7 days (Ganaway, 1976). The highest levels of morbidity and mortality due to *B. bronchiseptica* have been noted in young guinea pigs, as well as strain 2 animals (Fox, 2002; Ganaway, 1976). It is possible for infected animals to develop immunity and clear the organism. Yoda et al. (1972), noted that within 6–54 weeks of initial infection, 69 of 79 naturally infected guinea pigs completely recovered from infection.

**CLINICAL MANIFESTATIONS** Infection with *B. bronchiseptica* is often subclinical in nature (Fox, 2002). It has been suggested that the clinical signs associated with *Bordetella* in the past have actually been due to infections with a secondary invader, such as guinea pig adenovirus, which has not been recognized as an infectious agent of the guinea pig for as long as *B. bronchiseptica*. During an epizootic outbreak, death may follow respiratory disease and septicemia within a 24–72-hour period (Fox, 2002). Abortion and stillbirths can occur in pregnant dams (Percy and Barthold, 2007). In an enzootically infected colony, sporadic deaths may occur throughout the year, with highest levels during the winter months. Inappetance, depression, nasal discharge, dyspnea, and cyanosis may also be observed (Fox, 2002).

**PATHOLOGY** At necropsy, cranioventral pulmonary consolidation is seen, and whole lobes or individual lobules will present as dark red to red-gray in color (Ganaway, 1976; Percy and Barthold, 2007). A blood-tinged froth is noted in the trachea. Mucopurulent exudates may be noted in affected airways. Pleuritis and otitis media may be observed. Suppurative bronchopneumonia is noted histologically, with an influx of heterophils and mononuclear cells. Uterine infections may result in dead fetuses or pyosalpinx.

**DIAGNOSIS** *B. bronchiseptica* can be cultured on blood or MacConkey’s agar from nasal or other respiratory secretions (Songer and Post, 2005). In cases of otitis media, *B. bronchiseptica* can be isolated from the middle ear, and in cases of metritis, from the uterus (Fox, 2002; Yoda et al., 1972) at 35–37°C (Songer and Post, 2005). Smith and Baskerville medium selects for *B. bronchiseptica*, and is another option for culture (Songer and Post, 2005). ELISA and IFA tests have been developed for the detection of guinea pig *Bordetella*, and have been noted as equally successful in identifying infected animals as cultures of the respiratory tract (Boot et al., 1993a; Wullenweber and Boot, 1994).

**PREVENTION AND THERAPY** Purchasing *Bordetella*-free animals is the best means of control in laboratory colonies of guinea pigs. It is recommended that rabbits and guinea pigs not be co-housed since guinea pigs are highly susceptible to disease and rabbits are frequently sub-clinical carriers of *B. bronchiseptica* (Charles River Laboratories, 2011). Rats and other rodents can be additional sources of infection (Rigby, 1976). Antibiotic treatment with fluoroquinolones or trimethoprim-sulfonamides may successfully resolve clinical signs, but elimination of infection is rare, with animals often reverting to the sub-clinical state. If infection is suspected in a colony, restocking, test and cull, or rederivation may be more beneficial than treatment (Fox, 2002). The efficacy of canine, porcine, human, and autogenous *Bordetella* vaccines and bacterins has been evaluated by several individuals; reports suggest that these vaccines do not completely protect guinea pigs from infection, but a decrease in the incidence and severity of clinical disease has been noted in experimentally challenged animals (Matherne et al., 1987; Stephenson et al., 1989).

*B. bronchiseptica* apparently does not cause epidemic disease in man, but it can cause a whooping cough-like syndrome in immune-competent children or respiratory

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tract infections in immune-suppressed individuals (Songer and Post, 2005). Endocarditis, meningitis, and peritonitis have also been associated with B. bronchiseptica infections in humans. The ease of transmission between guinea pigs and humans in unknown.

**Brachyspira**

**BACKGROUND AND ETIOLOGY** Spirochetes of the genus Brachyspira (formerly Serpulina) have been associated with diarrhea and colitis in a variety of animals including birds and mammals. Brachyspira contains seven distinct species. Of these, two species have been implicated in guinea pigs, either in natural infections or as an animal model; B. hyodysenteriae, the primary cause of swine dysentery, and B. pilosicoli, a zoonotic agent associated with disease in chickens, pigs, and humans. Spirochetes have been associated with disease in guinea pigs in several publications, although purposeful infection to demonstrate causality has not been done and in many cases, identification of the species involved has also not been accomplished (Duhamel, 2001). Guinea pigs have been used as an animal model for B. hyodysenteriae infection.

**CLINICAL MANIFESTATIONS AND PATHOLOGY**

Two reports in the 1970s describing Tyzzer’s disease in guinea pigs also report observing spirochetes on histopathology (McLeod et al., 1977; Zwicker et al., 1978). The significance of the spirochete infections in the progression of the disease seen is unclear. A subsequent report describes a series of cases submitted for necropsy between 1992 and 1996 in Belgium (Vanrobaeys et al., 1998). In 29 of 33 cases when spirochetes were identified, the presenting complaints were either sudden death or a short course of diarrhea followed by sudden death. Flagellated parasites were seen in 12 animals and lesions consistent with vitamin C deficiency in six cases. Gross necropsy of affected animals most commonly demonstrated liquid, occasionally mucoid or hemorrhagic large intestinal contents, and dilation of the cecum and colon. Histologically, the cecum was characterized by hyperemia, mucosal infiltration of neutrophils, a mixed inflammatory infiltrate in the lamina propria, and occasionally, necrosis of crypt epithelium. Lesions involving other organs were present in 30 of the 37 animals identified, suggesting multifactorial disease processes. In a report of a single pet guinea pig, clinical signs of tenesmus, tachycardia, pale mucous membranes, and dehydration were associated with acute rectal prolapse (Helie et al., 2000). Histopathology identified superficial mucosal necrosis and ulceration and congestion with hemorrhage in the intussuscepted segment. Although spirochetes and organisms consistent with Eimeria spp. were seen in the rest of the intestinal tract, no other lesions were noted. B. pilosicoli was identified by PCR.

**DIAGNOSIS** Diagnosis can be made by identifying typical organisms on histopathology. PCR of intestinal contents is diagnostic (Helie et al., 2000).

**PREVENTION AND THERAPY** Treatment with ranidazole stopped the spread of the disease in some cases as described by Vanrobaeys et al. (1998), although cessation of treatment resulted in resumption of disease. As the majority of reports describe co-pathogens, controlling co-pathogens may be the most effective prevention.

**Brucella**

Brucella spp. are zoonotic, Gram-negative, strictly aerobic, intracellular, non-motile coccobacilli, which infect a variety of species, including guinea pigs (Martirosyan et al., 2011; Pappas, 2010; Van Hoosier and Robinette, 1976). Natural infections in guinea pigs have been described likely associated with contaminated food, bedding, or other biological materials (Van Hoosier and Robinette, 1976). In these outbreaks, guinea pigs developed disease similar to that seen in other species including testicular and joint swelling as well as abscesses in the liver and pancreas. Modern husbandry practices should limit transmission of Brucella spp. to guinea pigs.

**Campylobacter jejuni**

Campylobacter jejuni is a species of curved, rod-shaped, non-spore-forming, Gram-negative, microaerophilic bacteria that naturally colonize the digestive tract of birds and numerous other species, including domestic farm animals, dogs, cats, various wildlife, and rodents (Horrocks et al., 2009). It is a common cause of human gastroenteritis worldwide primarily from contamination of food. It was isolated from laboratory animal guinea pigs in one report where the prevalence of C. jejuni in a multispecies laboratory animal facility was investigated (Meanger and Marshall, 1989). In this report, no clinical signs were seen in any of the animals involved and pathological analysis was not done. Guinea pigs have been used as an animal model of C. jejuni infection (Burrough et al., 2009; Coid et al., 1987).

**Chlamydophilia caviae**

**BACKGROUND AND ETIOLOGY** Guinea pig inclusion conjunctivitis was first described in 1964 associated with an experiment to examine the correlation between vitamin deficiency and the development of trachoma virus (Murray, 1964). The organism was identified as a type of Chlamydia psittaci, a member of the psittacosis-lymphogranuloma-trachoma group, first thought to be protozoa, then viruses because they could pass through a 450-nm filter, and finally in 1966 recognized as bacteria (Longbottom and Coulter, 2003; Moulder, 1966; Songer and Post, 2005). As members of the family Chlamydiaceae, they are
Gram-negative, obligate intracellular pathogens that infect a variety of animals, including amoeba, birds, sheep, humans, and guinea pigs (Greenwood, 2007). Recently they have been divided into two genera: *Chlamydia* and *Chlamydophila*. *Chlamydophila* species include *C. caviae* as well as *C. pneumoniae* (humans, horses, koalas) and *C. psittaci* (birds) (Everett et al., 1999; Murray, 1964).

Unlike most bacteria, the cell walls of *Chlamydiaceae* do not have a peptidoglycan layer, but they do have a major outer-membrane protein, which is the determinant for serologic classification (Greenwood, 2007; Songer and Post, 2005). They also have a unique life cycle which consists of two forms; a small infectious elementary body which is more similar to a spore in that it is environmentally resistant and not metabolically active and a larger metabolically active, non-infectious reticulate body that is responsible for division within the host cell.

**EPIZOOTIOLOGY AND PATHOGENESIS** Generally, *C. caviae* infection is thought to be endemic in guinea pig colonies (Percy and Barthold, 2007), although its detection in colonies has been variable. In a survey done in 1964 of five herds of guinea pigs, conjunctival staining revealed the organism in four out of five herds, although not in any guinea pigs less than 4 weeks of age (Murray, 1964). In 2006, two breeding facilities of conventional guinea pigs in Korea were examined by conjunctival staining and no positive organisms were seen (Park et al., 2006). A survey of pet guinea pigs with normal conjunctiva, also revealed no positive staining (Coster et al., 1964), which may reflect the sensitivity of the test used or the actual prevalence of *C. caviae*. In a study using real-time PCR for diagnosis, *C. caviae* was detected in 12 out of 12 guinea pigs tested, four out of four rabbits, and one dog from samples obtained from a diagnostic laboratory (Pantchev et al., 2010). *C. caviae* in a second report was identified via PCR from conjunctival swabs from a rabbit, cat, and human that lived in the same household as infected guinea pigs (Lutz-Wohlgroth et al., 2006). Also utilizing PCR and DNA sequencing, *C. caviae* was detected in foals with conjunctivitis, rhinitis, and coughing, indicating the host range of the species of *Chlamydiaceae* may continue to be refined as new diagnostic tests are utilized (Gaede et al., 2010).

One study identified *Acanthamoeba* spp. via PCR from two guinea pigs with conjunctivitis that were also PCR positive for *C. caviae* (Lutz-Wohlgroth et al., 2006). Their role in the disease process is unclear.

Urogenital disease has been reported in natural infections with *C. caviae* and has been reproduced in experimental models (Lutz-Wohlgroth et al., 2006; Mount et al., 1973). In experimental infections, inoculation with *C. caviae* in the lower genital tract of female guinea pigs causes a self-limiting infection lasting 3–4 weeks. Typically, the infection involves the epithelium of the cervix with very little inflammation. However, in 80% of the animals, the infection progresses to involve the oviducts, with half of the animals developing pathologic changes in the oviducts including inflammation and fibrosis (Barron et al., 1979; Rank and Sanders, 1992). Infection can be transferred from infected male animals to females during sexual intercourse and vertically from dam to pups (Padilla-Carlin et al., 2008; Miyairi et al., 2010).

In experimental infections, both cell-mediated and humoral immunity are important in recovery and resistance to re-infection (Miyairi et al., 2010). Early infection is characterized by influx of polymorphonuclear cells while later in infection, lymphocytes predominate. T-cell depletion results in chronic infection and delayed clearance of the organisms. Decreased antibody response also correlates with delayed clearance of the organisms (Miyairi et al., 2010; Rank et al., 1979).

**CLINICAL MANIFESTATIONS** *C. caviae* has been primarily associated with conjunctivitis. Guinea pigs have reddened, swollen conjunctiva with serous to purulent discharge, follicular hypertrophy, and pannus (Deeb et al., 1989; Lutz-Wohlgroth et al., 2006; Murray, 1964; Padilla-Carlin et al., 2008; Strik et al., 2005). Generally the conjunctivitis resolves in 3–4 weeks. Occasionally, conjunctivitis is accompanied by rhinitis. In one study, nasal discharge was present in 31 of 39 of the animals with ocular discharge (Lutz-Wohlgroth et al., 2006). Vaginal discharge was seen in 25% (ten of 39) of the animals although the organism could not be recovered by PCR from either the nose or the vagina. Abortion was recorded in two animals. An early study also reported rhinitis, bronchopneumonia and abortions, although this study was complicated by infection with *Streptococcus pneumoniae* and *Bordetella bronchiseptica* (Schmeer et al., 1985).

**PATHOLOGY** Histological evaluation of the eyes and surrounding tissue reveals a mixed inflammatory response and congestion beneath the conjunctival epithelium (Deeb et al., 1989; Lutz-Wohlgroth et al., 2006). Histological examination of the urogenital tract has primarily been described following experimental infection and consists of inflammation of the endometrium, mesosalpinx, and oviduct with a mixed inflammatory infiltrate and fibrosis (Barron et al., 1979; Rank and Sanders, 1992).

**DIAGNOSIS** Diagnosis is by cytology, PCR, culture, tissue assays, and serology (Songer and Post, 2005). Giemsa, Gimenez, or Macchiavello stains on cytologic preparations reveal inclusions in the cytoplasm. Inclusions are a dark purple with Giemsa and red with Gimenez or Macchiavello stains. Cytology can be insensitive hence PCR can be used in addition (Pantchev et al., 2010; Strik et al., 2005). In one study, 31 samples
were tested via cytology and PCR (Lutz-Wohlgroth et al., 2006). Twenty-one were positive by PCR for C. caviae, however, no samples were positive by cytology. As C. caviae is an obligate intracellular pathogen, it cannot be cultured in cell-free media, but only on specific cell lines (Songer and Post, 2005). This is an insensitive and difficult process that is not typically used for diagnosis. Direct fluorescent antibody test and enzyme immunoassays can be used to detect antigens in cytology samples or tissues (Percy and Barthold, 2007; Songer and Post, 2005).

**PREVENTION AND THERAPY** Generally, the disease is self-limiting and treatment is not required (Percy and Barthold, 2007; Quesenberry and Carpenter 2004). No current vaccine prevents chlamydial infection, although vaccination studies have demonstrated a decrease in the intensity of the disease following vaccination (Padilla-Carlin et al., 2008). Recognition that zoonotic transmission is a possibility should guide appropriate personal protective equipment choices (Lutz-Wohlgroth et al., 2006).

**Citrobacter**

**BACKGROUND AND ETIOLOGY** *Citrobacter* is a genus of Gram-negative coliform bacteria of the family Enterobacteriaceae (Boone et al., 2001). In the 1960s and 1970s, a disease eventually named transmissible murine colonic hyperplasia caused by coliform bacteria of the genus *Citrobacter* was recognized (Mundy et al., 2005; Percy and Barthold, 2007; Petty et al., 2010). Originally described as unusual biotypes of *Citrobacter freundii*, these organisms were eventually separated into their own species, *Citrobacter rodentium*, on the basis of DNA sequencing studies (Luperchio et al., 2000; Petty et al., 2010). Whether the organisms that caused severe septicemia and death in guinea pigs in 1988 (Ocholi et al., 1988) and other disease syndromes in hysterectomy-rederived guinea pigs (Boot and Walvoort, 1986) are *C. freundii* as originally indicated or *C. rodentium* is unclear.

**PATHOGENESIS, CLINICAL MANIFESTATIONS, AND PATHOLOGY** There are two reports of disease associated with *Citrobacter* spp. in guinea pigs (Boot and Walvoort, 1986; Ocholi et al., 1988). First, *Citrobacter* spp. were isolated from germ-free guinea pigs that were exposed to defined flora from gnotobiotic mice (Boot and Walvoort, 1986). *Citrobacter* spp. were isolated from the middle ear, spleen, mammary gland, and kidney of some animals as well as the intestinal tract, suggesting an ability to cause varied disease in guinea pigs that are not populated with normal flora. Second, an epizootic of *Citrobacter* spp. septicemia in a large colony of conventional guinea pigs was reported (Ocholi et al., 1988). Animals presented with diarrhea, dyspnea, and decreased appetite. Mortality in weanlings and breeders was 115 of 1300 animals. Gross necropsy revealed lung consolidation with pleural adhesions as well as enteritis and thickening of the intestinal wall. Fibrinous pneumonia and septic thrombi in the capillaries of the lung, liver, and spleen were seen histopathologically. *Citrobacter* spp. were consistently isolated in pure culture from the lung, liver, spleen, and intestine.

**DIAGNOSIS** Culture is the traditional method of detecting *Citrobacter* spp. which grow well on normal media, are aerobic or facultative anaerobic, ferment glucose, produce catalase, but not oxidase, and are generally lactose-negative or later lactose-fermenting (Greenwood, 2007). However, PCR is more sensitive than bacterial culture for detection of *C. rodentium* in feces from mice (McKeel et al., 2002).

**PREVENTION AND THERAPY** *C. freundii* strains utilize a number of methods to encode resistance to ampicillin and cephalosporins (Pfeifer et al., 2010). Enrofloxacin has been successful in treating mice infected with *C. rodentium* (Maggio-Price et al., 1998). Prevention would include eliminating contact with *C. rodentium*-infected mice and other rodents.

**Clostridium piliforme (Tyzzer’s Disease)**

**BACKGROUND** *Clostridium piliforme*, first described in 1917 (Tyzzer, 1917), causes severe disease in many laboratory animals as well as other mammals (Percy and Barthold, 2007). Although rare in modern colonies, outbreaks in mice, rats, rabbits, and guinea pigs have been reported and *C. piliforme* is found in both wild (Wobeser et al., 2009) and domestic mammals (Borchers et al., 2006; Ikegami et al., 1999). While Tyzzer’s disease is not generally considered zoonotic, infection of an HIV-positive patient has been reported (Smith et al., 1996).

**ETIOLOGY** *Clostridium piliforme* (formerly *Bacillus piliformis*) is a Gram-negative, spore-forming, anaerobic rod that can survive for as long as five years in the environment (Percy and Barthold, 2007; Songer and Post, 2005).

**PATHOGENESIS** *C. piliforme* is thought to be transmitted via fecal–oral transmission. In experimental models, oral inoculation was successful when other routes of inoculation did not result in disease (Waggie et al., 1987). Vertical transmission has been reported in one case of hysterectomy-rederived guinea pigs (Boot and Walvoort, 1984). In outbreaks of Tyzzer’s disease in other species, usually predisposing factors such as stress, overcrowding, poor sanitation, or immune-modulating treatments contribute to the development of disease (Percy and Barthold, 2007).
**CLINICAL MANIFESTATIONS** Clinical signs generally consist of diarrhea, unthriftiness, dehydration, cachexia, or acute death (Boot and Walvoort, 1984; McLeod et al., 1977; Zwicker et al., 1978) typified seen in weanlings. Subclinical infections have been noted (Boot and Walvoort, 1984).

**PATHOLOGY** Lesions are usually found only in the gastrointestinal tract in young guinea pigs, although liver lesions have been reported in some animals (Sparrow, 1978; Waggie et al., 1987). Grossly, pinpoint gray foci occur on the ileum, cecum, and colon as well as enlarged, reddened mesenteric and colonic lymph nodes (McLeod et al., 1977; Sparrow, 1978; Waggie et al., 1987; Zwicker et al., 1978). White to tan pinpoint foci are also observed on the liver. Microscopically, foci of necrosis occur in the mucosa of the ileum, cecum, and colon as well as foci of periportal coagulative hepatic cellular necrosis when the liver is involved. Clusters of intracellular organisms can be observed via silver stain or Giemsa stain in affected enterocytes and hepatocytes. In two reports, affected animals have also had large numbers of spirochetes evident at necropsy (McLeod et al., 1977; Zwicker et al., 1978).

**DIAGNOSIS** *C. piliforme* cannot be cultured using standard media, although it can be isolated by inoculation of cell lines, embryonated hen's eggs, and primary mouse or chick embryo cell cultures (Niepceron and Licois, 2010; Percy and Barthold, 2007). Therefore, diagnosis typically relies on characteristic lesions and organisms observed on histopathology using a Warthin-Starry silver stain or Giemsa stain in affected enterocytes and hepatocytes. In two reports, affected animals have also had large numbers of spirochetes evident at necropsy (McLeod et al., 1977; Zwicker et al., 1978).

**TREATMENT AND CONTROL** Treatment of individual animals has not been reported. Tyzzer’s disease affects a wide variety of animals and immune-compromised people. Prevention entails modern husbandry and sanitation practices, preventing contamination of food and bedding, and separation of species.

**Escherichia coli**

*Escherichia coli* are aerobic, straight Gram-negative rods and are part of the normal intestinal flora of most vertebrates, including guinea pigs (Crecelius and Rettger, 1943; Songer and Post, 2005). Several pathotypes have been reported (e.g. EPEC-enteropathogenic strains), some which produce cytotoxins. Diarrhea, rough hair coats, wasting and death have been reported to be associated with *E. coli* infection in conjunction with other environmental stressors (Ganaway, 1976). In addition, there is one report of a compilation of cases of mastitis in guinea pigs from a diagnostic lab over a four year period (Kinkler et al., 1976). Of the 26 cases where cultures were taken, *E. coli* was found in 17 cases with the next most common isolate being *Klebsiella pneumoniae* in six cases. Diagnosis may be obtained by culture of affected organs on MacConkey agar and differentiation from other enteric Gram-negative bacteria by a number of biochemical reactions such as indole production and utilization of certain sugars (Greenwood, 2007).

**Klebsiella pneumoniae**

**BACKGROUND** Perkins (1901) described an epizootic outbreak in 25 laboratory guinea pigs that resulted in the death of all but two animals 18–24 hours after the onset of disease. A short bacillus, often paired, was isolated in the blood, spleen, liver, and peritoneal exudates. Disease was reproduced in naïve guinea pigs subsequently administered the bacterium by the intraperitoneal route. Perkins’ findings were similar to those of Howard (1899), who inoculated dogs, rabbits, mice, pigeons, and guinea pigs with a bacillus organism isolated from human patients.

**ETIOLOGY** *Klebsiella pneumoniae* is a Gram-negative, rod-shaped bacillus from the genus *Klebsiella* and family *Enterobacteriaceae* (Boone et al., 2001). *K. pneumoniae* is facultatively anaerobic, oxidase-negative, and produces acid and gas from lactose. It is an enteric bacterium, noted in the intestinal tract of 5% of healthy humans (Ganaway, 1976). It can also reside in the skin and mouth. *K. pneumoniae* causes pneumonia in guinea pigs of both sexes and all ages, although there are few reports of natural infections of this animal species with this organism.

**CLINICAL MANIFESTATIONS** In the epizooenic outbreak described by Perkins, animals presented as anorexic and ungroomed, and their illness escalated in severity until, in some animals, a comatose condition ensued (Perkins, 1901). Animals usually died 18–24 hours after the onset of clinical signs. In other epizootic outbreaks, dyspnea has been reported prior to reaching the comatose state (Ganaway, 1976). Less severely infected animals may be able to recover from disease and develop immunity to re-infection (Perkins, 1901). Otitis media and other signs consistent with a state of septicaemia have been associated with clinical disease (Fox, 2002; Ganaway, 1976; Kohn, 1974).

**PATHOLOGY** Seropurulent or serofibrinous peritonitis is noted at necropsy (Fox, 2002; Ganaway, 1976;
Perkins, 1901). Additionally, such exudates may be observed in the pleural cavity and pericardial sac. Congestion of the liver, spleen, and kidney has been noted, as has hepatic coagulative necrosis and degeneration of the renal tubule cells. An acute, necrotizing bronchopneumonia may be observed.

**DIAGNOSIS** Diagnosis of *K. pneumonia* is usually via culture of the upper respiratory tract. The bacterium has been isolated from blood, spleen, liver, peritoneal exudate, and cerebrospinal fluid (Fox, 2002; Ganaway, 1976; Perkins, 1901). *K. pneumoniae* can be differentiated from *K. oxytoca*, another *Klebsiella* spp. frequently recovered in animals, by the fact that it is indole-negative and does not grow at 10°C, while *K. oxytoca* is indole-positive and does grow at 10°C.

**PREVENTION AND THERAPY** Antibiotic treatment for *Klebsiella* infection should be based on sensitivity of culture isolates. Ceftriaxone and cefodizime were found effective at clearing *K. pneumoniae* in experimentally infected guinea pigs (Drago et al., 1999), although generally, chloramphenicol, enrofloxacin, trimethoprim-sulfa, and aminoglycoside drugs are considered the safest antibiotic choices for use in guinea pigs.

**Lawsonia intracellularis**

**BACKGROUND AND ETIOLOGY** Proliferative enteritis associated with *Campylobacter*-like organisms has been reported in many species including pigs, hamsters, rats, rabbits, foals, NHPs, ferrets, and deer (Lawson and Gebhart, 2000). In the early 1990s, molecular techniques resulted in the identification of *Lawsonia intracellularis* as the causative agent of many of these syndromes. Since that time, diagnostics, including PCR, have enabled the diagnosis of *L. intracellularis* infection (Collins et al., 2011).

**PATHOGENESIS, CLINICAL MANIFESTATIONS, AND PATHOLOGY** There have been two reports of disease in guinea pigs associated with *Campylobacter*-like organisms, both prior to the identification of *L. intracellularis*. In 1981, one 3.5-month-old guinea pig, treated with steroids for 90 days as part of a study, displayed no clinical signs of disease but on necropsy had marked duodenal mucosal hyperplasia with intracellular Warthin-Starry stained argyrophilic bacteria in affected epithelial cells (Elwell et al., 1981). Two cagemates of this guinea pig, that had the same steroid treatment, died at days 13 and 30. One had diarrhea for two days prior to death. Histopathology revealed acute enteritis with mucosal erosions without mucosal hyperplasia in both animals. Bacteria similar to that seen in the first case were found in the epithelial cells. The authors noted this organism was very similar to the organism associated with transmissible mucosal hyperplasia of hamsters (subsequently identified as *L. intracellularis*).

In 1983, two dams and five young guinea pigs in a laboratory in Japan developed diarrhea, anorexia, weight loss, and dehydration. Two young animals died 5–7 days post-onset of clinical signs. Grossly, there was thickened jejunum and ileum. Histopathologically, there was hyperplasia and proliferation of the epithelial cells and dilation of the glands primarily in the ileum and the distal part of the jejunum. Immature epithelial cells contained various numbers of intracytoplasmic, non-membrane-bound, curved organisms resembling *Campylobacter* spp. bacteria.

**DIAGNOSIS** Characteristic histopathological lesions, immunohistochemistry, and PCR are diagnostic (Collins et al., 2011; Lawson and Gebhart, 2000).

**PREVENTION AND THERAPY** Antibiotics have been used to treat a similar proliferative enteritis in swine with success (Lawson and Gebhart, 2000). Care should be taken to avoid penicillins and other antibiotics implicated in antibiotic-associated dysbacteriosis (Percy and Barthold, 2007).

**Leptospira**

**BACKGROUND AND ETIOLOGY** *Leptospira* are tightly coiled, aerobic, Gram-negative, flagellated spirochetes belonging to the genera *Leptospira*, family *Leptospiraceae*, phylum, Spirochaetes (Boone et al., 2001). Before 1989, the genus, *Leptospira*, was divided into two species, *L. interrogans* (pathogenic) and *L. biflexa* (non-pathogenic) which each contained strains separated into numerous serovars (Levett, 2001). More recently, DNA analysis has identified 20 species of *Leptospira* and revisions of these taxonomic groups are ongoing (Galloway and Levett, 2010; Levett, 2001).

**EPIZOOTIOLOGY AND PATHOGENESIS** *Leptospira* are zoonotic organisms with a world-wide distribution that infect a variety of mammals, including mice, rats, carnivores, and ruminants (Ko et al., 2009; Levett, 2001; Percy and Barthold, 2007). Wild guinea pigs in South America (*Cavia porcellus apera*), infected with *Leptospira* spp., have been implicated as the natural reservoir responsible for transmitting the disease to domestic cattle (Blood et al., 1963). In domestic guinea pigs, there have been only a few reports of natural infection, although the guinea pig infection models have been used extensively in *Leptospira* research (Ko et al., 2009; Van Hoosier and Robinette, 1976). Data from research models and infections in other species indicate that transmission occurs from direct contact with infected urine, soil, or water as *Leptospira* are excreted in the urine (Ko et al., 2009; Lourdault et al., 2009).
**CLINICAL MANIFESTATIONS AND PATHOLOGY** A report from 1937 describes a natural infection where one out of 12 guinea pigs died from leptospirosis (Ganaway, 1976). Pathological findings include jaundice, petechial hemorrhages in the skin, fascia, and muscles, and ecchymosis in the lung. A more recent report of a case of leptospirosis in a 21-year-old man, described 20 out of 50 guinea pigs that died on his farm in Germany. Three of the remaining guinea pigs were tested and were serologically positive for *Leptospira* serovar *bratislava* similar to the man. No necropsies of affected animals were described.

**DIAGNOSIS** Direct examination of infected tissue, urine, or blood with dark-field microscopy, immunofluorescence, or light microscopy with special stains is useful for diagnosis (Greenwood, 2007; Levet, 2001). Culture and PCR are additional diagnostic tools. Growth in culture can be slow. Generally, antibody detection is used to demonstrate previous infection.

**PREVENTION AND THERAPY** Antimicrobial treatment of individual animals is generally successful in other species (Pischke et al., 2010; van de Maele et al., 2008), although in guinea pigs, care must be taken to avoid antibiotic-associated dysbacteriosis (Percy and Barthold, 2007). Prevention includes preventing exposure to wild rodents and *Leptospira*-infected food, bedding, soil, or water.

**Listeria monocytogenes**

**BACKGROUND** *Listeria monocytogenes* was first discovered in 1926 by Murray et al. (1926), who isolated it from laboratory rabbits and guinea pigs. Since that time, few cases have been reported in guinea pigs, although guinea pigs are very susceptible and have been used extensively to model the pathogenesis of listeriosis (Cossart, 2007; Disson et al., 2009; Fox, 2002).

**ETIOLOGY** *Listeria monocytogenes* is a facultative intracellular, non-spore-forming, zoonotic, food, soil-, and silage-borne bacterium which causes disease in birds and many mammals.

**PATHOGENESIS, CLINICAL MANIFESTATIONS, AND PATHOLOGY** In spontaneous infections of guinea pig colonies, *L. monocytogenes* infection has been correlated with acute death, reproductive disorders such as abortions and still births, as well as conjunctivitis (Chukwu et al., 2006; Colgin et al., 1995; Fox, 2002). In an outbreak associated with feeding infected greens to a colony of 80 guinea pigs, the mortality rate was reported to be 80–100% with lung and liver lesions predominating (Chukwu et al., 2006).

Conjunctivitis was reported in one outbreak affecting 11 out of 49 newly arrived guinea pigs (Colgin et al., 1995). *L. monocytogenes* was cultured from 10 of 12 specimens submitted. The animals presented with unilateral or bilateral serous to purulent discharge with hyperemic conjunctiva. Histologically, there was corneal ulceration, stromal edema, and vascular proliferation. The conjunctiva contained an inflammatory infiltrate and the lacrimal gland had multifocal areas of inflammation and necrosis. Intracytoplasmic Gram-positive rods were seen in the conjunctival epithelium and no chlamydial organisms were identified on conjunctival scrapings or by histopathology. Experimentally, guinea pigs have been shown to be susceptible to *Listeria*-induced conjunctivitis.

**PREVENTION AND THERAPY** Prevention of contamination of food or bedding is essential to prevent this infection.

**Pasteurella multocida**

**BACKGROUND** Pasteurellosis is rare in present-day guinea pig laboratory colonies. Reports of epizootic outbreaks due to Gram-negative cocccobacilli were reported in Europe in the late 1800s (Wright, 1936).

**ETIOLOGY** *Pasteurella multocida*, a Gram-negative, non-spore-forming and non-motile rod is a member of the *Pasteurella* genus and the *Pasteurellaceae* family (Songer and Post, 2005).

**EPIZOOTIOLOGY AND PATHOGENESIS** *Pasteurella* spp. are mucosal commensal organisms of the oropharynx and gastrointestinal tract of many species, including man (Songer and Post, 2005). When stressed, the animal’s immune system can be overwhelmed and, in guinea pigs, pneumonia may result. *P. multocida* can be transmitted to man via contact with infected saliva, which is likely to occur as a result of a bite wound or scratch.

**CLINICAL MANIFESTATIONS** Wright detailed an outbreak of pasteurellosis that killed 600 guinea pigs over a 1-year period (Wright, 1936). Clinical signs were not noted prior to death. *P. multocida* has been isolated from cases of conjunctivitis (Percy and Barthold, 2007).

**PATHOLOGY** Fibrinopurulent serositis is present in cases of guinea pig pasteurellosis (Fox, 2002; Ganaway, 1976; Wright, 1936). Such serositis has been noted in the pericardium, pleura, and peritoneum. Lung consolidation may also be observed (Fox, 2002).

**DIAGNOSIS** *Pasteurella* infection is diagnosed via culture. The bacteria do not reliably grow well on MacConkey agar, therefore blood agar is routinely used for isolation (Ganaway, 1976; Songer and Post, 2005). Plates should be incubated at 3–5% CO₂ at 37°C for
24–48 hours (Songer and Post, 2005). In animal tissue or fluids, *P. multocida* appears as a bipolar rod after aniline dye staining, but in a smear taken from culture, it stains evenly (Ganaway, 1976). Unlike *P. pneumotropica*, *P. multocida* is o-nitrophenyl-β-D-galactoside (ONPG) and urease-negative (Songer and Post, 2005). *P. pneumotropica* is also positive for the fermentation of mannose, while *P. multocida* is negative. An ELISA-based assay has been developed to monitor antibodies to the SP group of *Pasteurellaceae*, which is one of five serologically distinct groups of *Pasteurellaceae* in guinea pigs (Boot et al., 1995).

**PREVENTION AND THERAPY** Antibiotic treatment of *P. multocida* should be based on culture sensitivities. Antimicrobial therapy will eliminate clinical signs, but will not eliminate the organism from the colony (Songer and Post, 2005).

**Pseudomonas and Aeromonas**

**BACKGROUND** Scherago (1937) reported on a fatal epizootic septicemia in a colony of young guinea pigs received from a local breeder. Animals died within 5–6 hours after showing clinical signs and “Gram-negative, non-spore-forming encapsulated rods with rounded ends and straight sides appearing singly and occasionally in pairs end to end” were found on smears from the peritoneal cavities of all examined animals. The route of infection was not determined in this colony, but Scherago did complete the required steps to fulfill Koch’s postulates and demonstrated that the infection was due to *Pseudomonas caviae*. *P. caviae* has since been reclassified as *Aeromonas caviae*, of the *Aeromonadaceae* family.

*Pseudomonas aeruginosa* was noted as the cause of pulmonary botryomycosis in two guinea pigs (Bostrom et al., 1969).

**ETIOLOGY** *P. aeruginosa*, a member of the genus *Pseudomonas*, is part of the *Pseudomonadaceae* family (Songer and Post, 2005). *Pseudomonas* spp. are Gram-negative rods that are aerobic, non-spore-forming, oxidase-positive, and non-fermentative.

**EPIZOOTIOLOGY AND PATHOGENESIS** *Pseudomonas* organisms thrive in aqueous environments (Songer and Post, 2005). Additionally, they are ubiquitous in soil, decaying organic matter, and vegetation. *Pseudomonas* spp. are opportunistic pathogens of both humans and animals, yet, there are few reports of infections caused by these agents in guinea pigs (Fox, 2002).

**CLINICAL MANIFESTATIONS** Bostrum et al. (1969), did not describe the clinical signs associated with the epizootic outbreak of pulmonary botryomycosis. Otitis media, conjunctivitis, and an inflamed prostate gland are signs that have been associated with *Pseudomonas* in other reports of guinea pig infection (Fox, 2002).

**PATHOLOGY** A focal, necrotizing bronchopneumonia, along with pulmonary consolidation has been described in cases of guinea pig *Pseudomonas* infection (Bostrum et al., 1969; Fox, 2002; Ganaway, 1976; Percy and Barthold, 2007). Bostrum noted atypical “sulfur granules”, resembling the spherules of *Coccidioides immitis*, in the lungs of affected animals (Bostrom et al., 1969).

**DIAGNOSIS** *P. aeruginosa* can be cultured from infected tissues (Songer and Post, 2005). *P. aeruginosa* grows well on MacConkey agar and trypticase soy agar. Additionally, Cetrimide agar, a commercial formulation, selectively isolates *P. aeruginosa*.

**PREVENTION AND THERAPY** The best means of controlling *Pseudomonas* is to reduce possible sources of infection, such as damp bedding or stagnant water. Animal drinking water should be monitored for *P. multocida*. Reducing stressors, such as overcrowding and concurrent infection, also aids in control. *Pseudomonas* spp. have an inherent resistance to many antimicrobials.

**Salmonella**

**BACKGROUND** Some of the earliest reports of salmonellosis in guinea pigs date back to the 1800s (Nelson and Smith, 1927). Multiple outbreaks of natural infections in guinea pig colonies in the United States were documented throughout the early 1900s (Holman, 1916; Nelson and Smith, 1927). Since this period of time, as laboratory standards have grown more stringent and general hygiene and sanitation have improved, the occurrence of salmonellosis in laboratory guinea pigs has declined greatly (Fox, 2002; Harkness and Wagner, 1995; Percy and Barthold, 2007).

**ETIOLOGY** Members of the genus *Salmonella* are Gram-negative, non-spore-forming bacilli that are facultative anaerobes. *Salmonella* other than *S. typhi* or *S. paratyphi* produce hydrogen sulfide, as well as acid and gas from glucose, but not lactose (Ganaway, 1976; Songer and Post, 2005). *Salmonella* is a member of the *Enterobacteriaceae* family. While multiple serovars have been recovered from guinea pigs, the most frequently isolated are *S. typhimurium* and *S. enteritidis* (Fox, 2002; Ganaway, 1976; Harkness and Wagner, 1995; Quesenberry and Carpenter, 2004; Percy and Barthold, 2007). Humans are susceptible to disease from the same serovars and phage types as guinea pigs (Fish et al., 1968; Percy and Barthold, 2007; Rigby, 1976).
**EPIZOOTIOLOGY AND PATHOGENESIS** Guinea pigs are extremely susceptible to *Salmonella* (Fox, 2002). Transmission of *Salmonella* is primarily fecal-oral or via ingestion of contaminated feed (contaminated with feces of infected guinea pig or a wild rodent) (Fox, 2002; Harkness and Wagner, 1995; Percy and Barthold, 2007; Quesenberry and Carpenter, 2004). Entry via the conjunctiva has also been reported in guinea pig epizootics (Iijima et al., 1987; Moore, 1957). Additionally, ingestion of contaminated blood or tissue can transmit *Salmonella* (Fox, 2002). Stressed animals, due to conditions such as weaning, parturition, old age or poor nutrition, are more susceptible to infection (Quesenberry and Carpenter, 2004). Recovered animals can develop an asymptomatic carrier state with intermittent shedding in the feces, making elimination of this bacterium from a colony difficult (Fox, 2002; Harkness and Wagner, 1995; Percy and Barthold, 2007). The incubation time for *Salmonella* is 5–7 days and epizootic or enzootic patterns of infection are possible (Fox, 2002; Ganaway 1976).

**CLINICAL MANIFESTATIONS** Disease due to *Salmonella* occurs as peracute septicemia or acute, subacute, or chronic enteritis (Songer and Post, 2005). Acute disease is characterized by high morbidity and low to moderate mortality. Clinical signs include depression, weakness, and fever. Dehydration and electrolyte imbalance may be severe. Infection spreads rapidly within a colony. Conjunctivitis and abortions have also been noted (Percy and Barthold, 2007). Although weight loss is present, diarrhea may or may not occur in guinea pigs. In an epizootic outbreak, young guinea pigs may die suddenly without prior signs of illness.

**PATHOLOGY** In acute and peracute cases, there may be no lesions seen at necropsy (Harkness and Wagner, 1995; Percy and Barthold, 2007). Splenomegaly may be observed in subacute and chronic infections. Minute white foci and/or yellowish-white nodules, up to several millimeters in diameter, may occur in the spleen, liver, or other lymph nodes. Similar foci or nodules may also occur in the lung, pleura, peritoneum, and in the wall of the uterus. Rupture of the nodules may result in a suppurative pleuritis, peritonitis, and/or pericarditis. Gas may be observed in the small and large intestine, along with catarrhal enteritis (Fish et al., 1968).

On histopathology, lesions support bacterial invasion, with subsequent necrosis and abscess formation (Ganaway, 1976). Nodules are noted to be “typhoid-like” granulomas, with areas of central necrosis, surrounded by histiocytes. Polymorphonuclear leukocytes and histiocytes are present in the Peyer’s patches of the ileum and jejunum.

**DIAGNOSIS** *Salmonella* can be isolated from blood, feces, and affected organs (most commonly from the spleen) (Fox, 2002). Recovery requires special conditions: enrichment in a broth such as selenite-F or tetracycline and culture at 37°C on MacConkey’s or brilliant green agar (Fox, 2002; Songer and Post, 2005).

**PREVENTION AND THERAPY** Prevention is the best approach (Harkness and Wagner, 1995; Rigby, 1976). All fresh fruit and vegetables should be thoroughly washed and stored in airtight containers. Since so many species of mammals are potential carriers, the exclusion of wild rodents, birds, and other vermin is essential. When increased colony mortality is apparent and a chronic case is recognized at necropsy, *Salmonella* infection is likely widespread and well established in the colony. In situations such as this, it is reasonable to depopulate the colony, sanitize the premises, and restock with *Salmonella*-free guinea pigs.

Treatment on an individual basis will include the appropriate antibiotics with fluid therapy. Animals that become asymptomatic after treatment may become carriers, a problem with zoonotic potential. Antimicrobial resistance is expanding; 90% of *Salmonella* isolates from domestic animals demonstrate multi-drug resistance (Songer and Post, 2005).

**Streptobacillus moniliformis**

**BACKGROUND** *Streptobacillus moniliformis* is one of the causative agents of rat bite fever, a significant worldwide, zoonotic, systemic infection of humans associated with contact with rats (Gaasta et al., 2009; Khatchadourian et al., 2010). It was described in early recorded history in India and was recognized in the US as early as 1839 as a syndrome that developed following contact with rats (Gaasta et al., 2009). *S. moniliformis* also causes Haverhill fever, a systemic infection of those who eat food contaminated with rat urine or feces (Abdulaziz et al., 2006; McEvoy et al., 1987; Shanson et al., 1983).

**ETOLOGY** *Streptobacillus moniliformis*, a facultative anaerobic, non-motile, non-capsulate, pleomorphic, Gram-negative rod, is the type species of the genera, *Streptobacillus*, family *Leptotrichiaceae* within the phylum *Fusobacteria* (Greenwood, 2007; Nolan et al., 2009). Its genome has been completely sequenced (Nolan et al., 2009).

**EPIZOOTIOLOGY AND PATHOGENESIS** *S. moniliformis* is commonly found in the nasopharynx of wild and pet rats (Gaasta et al., 2009; Wullenweber, 1995), although typically excluded from modern SPF laboratory animal facilities (Nicklas et al., 2002; Pritchett-Corning et al., 2009). The organism has also been found in carnivores, calves, pigs, turkeys, and a variety of rodents including guinea pigs presumably following contact with infected rats (Gaasta et al., 2009; Wullenweber, 1995).
CLINICAL MANIFESTATIONS AND PATHOLOGY  Most commonly, *S. moniliformis* in guinea pigs has been associated with cervical lymphadenitis and other localized abscesses (Aldred et al., 1974; Fleming, 1976; Percy and Barthold, 2007; Van Hoosier and Robinette, 1976; Wullenweber, 1995). Severe necrotizing bronchopneumonia with pyogranuloma formation was reported in one guinea pig by Kirchner et al. (1992). No clinical signs of disease were noted in their report.

DIAGNOSIS  Gram stain of smears can be suggestive of infection by demonstrating short bacilli in chains or long filaments followed by bacterial culture and isolation (Greenwood, 2007; Kirchner et al., 1992; Wullenweber, 1995) although because of the fastidious nature of *S. moniliformis*, PCR is more commonly used for detection (Boot et al., 2002). If culture is attempted, samples must be cultured on a media containing serum, blood or ascitic fluid, such as Loeffler’s serum medium (Greenwood, 2007). Cross-reactive sequences between *Leptotrichia* spp. and *S. moniliformis* have been demonstrated and can result in false positives when PCR is used for diagnosis (Boot et al., 2008; Wouters et al., 2008). Sequence of the amplicon can differentiate these outcomes. As the entire sequence of *S. moniliformis* has recently been completed (Nolan et al., 2009), new primers for diagnosis may be forthcoming. Antibodies to *S. moniliformis* can be demonstrated by ELISA (Boot et al., 1993b, 2006).

PREVENTION AND THERAPY  Because the organism is not spread easily, outbreaks can be controlled by culling affected guinea pigs (Van Hoosier and Robinette, 1976). Treatment of individual animals with antibiotics is effective in other species (Gaastra et al., 2009; Van Hoosier and Robinette, 1976; Wullenweber, 1995). Severe necrotizing bronchopneumonia with pyogranuloma formation was reported in one guinea pig by Kirchner et al. (1992). No clinical signs of disease were noted in their report.

**Yersinia pseudotuberculosis**  
**BACKGROUND**  Ganaway states that “one of the earliest recognized bacterial disease of the guinea pig was caused by *Yersinia pseudotuberculosis*” (Ganaway, 1976). In present day colonies of laboratory guinea pigs, natural outbreaks of pseudotuberculosis are rare (Fox, 2002; Percy and Barthold, 2007).

**ETIOLOGY**  *Yersinia pseudotuberculosis*, an ubiquitous enteropathogen, is a Gram-negative, non-spore-forming, facultative anaerobic rod that is oxidase-negative and catalase-positive (Ganaway, 1976). It is non-hemolytic and produces both exotoxin and enzyme (Fox, 2002). Growth is optimal at 20–30°C (Fox, 2002; Ganaway, 1976). The genus *Yersinia* is part of the family *Enterobacteriaceae* and, in addition to guinea pigs, it causes pseudotuberculosis in other rodents, cats, and turkeys (Soner and Post, 2005).

**EPIZOOTIOLOGY AND PATHOGENESIS**  *Y. pseudotuberculosis* can result in clinical disease or a subclinical carrier state. Guinea pigs are very susceptible to infection with this bacterium (Fox, 2002; Ganaway, 1976). *Y. pseudotuberculosis* is shed in feces, therefore ingestion of food contaminated with feces from a carrier guinea pig, wild rodent, or bird can transmit the organism, as can aerosol spread, or entry via a bite wound or skin laceration (Fox, 2002; Ganaway, 1976; Rigby, 1976). Dams can pass infection to their pups (Fox, 2002). Orally absorbed organisms disseminate from the intestinal tract to the mesenteric lymph nodes.

Acute and chronic forms of disease have been described (Ganaway, 1976; Rigby, 1976). An acute septicemic form of infection can lead to mortality in 24–48 hours. A chronic infection that often lasts several weeks to months and ultimately results in death is the more classic pseudotuberculosis presentation.

**CLINICAL MANIFESTATIONS**  The classic clinical presentation associated with *Y. pseudotuberculosis* is that of wasting and lymphadenitis, sometimes with accompanying diarrhea, and frequently resulting in death about a month after initial infection (Obwolo, 1977; Sebesteny, 1976). The acute form of the disease can present with no clinical signs or consist of one to two days of coughing and respiratory distress prior to death (Rigby, 1976).

**PATHOLOGY**  Necropsy of animals chronically or sub-acutely infected with *Yersinia pseudotuberculosis* reveals nodules throughout the body, including the regional lymph nodes, spleen, liver, lung, and bone marrow (Fox, 2002; Percy and Barthold, 2007). The grayish-white spherical nodules vary from miliary pinpoint to 2–3 cm in diameter and may contain creamy to caseous exudate. In acute cases, nodules are noted in the intestinal wall, especially at the location of the terminal ileum and cecum, and often with accompanying mucosal ulceration and acute enteritis (Percy and Barthold, 2007). Lung congestion may be seen in acute cases (Rigby, 1976).

*Yersinia* nodules often have a central area of necrosis with neutrophilic infiltration; foamy macrophages are often noted in the periphery (Fox, 2002; Ganaway, 1976). Blood vessels within the nodule may contain bacterial emboli. In chronic lesions, fibroblasts and epithelial cells proliferate and nodules may become granulomatous, but do not calcify.

**DIAGNOSIS**  *Y. pseudotuberculosis* can be cultured from abscesses (Rigby, 1976). Direct smears may also
be beneficial. In acute septicemic cases, *Yersinia* may be cultured from the blood (Ganaway, 1976). *Yersina* spp. can be cultured on standard media and *Y. pseudotuberculosis* can be differentiated from *Y. pestis*, the causative agent of plague, by the fact that it is urease, and rhamnose-positive, while *Y. pestis* is negative for both of these growth conditions (Songer and Post, 2005).

**TREATMENT AND CONTROL**  Euthanasia of infected animals is advised due to the fact that antibiotic treatment can result in a carrier state, which, due to its zoonotic potential, puts human handlers and staff at risk. A killed vaccine has been unsuccessful at protecting guinea pigs from infection, but a more recent live vaccine has produced promising results (Quintard et al., 2010).

**FUNGAL INFECTIONS**

Dermatophytosis – *Trichophyton mentagrophytes*, *Microsporum canis*, *Microsporum gypseum*

**BACKGROUND** Dermatophytosis, also known as ringworm or tinea, indicates infection with pathogenic fungi in the phylum Ascomycota that cause the bulk of superficial fungal infections in humans and animals (Ameen, 2010; Howard et al., 2003). The fungi are keratinolytic and keratinophilic and infection is usually limited to cornified layers of the skin, hair, or nails (Howard et al., 2003; Weitzman and Summerbell, 1995). Their importance as pathogens is clear in that the majority of dermatophytes infecting animals are zoonotic (Chermette et al., 2008). Originally, the dermatophytes were organized into three anamorphic, or asexual, genera, *Microsporum*, *Trichophyton*, and *Epidermophyton*. The primary structure associated with asexual reproduction is the conidium and classification into these genera was based on the morphology of the macroconidia in culture. Subsequent studies revealed sexual reproduction in certain *Microsporum* and *Trichophyton* spp. that occurs by means of an ascospore found within an ascus. The dermatophyte sexual states (teleomorphs) are classified in the genus, *Arthroderma* (Weitzman and Summerbell, 1995). Recent efforts at phylogenetic analysis and identification of dermatophytes have been achieved by sequencing 28S ribosomal DNA (rDNA) and internal transcribed spacer (ITS) regions flanking 5.8S rDNA (Drouot et al., 2009; Frealle et al., 2007; Symoens et al., 2011). Dermatophyte species can also be divided into three groups determined by their adaptation to a certain habitat. Human-associated dermatophytes are anthropophilic (e.g. *Trichophyton rubrum*), those primarily found on animals and occasionally infecting humans are zoophilic (e.g. *Trichophyton mentagrophytes*), and species persisting in the soil are termed geophilic (e.g. *Microsporum gypseum*) (Weitzman and Summerbell, 1995), however some overlap does occur. Zoophilic and geophilic dermatophytes infecting humans cause a more intense inflammatory reaction than anthropophilic species (Weitzman and Summerbell, 1995).

**ETIOLOGY** Dermatophytosis in animals is most often caused by the anamorph species *Microsporum* and *Trichophyton*, however the infecting species can vary with the geographic region (Bond, 2010). Of these genera, *Trichophyton mentagrophytes* is the most common cause (Aho, 1980; Balsari et al., 1981; Drouot et al., 2009; Feuerman et al., 1975; Lopez-Martinez et al., 1984; McAleer, 1980a, 1980b; Papini et al., 1997; Pombier and Kim, 1975; Stenwig, 1985; Vangeel et al., 2000). *T. mentagrophytes* is a species complex with several variants including both anthropophilic and zoophilic pathogens. Pollock (2003) considered *T. mentagrophytes* var *mentagrophytes* as the most common variant infecting rodents, however the specific variant is not always reported in the literature. The teleomorphs are known for the *T. mentagrophytes* complex and there are two, *Arthroderma benhamiae* and *A. vanbreuseghemii*. The *A. benhamiae* genome has been sequenced (Burmester et al., 2011). The different variants and sexual states of the *T. mentagrophytes* complex coupled with more recent phylogenetic analyses presents confusion about proper nomenclature and species assignment (Drouot et al., 2009; Fumeaux et al., 2004). Infection with either *M. canis* or *M. gypseum* has also been reported in the guinea pig but less frequently (Feuerman et al., 1975; Papini et al., 1997).

**EPIZOOTIOLOGY AND PATHOGENESIS** Guinea pigs, and other animals, are infected by direct exposure to an infected animal, contaminated environments, or fomites. Arthroconidium produced by septation of hyphae are infectious and persist in the environment for months to years (Bond, 2010; Weitzman and Summerbell, 1995). Hyphae invade the stratum corneum eventually colonizing the hair follicles. The sequenced genome of *A. benhamiae* revealed numerous predicted protease-encoding genes and their secretion was confirmed experimentally in a keratin digestion assay indicating an important role in invasion and pathogenesis (Burmester et al., 2011). Young guinea pigs appear to be more susceptible to disease and other predisposing and susceptibility factors include pregnancy, high temperature and humidity, health status, and genetics (Pollock, 2003; Pombier and Kim, 1975). Surveys of dermatophytosis in guinea pigs have been reported from around the world, with prevalence ranging from 1.3–56% (Balsari et al., 1981; Drouot et al., 2009; Feuerman et al., 1975; Lopez-Martinez et al., 1984; Papini et al., 1997; Vangeel et al., 2000).
CLINICAL MANIFESTATIONS  Infected guinea pigs are most often asymptomatic but can exhibit lesions typical of dermatophytosis. When present, lesions are most common on the head and appear to begin on the nose or muzzle and then can spread over the body to the trunk and limbs (Figure 23.2). Circumscribed or irregular lesions with combinations of alopecia, scale, crust, erythema, and ulceration develop, with or without pruritis, and spontaneous remission is possible (Drouot et al., 2009; McAleer, 1980a; Pollock, 2003; Pombier and Kim, 1975). Pustules may be associated with the lesions due to secondary bacterial infections. Furthermore, in one outbreak of *T. mentagrophytes*, affected animals were in poor body condition and there was approximately 50% mortality in young guinea pigs (Pombier and Kim, 1975). Onychomycosis is rare in the guinea pig (Drouot et al., 2009).

PATHOLOGY  Microscopic analysis of affected epidermis and adnexa can include acanthosis, vascular congestion, dermal lymphocytic infiltration, folliculitis, perivascular, and interstitial dermatitis, and intra-epidermal pustules (Chermette et al., 2008; Pombier and Kim, 1975).

DIAGNOSIS  Microscopy and culture are the primary means of diagnosing dermatophytosis. Wood’s lamp can be used as a screening tool for *M. canis* and infected hairs will fluoresce with an apple-green color. However, false negatives can occur (Chermette et al., 2008). Hairs are plucked or the skin scraped from the periphery of an active lesion or from the whole lesion if there is no evidence of inflammation and samples placed in 10% potassium hydroxide to remove keratin. The samples are then examined for hair or skin invasion with hyphae and/or arthroconidia. To increase sensitivity, fluorescent microscopy with Calcofluor white and Congo red can be used (Bond, 2010; Robert and Pihet, 2008). Geimsa staining will also identify arthroconidia. All the dermatophytes infecting guinea pigs will have ectothrix hair shaft involvement. Prior to obtaining a skin or hair sample for culture, the area should be wiped with alcohol to reduce contamination. Saprophytic fungi contamination of the fur may hinder isolation of dermatophytes (Aho, 1983). Hair, skin, or crusts are collected using a sterile toothbrush, swab, forceps, scalpel blade, or surgical scrub brush and placed onto culture medium. Sabouraud’s dextrose agar supplemented with cyclohexamide and chloramphenicol is commonly used. Dermatophyte Test Medium is available, however contamination can cause both false-positive and false-negative results (Robert and Pihet, 2008). If the animal is simply a mechanical carrier, results of repeated testing will vary (Chermette et al., 2008). Biopsy samples can be stained with periodic acid-Schiff or silver stains to detect arthroconidia and hyphae (Figure 23.3) (Chermette et al., 2008). As mentioned earlier, polymerase chain reaction (PCR) amplification and sequencing of ITS and 28S ribosomal DNA (Drouot et al., 2009; Fumeaux et al., 2004; Symoens et al., 2011) will identify isolates, and mating experiments can be performed (Hironaga et al., 1981).

PREVENTION AND THERAPY  Reducing exposure to infected animals and contaminated environments is critical in preventing dermatophytosis. Assuring a well-managed facility with no overcrowding, parasite control, and proper temperature and humidity regulation are important preventive components (Pollock, 2003;
Pombier and Kim, 1975). Infected animals should be removed, the environment thoroughly decontaminated and any items that cannot be disinfected should be discarded. Animal care staff should wear proper personal protective equipment when handling potentially contaminated items or bedding since zoonosis is a concern (McAleer, 1980a). Dilute bleach, benzalkonium chloride, and glutaraldehyde are effective surface disinfectants (Pollock, 2003). In a laboratory setting, it is doubtful that animals will be treated for ringworm. Readers are referred to other summaries of available topical and systemic treatments (Pollock, 2003).

**Encephalitozoonosis/Microsporidiosis**

**BACKGROUND** The Microsporida (members of the phylum Microspora) are a group of single-celled intracellular spore-forming eukaryotic parasites that infect a wide range of animals, from insects to mammals. The defining and unique feature of the phylum is the presence of a polar filament (tube) in the mature spore (Wasson and Peper, 2000). The microsporidia also have one of the smallest genomes of any eukaryote and lack several key features, such as typical mitochondria. Long thought to be protozoa, certain characteristics indicated that these organisms were fungi-like such as presence of a chitinous spore wall, genes for trehalose metabolism, and intranuclear division (Brosson et al., 2006; Dunn and Smith, 2001). Recently, Lee et al. (2008) concluded that microsporidia are true fungi related to zygomycetes. Of the microsporidial species infecting humans, Enterocytozoon bieneusi is the most common with lesser, but still significant, numbers of cases due to the Encephalitozoon spp. The majority of patients are immunocompromised as a result of HIV infection, AIDS, or are organ transplant recipients. However, healthy immune-competent persons are also susceptible to disease (Didier and Weiss, 2006; Mathis et al., 2005). Animals are hosts for those common species strongly supporting their zoonotic potential.

**ETIOLOGY** The primary agent of microsporidiosis in guinea pigs is Encephalitozoon cuniculi (syn. Nosema). E. cuniculi was first reported in the rabbit as the cause of “Infecitious Motor Paralysis” (Percy and Barthold, 2007) and subsequently has been identified in a wide range of animal species (Wasson and Peper, 2000). Katinka et al. (2001) have sequenced the 11 chromosomes of the approximately 2.9-Mb genome, highlighting the genome compaction and shortened protein sequences that reflect its intracellular location and host dependence.

**EPIZOOTIOLOGY AND PATHOGENESIS** Wasson and Peper (2000) provide an informative summary of the mammalian microsporidian life cycle. Environmentally resistant spores are shed in feces, urine, and mucus and then ingested or inhaled. Transplacental transmission has been documented in the rabbit (Baneux and Pognan, 2003) and has been claimed in the guinea pig (Boot et al., 1988). Predictably, primary sites of infection commonly include the small intestine, respiratory tract, and placenta. An unknown signal triggers the polar filament (tube) to be extruded from the spore and infectious sporoplasm is injected into the host cell cytoplasm. The sporoplasm then divides into meronts (merogony) that differentiate through intermediary forms before becoming mature spores (sporogony). For E. cuniculi and other Encephalitozoon spp., developing spores are packaged in a parasitophorous vacuole. The host cell ruptures releasing spores that commonly disseminate to the kidney, liver, and brain. Host protection from infection is primarily achieved by cell-mediated immunity with lesser contributions from the humoral immune system (Khan et al., 2001).

From serologic surveys, prevalence of encephalitozoonosis in guinea pig colonies has ranged from 13%–63%. This variability may be due to differences in housing and husbandry for the particular colony and diagnostic methodology (Boot et al., 1988; Gannon, 1980).

**CLINICAL MANIFESTATIONS** Encephalitozoonosis is subclinical in the guinea pig (Boot et al., 1988; Gannon, 1980; Illanes et al., 1993; Moffatt and Schiefer, 1973; Wan et al., 1996).

**PATHOLOGY** Gross lesions of encephalitozoonosis in the guinea pig are not consistently found and when present have only been described in the kidney. Infected animals may have pale kidneys and/or pitting of the renal cortex (Gannon, 1980; Moffatt and Schiefer, 1973). Histologic lesions are found primarily in the brain and kidney. Focal to multifocal granulomatous encephalitis may be evident in different regions of the brain, with or without associated necrosis, and perivascular and meningeal mononuclear cell infiltrate (Moffatt and Schiefer, 1973; Wan et al., 1996). Organisms approximately 1–1.5 µm in width × 1.5–2.5 µm in diameter (Illanes et al., 1993; Wasson and Peper, 2000) can be found within or adjacent to lesions or free in the tissue with no associated inflammation. In the kidney, interstitial nephritis and necrosis, fibrosis, perivascular cuffing and tubular ectasia have all been described (Boot et al., 1988; Gannon, 1980; Moffatt and Schiefer, 1973). Here, organisms may occasionally be visualized in renal epithelial cells and collecting tubule lumens. Absence of typical lesions in the brain or kidney in a seropositive animal may be due to the multifocal nature of the lesions and insufficient sections being analyzed (Gannon, 1980; Wan et al., 1996). Other lesions reported include necrotic liver foci and interstitial pneumonia.
thought to occur in guinea pigs (Boot et al., 1988), so hysterectomy rederivation should be used with caution and offspring extensively tested. It is unlikely that laboratory guinea pigs would be treated for encephalitozoonosis.

Miscellaneous Diseases

**Candida pintolopesii (Formerly Known as Torulopsis pintolopesii)**

Two of four laboratory-bred guinea pigs were found dead several days to two weeks after adoption (Kunstyr et al., 1980). Diarrhea was noted in one animal prior to death and each had gross evidence of enteritis at necropsy which was confirmed histologically. The yeast *Candida pintolopesii*, a normal inhabitant of the gut, was isolated from the small intestine, lung, and ascitic fluid of one animal. The authors hypothesized that a change in social structure, diet, and environment precipitated disease.

**Cryptococcus neoformans**

*Cryptococcus neoformans* is a basidiomycetous yeast causing serious infections of the lungs and central nervous system in immunocompromised persons (Boekhout and Guého, 2003). Betty (1977) reported chronic, subclinical cryptococcal meningitis in laboratory-reared Dunkin Hartley guinea pigs with no evidence of generalized infection. The source of infection was not identified. Van Herck et al. (1988) described dermal cryptococcosis of an adult male pet guinea pig. Histopathologic analysis of a large ulcerative lesion on the dorsal aspect of the nose showed extensive focal ulcerative dermatitis with infiltrating neutrophils, plasma cells, lymphocytes, and macrophages with edema and ovoid organisms. Dermal and subcutaneous tissue also contained large numbers of these thick-walled organisms that were positive by periodic acid-Schiff staining.

**Enterocytozoon bieneusi**

*Enterocytozoon bieneusi* is a significant cause of intestinal microsporidiosis in immunocompromised persons and has been identified in many mammalian and nonmammalian hosts (Mathis et al., 2005). Microsporidian spores were found in the feces of a two-year-old male entered into a prospective study of pediatric enteric parasites in Peru. To investigate the source of infection, stool was analyzed from animals in the household, including guinea pigs, chickens, dogs, and cats. Seven of eight asymptomatic guinea pigs were positive for spores, whereas all the other animals were negative. Polymerase chain reaction and sequence analysis confirmed that both the child and guinea pigs were infected with *E. bieneusi* and with the same genotype. Furthermore, this specific genotype was found in guinea pigs from other unrelated...
households suggesting that guinea pigs are the natural host and there is zoonotic potential for this organism.

**Histoplasma capsulatum**

There is a single report from Brazil of a naturally occurring histoplasmosis outbreak in laboratory guinea pigs (Correa and Pacheco, 1967). Clinical signs of disease in adults included progressive emaciation and hindlimb dysfunction before death. Young animals exhibited a hunched back, ruffled fur, and conjunctivitis with discharge before dying at two months of age. Gross and histologic lesions were numerous; however, for these authors a characteristic lesion of colitis with the wall expanded by numerous lymphocytes, macrophages, epithelioid and giant cells with basophilic organisms free or inside macrophages and culture results established the diagnosis. There may have been a link between this outbreak and histoplasmosis diagnosed in a cow on a farm from which the grass used to feed the guinea pigs was sourced.

**Hortaea werneckii**

*Hortaea werneckii*, the causative agent of tinea nigra in people, was diagnosed in a household guinea pig in Japan (Sharmin et al., 2002). Lesions included a focal area of ulceration and alopecia on the back and black pigmentation on the palmar aspect of the right forepaw. *H. werneckii* was detected by mycologic culture of the back lesion and DNA sequencing of an amplified region of large subunit ribosomal DNA. The authors hypothesized that the animal contracted the infection from the environment, but could not definitively rule out contamination with the fungus rather than a real infection.

**Paecilomyces**

*Paecilomyces* spp. are occasional opportunists in humans and animals (Summerbell, 2003). This fungus was identified during routine monitoring from a single conventionally housed laboratory guinea pig with no apparent clinical signs (Kunstyr et al., 1997). *Paecilomyces* spp. were most commonly identified in specific pathogen-free rats from one particular animal facility with the trachea and lungs being the most common site of infection in all animals analyzed. Mild dermatitis was noted in a group of hairless mice; however, the vast majority of animals had no clinical or histologic evidence of disease.

**Pneumocystis carinii**

A hairless mutant arose in a closed colony of Hartley guinea pigs. In addition to abnormal haircoat development, affected guinea pigs were smaller than their haired siblings and died early due to infections otherwise associated with an abnormal immune system such as systemic cytomegalovirus and balantidiasis, and *Pneumocystis* pneumonia (Reed and O'Donoghue, 1979). Abnormal thymic and lymphoid follicle morphology and agammaglobulinemia confirmed the immunodeficiency.

**PROTOZOA INFECTIONS**

Protozoa rarely cause disease in guinea pigs and intestinal protozoa are often considered part of the normal flora. In this review, the more frequently reported protozoa of domestic guinea pigs will be discussed. The reader is referred to *Parasites of Laboratory Animals* (Baker, 2007) and *Morphology and Taxonomy of the Intestinal Protozoa of the Guinea Pig* (Nie, 1950) for a more detailed description of the protozoa of this species. The nomenclature used in this section is in accordance with the 2007 reference.

**Amoebiasis**

**ETIOLOGY** *Endolimax caviae* and *Entamoeba caviae* (syn. *Entamoeba cobayae*) are the causative agents of amoebiasis in guinea pigs (Levine, 1985). Nie (1950) reported the incidence of *Endolimax caviae* to be 18% and the incidence of *Entamoeba caviae* to be 14% in a colony of guinea pigs studied at the University of Pennsylvania.

**PATHOGENESIS** *Endolimax caviae* and *Entamoeba caviae* are observed in the cecum of the guinea pig (Nie, 1950). Both of these organisms are thought to feed upon the fecal material and microflora of the host intestine, without invasion of tissue or consumption of blood. Transmission is via ingestion of cysts passed in the feces.

**CLINICAL MANIFESTATIONS** Infection with either organism does not generally result in clinical signs (Levine, 1985).

**PATHOLOGY** *Entamoeba* and *Endolimax* are usually non-pathogenic (Baker, 2007; Levine, 1985).

**DIAGNOSIS** Trophozoites can be observed in a smear of intestinal contents (Baker, 2007; Levine, 1985). Cysts are detected by zinc sulfate float. *Endolimax caviae* trophozoites are smaller than those of *Entamoeba caviae*, with an average diameter of 1.6µm and 14.4µm, respectively (Nie, 1950). The cyst forms of either organism have rarely been observed, and little detail has been recorded on their appearances.

**PREVENTION AND THERAPY** Generally, treatment is not necessary for guinea pig amoebiasis.

**Balantidia caviae**

**BACKGROUND** Upon initial description, controversy developed over whether *B. caviae* was the same organism as *B. coli* in swine (Vetterling, 1976). Morphological
descriptions and infection studies have since proved that the two species are distinct.

**ETIOLOGY** *Balantidium caviae* is the causative organism.

**PATHOGENESIS** *B. caviae* transmission is via ingestion of cysts in the feces (Baker, 2007).

**CLINICAL MANIFESTATIONS** If the mucosal barrier of the intestine is compromised, *B. caviae* can become invasive and result in enteritis; otherwise infection is non-pathogenic (Baker, 2007).

**PATHOLOGY** *B. caviae* may be observed in the walls of the cecum and colon, but penetration can occur post-mortem, a consideration that should be made when diagnosing infection at the time of necropsy (Baker, 2007; Nie, 1950). If invasion is ante-mortem, intestinal inflammation should be present; more often, though, *B. caviae* is considered a commensal protozoan.

**DIAGNOSIS** In addition to diagnosing *B. caviae* in histologic sections of the cecum or colon, ciliated organisms with micro- and macro-nuclei can be observed in fresh fecal smears (Baker, 2007; Fox, 2002).

**PREVENTION AND THERAPY** Proper hygiene is most important in controlling *B. caviae* infection in guinea pigs (Baker, 2007). Tetracyclines have been used to treat balantidiasis in other species.

**Cryptosporidiosis**

**BACKGROUND** *C. wrairi* is named after the Walter Reed Army Institute of Research where the organism was first identified in a colony of laboratory guinea pigs (Vetterling et al., 1971).

**ETIOLOGY** *Cryptosporidium wrairi* is the causative organism.

**PATHOGENESIS** The route of infection for *C. wrairi* is likely fecal–oral, with ingestion of oocysts in feces (Baker, 2007; Fox, 2002). Experimental infection has shown that the duration of infection for animals older than 16 weeks is usually short, lasting as little as 1–2 weeks, after which the organism is cleared (Chrisp et al., 1990). Younger animals have a longer duration of infection. Recovered animals appear to be refractory to subsequent infection.

**CLINICAL MANIFESTATIONS** Clinical signs are more likely to be seen in young animals, with weight loss noted most commonly (Baker, 2007; Fox, 2002). If infection is severe, anorexia, a potbellied appearance and a greasy hair coat may be observed with or without accompanying diarrhea (Baker, 2007). Morbidity and mortality, especially in young animals, can reach levels of 50% during an outbreak (Harkness and Wagner, 1995; Percy and Barthold, 2007). *Echinococcus colii* has been associated with clinical cases of *C. wrairi*, but the significance of this infection is unknown (Percy and Barthold, 2007). Subclinical infections with *C. wrairi* are thought to be possible (Baker, 2007; Fox, 2002).

**PATHOLOGY** Erosion, hyperemia, and inflammation of the small intestine have been observed with *C. wrairi* infection (Baker, 2007; Chrisp et al., 1992; Harkness and Wagner, 1995). Edema of the lamina propria and hyperplasia of the crypt epithelium occurs. In chronic infections, villous atrophy and bridging, metaplasia of the mucosal epithelium, and lymphocyte infiltration of the lamina propria have been noted. Developmental stages of *C. wrairi* can be seen throughout the intestine, with highest concentrations of the organism noted in the brush border of the ileum.

**DIAGNOSIS** Oocysts can be seen in fecal floats (Gressler et al., 2010; Percy and Barthold, 2007). Kinyoun staining of fecal smears and microscopic examination of mucosal scrapings or histological sections are also diagnostic options.

**PREVENTION AND THERAPY** Prevention is the best means of control for *C. wrairi*. Oocysts are resistant to many disinfectants or require high concentrations and/or long contact times before being rendered non-infectious. Heating above 65°C for greater than 5 minutes has been described to be successful for the destruction of *Cryptosporidium* organisms, as has exposure to temperatures below 0°C (Baker, 2007; Harkness and Wagner, 1995). Successful treatment with sulfonamides has been reported, but the efficacy of this treatment has been questioned (Fox, 2002; Percy and Barthold, 2007; Sebesteny, 1976). Harkness suggests the “extra-label” use of high doses of the coccidiostat, Decoquinate, to treat cryptosporidiosis (Harkness and Wagner, 1995). While *C. wrairi* is not known to infect humans, the genus has a general lack of specificity and precautions should be taken to prevent zoonotic transmission (Baker, 2007; Harkness and Wagner, 1995).

**Eimeria**

**BACKGROUND** Reports of coccidia in guinea pigs date back to the late 1800s, although the observed organisms were initially thought to be a variety of rabbit coccidian (Vetterling, 1976). In the early 1920s, Bugge and Heinke showed that coccidia noted in the guinea pig were indeed distinct from those of the rabbit and in 1924 Sheather named the guinea pig coccidia *E. caviae*. 

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**ETIOLOGY**  *Eimeria caviae* is the causative organism.

**PATHOGENESIS** Transmission of *E. caviae* is fecal–oral, with ingestion of oocysts in feces (Baker, 2007).

**CLINICAL MANIFESTATIONS** Clinical signs due to *E. caviae* are noted in severe infections and include diarrhea, anorexia and a rough hair coat (Baker, 2007; Ellis and Wright, 1961; Rigby, 1976). The first appearance of diarrhea is often 10–11 days after initial infection (Baker, 2007; Elsheikha et al., 2009; Percy and Barthold, 2007). Watery, pasty, and hemorrhagic forms of diarrhea have all been reported (Baker, 2007; Elsheikha et al., 2009; Fox, 2002; Percy and Barthold, 2007). Severe infections can result in death (Baker, 2007; Fox, 2002). In mild infections or infections of older animals, diarrhea is likely to resolve in 4–7 days (Baker, 2007; Fox, 2002), after which constipation may follow (Fox, 2002). Stress, such as a diet change or transport, may exacerbate an otherwise non-pathogenic infection of *E. caviae* in the guinea pig (Ellis and Wright, 1961; Elsheikha et al., 2009; Rigby, 1976).

**PATHOLOGY** The large intestine is most affected by *E. caviae*, with organisms most often settling in the proximal colon (Baker, 2007; Elsheikha et al., 2009). Hyperemia, edema, and petechial hemorrhage of the colonic mucosa may be seen (Baker, 2007). White or yellow plaques may be present in the colon or cecum. Watery intestinal contents can contain blood (Baker, 2007; Percy and Barthold, 2007). Dilated cystic crypts of Liekberkuhn may be observed (Baker, 2007). Developmental stages of *E. caviae* can be seen in intact epithelial cells or free in the intestinal lumen. Enterocytes may slough and an infiltration of polymorphonuclear and mononuclear cells is possible (Baker, 2007; Percy and Barthold, 2007). Microgametocytes and macrogametocytes may be present in the cecal and colonic mucosa (Percy and Barthold, 2007).

**DIAGNOSIS** Oocysts are seen on fecal float (Baker, 2007; Fox, 2002; Percy and Barthold, 2007). Fox et al. (2002) recommend using a flotation medium of 1.33 specific gravity. The prepatent period of *E. caviae* is 11–12 days, yet diarrhea may occur before day 11; therefore, a fecal float performed at the beginning of diarrhea may result in a false-negative finding. Multiple floats performed every 4 or 5 days for several weeks is recommended (Vetterling, 1976). Organisms may also be identified on mucosal scrapings or histopathology sections (Baker, 2007; Fox, 2002; Percy and Barthold, 2007).

**PREVENTION AND THERAPY** Sulfonamides are recommended for treatment. Minimizing stress and providing an adequate level of vitamin C help to prevent clinical infection. Oocysts in the feces take 6 days to become infective, therefore regular cleaning of pans will help to minimize the spread of infection (Rigby, 1976). Ammonia, followed by a thorough rinsing, has been used to clean cages and pans of infected animals (Elsheikha et al., 2009). Steam has also been used to clean enclosures. Calhoon notes that *Eimeria*-free colonies can be achieved via cesarean rederivation (Calhoon and Matthews, 1964).

**Giardia duodenalis**

**ETIOLOGY** The causative agent of guinea pig giardiasis is *Giardia duodenalis*, formally referred to as *G. caviae* (Baker, 2007; Vetterling, 1976).

**PATHOGENESIS** *Giardia duodenalis* is a flagellate of guinea pigs that is transmitted by the fecal–oral route or via ingestion of contaminated food or water (Baker, 2007).

**CLINICAL MANIFESTATIONS** Overt signs of infection, such as diarrhea, are rare, although some animals are severely infected and may present as weak and moribund (Baker, 2007).

**PATHOLOGY** The small intestine, primarily the duodenum, is colonized by trophozoites (Baker, 2007). Colonization may result in mild inflammatory lesions, decreased villar height, and cystic enlargement of duodenal crypts.

**DIAGNOSIS** Diagnosis of *G. duodenalis* is via direct fecal smear, where trophozoites or cysts may be observed (Baker, 2007). Only trophozoites, and not cysts, are found in diarrheic feces (Vetterling, 1976). Shedding of *G. duodenalis* is intermittent, so unless multiple fecal smears are performed, there is a high likelihood of obtaining a false-negative result. FELASA recommends including *Giardia* spp. on guinea pig breeding colony health monitoring reports (Rehbinder et al., 1996).

**PREVENTION AND THERAPY** Metronidazole and fenbendazole are treatment options for guinea pig giardiasis (Baker, 2007). Infection can be prevented by thorough environmental sanitation using a quaternary ammonium product or sodium hypochlorite. Hot temperatures will destroy cysts. Cysts thrive in moist areas, so environments must be kept dry. The zoonotic potential of *G. duodenalis* of guinea pigs is unknown, but the possibility of transmission between guinea pigs and humans is suspected.

**Klossiella cobayae**

**BACKGROUND** *K. cobayae* is also known as *Klassia caviae*, as it was described and named simultaneously by two individuals, Pearce and Sangiori (respectively) working independently of each other (Vetterling, 1976). Occurrence in modern laboratory guinea pigs is rare (Percy and Barthold, 2007).
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**Klossiella cobayae** is the causative organism.

**PATHOGENESIS** *K. cobayae* is a parasite of the epithelial cells of the renal tubules, as well as the endothelial cells associated with glomerular capillaries and other organs, such as the spleen and lungs (Griffiths, 1971; Van Andel et al., 1995; Vetterling, 1976). Transmission is via ingestion of sporocysts in urine (Baker, 2007).

**CLINICAL MANIFESTATIONS** Clinical signs associated with *K. cobayae* are rare. If infection is severe, signs secondary to renal damage may result.

**PATHOLOGY** Infection can be non-pathogenic or result in nephritis (Figure 23.5) (Baker, 2007; Sebesteny, 1976). Heavy infection can lead to an irregular surface and a gray mottled appearance of the kidney (Baker, 2007; Fox, 2002). Interstitial and perivascular lymphocytic and histiocytic infiltration may occur (Baker, 2007). A large number of interstitial fibroblasts may also be observed.

**DIAGNOSIS** Sporocysts are passed in the urine, yet observation of this stage in the urine is difficult (Baker, 2007). Most often, diagnosis is made at the time of necropsy by identifying the different developmental stages of *K. cobayae* in glomerular capillaries or in the cytoplasm of epithelial cells lining the renal tubules (Baker, 2007; Percy and Barthold, 2007). FELASA recommends including *Klossiella* spp. as part of a health monitoring report for guinea pig breeding colonies (Rehbinder et al., 1996).

**PREVENTION AND THERAPY** Control of *K. cobayae* is best achieved through prevention. Contamination of food and bedding with infective urine should be minimized (Baker, 2007). Sulfonamides might be effective forms of treatment.

**Leishmania enrietti**

**BACKGROUND** *Leishmania enrietti* was first noted in laboratory guinea pigs in 1948 in Brazil (Medina, 1946). According to the review by Machado et al., this flagellate was next reported in 1967 in a guinea pig captured from the outskirts of Curitiba (Machado et al., 1994). The sandfly, *Lutzomyia monticola*, which is frequently noted on the trunks of Curitiba pine trees, was proposed as a possible vector.

**ETIOLOGY** *Leishmania enrietti* is the causative organism.

**PATHOGENESIS** Little is known about the lifecycle of *L. enrietti*, but other members of the genus *Leishmania* have indirect lifecycles and sandfly vectors (Baker, 1998, 2007; Nie, 1950). *L. enrietti* results in cutaneous infection.

**CLINICAL MANIFESTATIONS AND PATHOLOGY** An infected guinea pig may present with a cutaneous nodule at the site of entry 1–2 weeks after infection (Baker, 2007). Additionally, ulcers can develop on the feet, ears, nose, and genitalia of infected animals. Ulcers will go through a series of pathologic changes, such as necrosis of surrounding macrophages 4–5 weeks after initial infection (especially in naive animals), followed by an infiltrate of giant cells, plasma cells, and lymphocytes at the periphery of the ulcer. By 7 weeks, giant cells are gone and fibroblasts appear, indicating resolution. Resolution is usually complete by 10 weeks post-infection. Hematogenous spread of the organism can occur and *L. enrietti* may be observed in the lymph nodes.

**DIAGNOSIS** Detection is via identification of amastigotes in lesion histology or via culture of the organism (Baker, 2007).

**PREVENTION AND THERAPY** Control is achieved by elimination of vectors. Treatment with meglumine antimoniate has been attempted, with inconsistent success (Thomaz-Soccol et al., 1996). Contact with possible sandfly vectors should be avoided.

**Toxoplasma gondii**

**BACKGROUND** This organism was first reported in Brazil by Carini and Migliano (Vetterling, 1976). In early reports, *T. gondii* was mistaken for *Sarcocystis* in the guinea pig (Kean and Grocott, 1945).

**ETIOLOGY** *Toxoplasma gondii* is the causative organism.
**PATHOGENESIS** Cats are the definitive hosts of *T. gondii* (Baker, 2007). Oocysts are released in cat feces and are ingested by guinea pigs which act as intermediate hosts for *T. gondii*. Cysts can remain viable in a guinea pig for up to five years before ingestion by the definitive host. In addition to the guinea pig, a large number of mammalian and avian species are intermediate hosts to *T. gondii*, including humans. Ingestion of contaminated biological material and transplacental transmission are alternative routes of transmission for the guinea pig (Baker, 2007; Percy and Barthold, 2007).

**CLINICAL MANIFESTATIONS** *T. gondii* infection in guinea pigs is often asymptomatic and, therefore, frequently goes undiagnosed (Baker, 2007; Griffiths, 1971; Percy and Barthold, 2007). Infection in pregnant sows can result in vulvar bleeding and abortion (Fox, 2002). In a case of spontaneous toxoplasma encephalitis in a guinea pig, spastic paralysis, opisthotonos, and loss of urethral and anal sphincter control were reported (Markham, 1937).

**PATHOLOGY** Hepatitis, pneumonia, encephalitis, and uterine infection (possibly blood-filled), have been noted in infected animals, as have cysts in both the myocardium and central nervous system (Baker, 2007; Fox, 2002; Percy and Barthold, 2007). In spontaneously infected animals that develop toxoplasma encephalitis, congested blood vessels of the meninges were noted and were surrounded by mononuclear leukocytes (Markham, 1937).

**DIAGNOSIS** Serology is often used for diagnosis in guinea pigs (Baker, 2007). Cysts can be observed on histology. Mice or hamsters can be inoculated with tissue homogenate from suspected positives and act as sentinels of infection. FELASA recommends including *Toxoplasma gondii* on guinea pig breeding colony health monitoring reports (Rehbinder et al., 1996).

**PREVENTION AND THERAPY** Sulfadiazine and pyrimethamine are reported treatment options for clinical cases of *T. gondii*, yet the effectiveness of such treatments is questionable (Baker, 2007; Fox, 2002). Temperatures above 60°C kill oocysts (Baker, 2007). Strict sanitation and periodic colony monitoring are necessary for *T. gondii* control.

**Trypanosoma cruzi**

Guinea pigs, among other mammals, are reservoirs for the flagellate *T. cruzi* (Baker, 2007; Vetterling, 1976). Reduviid bugs act as vectors, becoming infected after a blood meal from a positive animal. *T. cruzi* mature and reproduce within the vector. The bugs then go on to deposit *T. cruzi*-containing feces on humans during another blood meal. The organism enters human skin through a wound (potentially the bug bite) or contact with mucous membranes. Chagas disease may result in humans.

In the guinea pig, *T. cruzi* can encyst in multiple organs, including the skin and cardiac muscule. *T. cruzi* has been noted in domesticated guinea pigs of South America exposed to reduviid vectors. Clinical and pathological signs are not described.

**PARASITIC INFECTIONS**

The reader is once again directed to Flynn’s *Parasites of Laboratory Animals* for further discussion on many of the parasites discussed below, including anatomical appearances and detailed life cycles (Baker, 2007). The nomenclature used in this section is also in accordance with this reference.

**Arthropods**

Note: the common names of arthropod organisms have been used in place of the name of the resulting condition (e.g. Flies instead of Myiasis).

**Fleas**

*Ctenocephalides felis* has been noted on pet guinea pigs living in a household with cats and/or dogs.
Infected guinea pigs presented with pruritus, alopecia, dermal crusts, and anemia (White et al., 2003). Aqueous-based pyrethrin sprays have been recommended as the safest treatment option for such infection. *Nosopsyllus fasciatus*, the northern rat flea, can also inhabit guinea pigs, although similarly to *C. felis*, infection of laboratory guinea pigs is rare (Fox, 2002).

**Flies**

It has been stated that “fatal myiasis involving at least three species of flies, *Lucilia sericata*, *Calliphora vicina* and *Calliphora vomitoris*, have been reported in guinea pigs” (Baker, 2007). Eggs are deposited on the skin of a guinea pig by an adult fly, where larvae will develop and then feed on living or necrotic animal tissue (Baker, 2007).

### TABLE 23.1 Other Parasites of Wild Guinea Pigs

| Parasite                  | Location in Host | Method of Infection | Pathologic Effects |
|---------------------------|------------------|---------------------|--------------------|
| **FLEAS**                 |                  |                     |                    |
| *Hectopsylla* spp.        | Pelage           | Direct contact      | Unknown            |
| *Leptopsylla seginis*     | Pelage           | Direct contact      | Unknown            |
| *Nosopsyllus fasciatus*   | Pelage           | Direct contact      | Unknown            |
| *Pulex irritans*          | Pelage           | Direct contact      | Dermatitis         |
| *Rhopalopsylla clavicola* | Pelage           | Direct contact      | Unknown            |
| *Tiamastus cavicola*      | Pelage           | Direct contact      | Unknown            |
| **LICE**                  |                  |                     |                    |
| *Polyplax spinula*        | Pelage           | Direct contact      | Unknown            |
| *Pteropthirus* spp.       | Pelage           | Direct contact      | Unknown            |
| **MITES**                 |                  |                     |                    |
| *Ornithonyssus bacoti*    | Skin             | Direct contact      | Dermatitis         |
| *Ornithonyssus braziliensis* | Skin              | Direct contact      | Unknown            |
| *Ornithonyssus wernecki*  | Skin             | Direct contact      | Unknown            |
| *Eutrombicula* spp.       | Skin             | Direct contact      | Unknown            |
| **CESTODES**              |                  |                     |                    |
| *Anoplocephala* spp.     | Intestine        | Unknown             | None               |
| *Monocoecestus parcitesticulatus* | Intestine   | Unknown             | None               |
| **NEMATODES**             |                  |                     |                    |
| *Ackertia* borgosi        | Abdominal cavity | Arthropod host      | None               |
| *Capillaria hepatica*     | Liver            | Ingestion of embryonated egg | None |
| *Graphidioides mazzai*    | Small intestine  | Ingestion of infective larvae | None |
| *Trichuris* gracilis      | Large intestine  | Ingestion of embryonated egg | None |
| *Viannella travassosi*    | Small intestine  | Ingestion of infective larvae | None |
| **TREMATODES**            |                  |                     |                    |
| *Pseudoquinqueserialis* caviae | Intestine   | Ingestion of metacercaria | None |
| *Taxorchis caviae*        | Cecum            | Ingestion of metacercaria | None |
| *Taxorchis ringueleti*    | Cecum            | Ingestion of metacercaria | None |

*Adapted from Baker (2007).*
**Lice**

**ETIOLOGY** Biting lice from the order Mallophaga, *Gyropus ovalis*, *Gliricola porcelli*, and *Trimenopon hispidum* (previously *Trimenopon jenningsi*) are often observed in guinea pigs (Baker, 2007). *G. porcelli*, the most commonly observed of the three, is known as the “slender louse” due to its general appearance, especially when compared to *G. ovalis* or the “oval louse” (Baker, 2007; Harkness and Wagner, 1995; Kim et al., 2008). Several species of sucking lice (order Anoplura) have been noted on wild guinea pigs in South America: *Pterophthirus alata* and *Polyplax spinulosa* (Dittmar, 2002). These later lice are listed in Table 23.1, but not discussed here in detail.

**PATHOGENESIS** Biting lice attach to hair shafts and abrade the skin to ingest cutaneous fluids (Fox, 2002; Kim et al., 2008). Transmission is via direct contact (Harkness and Wagner, 1995; Kim et al., 2008). The life cycles of guinea pig lice are not specifically described, but in general, biting lice go through the following stages: egg, three nymphal stages, and adult (Baker, 2007).

**CLINICAL MANIFESTATIONS** *G. ovalis*, *G. porcelli* or *T. hispidum* infection of a guinea pig can be asymptomatic or may result in pruritus and a rough hair coat or alopecia (Baker, 2007; Coman et al., 2009; Harkness and Wagner, 1995; Kim et al., 2008). Scabs and crusts are sometimes noted secondary to scratching, especially around the ears (Harkness and Wagner, 1995).

**PATHOLOGY** Signs of louse infection are usually superficial. Dermatitis may be noted grossly.

**DIAGNOSIS** Lice (adults or nits) can be seen on the haircoat of an infected animal, with or without the aid of a magnifying lens (Figure 23.6) (Baker, 2007; Griffiths, 1971). On a dead animal, lice will migrate to the warm tips of the hair as the skin cools (Griffiths, 1971). Tape tests and flea combing can also be used to diagnose louse infestation (Coman et al., 2009). As stated previously, *G. porcelli* is slender in appearance (1.0–1.5 mm × 0.3–0.4 mm), compared to *G. ovalis* (1.0–1.2 mm × 0.5 mm) (Figure 23.7) (Huerkamp et al., 1996). *T. hispidum*’s dimensions are similar to those of *G. ovalis*, yet can be differentiated by the fact that *T. hispidum* has five abdominal segments as compared to *G. ovalis*’ eight.

**PREVENTION AND THERAPY** In reports of successful control of guinea pig louse infestations, both infected animals and the environment have been treated (Harkness and Wagner, 1995; Kim et al., 2008). Systemic ivermectin (Baker, 2007; White et al., 2003), carbamate or pyrethrin-based powders (Baker, 2007; Griffiths, 1971), Romavermectin B1 (Coman et al., 2009) and a combination of imidacloprid and moxidectin (Kim et al., 2008) have been noted as effective drug choices for treating infected guinea pigs. Hypochlorite bleach has been used for environmental decontamination (Kim et al., 2008).

**Mites**

Guinea pigs are susceptible to infection with several species of mites, some occurring more commonly than others. *Chirodiscoides caviae* and *Trixacarus caviae* are the most commonly noted infectious mites in guinea pigs, with *Demodex caviae*, *Myocoptes musculinus*, *Sarcoptes scabiei* and *Notoedres muris* reported less frequently (Baker, 2007; Fox, 2002; White et al., 2003). Infection with the astigmatic mite, *Acarus farris*, was described in a case report of two guinea pigs (Linek and Bourdeau, 2005). *Psocoptes cuniculi* has been described on a pet guinea pig in close contact with a pet rabbit (Yeatts, 1994). White et al. (2003) note *Cheyletiella parasitivorax* as a cause of pruritus and scaling along the dorsum of guinea pigs. The more commonly noted mites, *C. caviae* and *T. caviae*, will be discussed below.

**CHIRODISCOIDES CAVIAE**

**BACKGROUND** The first reports and illustrations of *C. caviae* were by Stanley Hirst in the early 1900s (Hirst 1922). Hirst noted this mite attached to the hairs of the back of the guinea pig.

**ETIOLOGY** *Chirodiscoides caviae* is the causative organism (Figure 23.8).

**PATHOGENESIS** *C. caviae* is a species-specific fur mite that tends to concentrate in the lumbar area and the lateral aspects of the hindquarters (Harkness and Wagner, 1995; Percy and Barthold, 2007; Schonfelder et al., 2010). *C. caviae* feed on the scales of hair shafts (Hirsjarvi and Phyala, 1995) and transmission is via direct contact with...
an infected animal (Fox, 2002; Schonfelder et al., 2010) or with infected cage debris or bedding (Fox, 2002). The life cycle of *C. caviae* has not been specifically described, although mites in general commonly go through egg, larval, nymphal, and adult stages (Baker, 2007). Concurrent infection with lice is not uncommon (White et al., 2003), and mixed infection with *Demodex caviae* (detected via deep skin scrapping) has also been reported (Schonfelder et al., 2010).

**CLINICAL MANIFESTATIONS** Infection with *C. caviae* can be asymptomatic or, if infestation is heavy, pruritis, alopecia, hyperemia, and dermal crusts may be seen (Coman et al., 2009; Fox, 2002; Hirsjarvi and
Phyala, 1995; Lumeij and Cremers, 1986; Schonfelder et al., 2010). Anorexia may result secondary to grooming pruritic areas (Schonfelder et al., 2010).

**PATHOLOGY** The appearance of *C. caviae* mites themselves is the major pathologic finding (Fox, 2002). Mites and ova are located on the hair shafts of the guinea pigs, not burrowed into the skin.

**DIAGNOSIS** Mites may be seen with the unaided eye, hand lens or dissecting microscope. *C. caviae* can also be found on a superficial scrape (Harkness and Wagner, 1995; Percy and Barthold, 2007; Schonfelder et al., 2010). Combing, hair plucking, and cellophane tape testing can aid in isolating mites for observation (White et al., 2003).

**PREVENTION AND THERAPY** Many treatment options have been described in the literature for *C. caviae*. Dilute ivermectin (diluted in aqua/propylene glycol) sprays have been successful, especially for treating large colonies of infected animals (Baker, 2007; Hirsjarvi and Phyala, 1995; White et al., 2003). Selamectin, 12–15mg/kg, applied twice at 2-week intervals has also eliminated infection (Baker, 2007; Fox, 2002; Schonfelder et al., 2010). Pyrethrin sprays and powders have been used to rid the environment of *C. caviae* (Harkness and Wagner, 1995; Hirsjarvi and Phyala, 1995). 1% Virkon S® was used to treat an automatic watering system (Hirsjarvi and Phyala, 1995). Older successful treatments include the use of dichlorvos vapors (Henderson, 1973) as well as immersion of shaved animals in 0.15% trichlorfon (Lumeij and Cremers, 1986).

**TRIXACARUS CAVIAE**

**BACKGROUND** *T. caviae* was discovered in a colony of albino guinea pigs in the early 1970s by Fain and was described as a disease very similar in appearance to sarcoptic mange in other animals (Dorrestein and Vanbronzwijk, 1979; Fain et al., 1972). The first report of *T. caviae* in North America was in 1980 at Davis, California (McDonald and Lavoipierre, 1980).

**ETIOLOGY** *Trixacarus caviae* is the causative organism (Figure 23.8).

**EPIZOOTIOLOGY AND PATHOGENESIS** *Trixacarus caviae* is a species-specific sarcoptic mite that most commonly affects guinea pigs that are 1–3 years of age (Dorrestein and Vanbronzwijk, 1979). If left untreated, the parasite load peaks 1 month post-infection, after which it slowly regresses (Fuentealba and Hanna, 1996). The life cycle of *T. caviae* includes an egg, larval, two nymphal, and a final adult stage, all of which inhabit the host guinea pig (Baker, 2007). Transmission is by direct contact, with nymphal or larval stages indicated in establishing new infestations (Baker, 2007; Rothwell et al., 1991). Within 72 hours, pups born to an infected guinea pig dam will show clinical signs consistent with *T. caviae* infestation (Beck et al., 2007; Kummel et al., 1980).

Humans have been reported to develop transient pruritic, papulovesicular dermatitis after contact with infected animals, although mites appear to be incapable of persisting on human skin (Fuentealba and Hanna, 1996; Kummel et al., 1980; Mederle and Indre, 2009).

**CLINICAL MANIFESTATIONS** While infection with *T. caviae* may be asymptomatic and result in non-clinical carrier animals, *T. caviae* has been reported as the most common and important cause of dermatitis in guinea pigs (Dorrestein and Vanbronzwijk, 1979; Fuentealba and Hanna, 1996; Percy and Barthold, 2007; White et al., 2003). Severe pruritis and excoriation along with erythema and alopecia can accompany dermatitis in some animals (Ackerman, 1987; Beck et al., 2007; Dorrestein and Vanbronzwijk, 1979). In those guinea pigs that are clinical, grayish to yellow or white crusts may be present on the skin and can be dry or slightly greasy (Ackerman, 1987; Dorrestein and Vanbronzwijk, 1979). Secondary bacterial infections of infected skin areas are possible (Fuentealba and Hanna, 1996). Infection usually starts on the face and ears, spreading to the lumbar regions and lateral aspects of the legs (Dorrestein and Vanbronzwijk, 1979; Percy and Barthold, 2007). The intense pruritic response in some guinea pigs is reported to be due to an initial allergic reaction to mite antigen (Fox, 2002). Extreme restlessness and emaciation have been noted in affected animals, especially in those that seemingly scratch uncontrollably (Beck et al., 2007). This constant scratching can lead to “fits” of muscular spasms or sporadic epileptiform seizures (Ackerman, 1987; Beck et al., 2007; Dorrestein and Vanbronzwijk, 1979; Kummel et al., 1980) caused by generalized pruritus-induced hypersensitivity (Baker, 2007).

**PATHOLOGY** Orthokeratotic hyperkeratosis and acanthosis have been noted in animals showing clinical signs of *T. caviae* infection (Ackerman, 1987; Dorrestein and Vanbronzwijk, 1979; Fuentealba and Hanna, 1996; Zenoble and Greve, 1980). A polymorphonuclear leukocytic infiltrate is present in the dermis (Dorrestein and Vanbronzwijk, 1979; Percy and Barthold, 2007; Rothwell et al., 1991; Zenoble and Greve, 1980). Adult mites may be noted in “tunnels” or burrows located in the hyperkeratotic areas (Dorrestein and Vanbronzwijk, 1979; Zenoble and Greve, 1980). Such tunnels approach the epidermis perpendicularly, with some entering the mouth of hair follicles (Zenoble and Greve, 1980). Eggs may also be present in tunnels (Dorrestein and Vanbronzwijk, 1979). *T. caviae* mites have sharp spines on
the cuticle of their dorsums (Zenoble and Greve, 1980), which differentiates them from *Notoedres* (Ackerman, 1987). The anus of the female *T. caviae* mite is located dorsally, while this structure is located terminally on *S. scabiei* (Ackerman, 1987; Baker, 2007; Fuentealba and Hanna, 1996).

**DIAGNOSIS** Deep skin scrapes of crusted areas with 10% KOH reveal *T. caviae* (Dorrestein and Vanbronswijk, 1979; Fain et al., 1972; Fuentealba and Hanna, 1996; Mederle and Indre, 2009). Zajac et al. (1980) report that live mites could be demonstrated for 5 days postmortem from deep skin scrapings taken from a guinea pig held at 4°C after death.

**PREVENTION AND THERAPY** Treatment of both affected animals and the environment has been employed to rid guinea pig colonies of *T. caviae*. Multiple treatment regimens have been reported as successful over the years, including lindane baths (Dorrestein and Vanbronswijk, 1979; Zajac et al., 1980), weekly lime sulfur dips (Ackerman, 1987; McDonald and Lavoipierre, 1980; Zenoble and Greve, 1980), ivermectin injections (White et al., 2003), and monthly spot-on treatment with 10% imidacloprid and 1% moxidectin (Beck et al., 2007). Dilute lime sulfur can also be used to treat the environment (White et al., 2003). Valium has been used to control seizure-like activity related to *T. caviae* infection by some, whereas others suggest that treating the mite infection alone eliminates this sequela to infection (Beck et al., 2007; White et al., 2003).

### Cestodes

According to Harkness and Wagner (1995), tapeworms rarely infect guinea pigs. *Anoplocephala* spp. and *Monoecestus parcesticulatus* (Table 23.1) have been reported in the intestines of South American guinea pigs (Baker, 2007; Sardella and Fugassa, 2009).

### Nematodes

**Baylisascaris procyonis**

**ETIOLOGY** *Baylisascaris procyonis* is the causative organism.

**PATHOGENESIS** Guinea pigs are paratenic hosts of *B. procyonis* and contract infection by ingesting eggs in raccoon feces (Baker, 2007). Once ingested, larvae will hatch and penetrate the small intestine of the guinea pig, migrate through the liver to the lungs and disseminate throughout the body via the circulatory system. Larvae then encapsulate where they remain until ingested by a raccoon.

**CLINICAL MANIFESTATIONS** No signs are present in the guinea pig due to *B. procyonis* unless organisms migrate to the brain. Migration can result in lethargy, head tilt and ataxia, which may progress to cachexia, stupor, hyperexcitability, lateral recumbency, torticollis, or opisthotonos (Van Andel et al., 1995).

**PATHOLOGY** In cases were *B. procyonis* migrates to the brain, multifocal eosinophilic granulomatous inflammation and neutrophilic infiltration is seen, along with perivascular lymphoid cuffing and malacia (Van Andel et al., 1995). Eosinophilic granulomata have been noted in the lungs of some infected animals.

**DIAGNOSIS** Histology is diagnostic for *B. procyonis* (Baker, 2007). The Baermann extraction technique can be used to extract organisms from the cerebral tissue of clinical animals (Van Andel et al., 1995).

**PREVENTION AND THERAPY** Prevention, rather than treatment, is the most logical approach for *B. procyonis* control, as clinical signs are often not noted until the end stage of infection and diagnosis relies on histopathology. Contamination of bedding or food with raccoon feces must be avoided. Ova can be viable for years in soil and weeks to months in straw and are resistant to most disinfectants (Fox, 2002). Removal of contaminated bedding and the autoclaving of caging may be required (Baker, 2007). Humans, similarly to guinea pigs, can contract infection by ingesting raccoon feces, but transmission from guinea pigs to humans is not feasible (Fox, 2002).

**Paraspidodera uncinata**

**ETIOLOGY** *Paraspidodera uncinata* is the causative organism.

**EPIZOOTIOLOGY AND PATHOGENESIS** *P. uncinata* is the cecal worm of guinea pigs and the most common nematode infecting this species (Griffiths, 1971). The prevalence of *P. uncinata* in wild guinea pigs of South America was found to be 37%, while the prevalence was noted as 23.8% in a laboratory colony of guinea pigs (Coman et al., 2009; Dittmar, 2002). Transmission is via ingestion of an embryoalted egg in feces (Baker, 2007; Fox, 2002). Eggs become infectious 3–5 days after they are initially shed (Fox, 2002). The life cycle is not well described (Baker, 2007).

**CLINICAL MANIFESTATIONS** Infections are normally asymptomatic, but with heavy parasitic loads weight loss, diarrhea, and disability are possible (Fox, 2002).

**PATHOLOGY** Infection can, and often does, occur without pathologic changes (Baker, 2007; Percy and...
If cecal worms migrate through the intestinal mucosa, a hemorrhagic typhlitis may be seen along with capillary ectasis in the submucosa (Coman et al., 2009).

**DIAGNOSIS** Adult worms may be seen in the cecum at necropsy and eggs may be observed in feces (Figure 23.9) (Baker, 2007; Rigby 1976).

**PREVENTION AND THERAPY** Levimasole administered at 25 mg/kg, either orally or subcutaneously, has most often been reported as an effective treatment for *P. uncinata* in the guinea pig (Baker, 2007; Eliazian et al., 1975). Other reported treatment regimens include oral mebendazole at 50 mg/kg (Baker, 2007) and Romavermectin B1 given subcutaneously at a dose of 0.2 mg/kg twice at a three-week interval (Coman et al., 2009).

**Pelodera strongyloides**

**ETIOLOGY** *Pelodera strongyloides* is the causative organism.

**PATHOGENESIS** *P. strongyloides* organisms are usually found in damp soil or vegetation (White et al., 2003). Bedding can be a possible source of infection.

**CLINICAL MANIFESTATIONS** While typically non-pathogenic, if *P. strongyloides* invade hair follicles dermatitis can result (Baker, 2007; White et al., 2003).

**PATHOLOGY** Organisms may be found in hair follicles of clinically infected animals.

**DIAGNOSIS** The observation of larvae in skin scrapings or biopsies signifies infection (White et al., 2003). Adults may be observed in the bedding.

**PREVENTION AND THERAPY** Cages should be kept dry, as organisms thrive in moist environments (White et al., 2003). The bedding of any positive animal should be replaced. A 1–2% chlorhexadine bath has been recommended for infected animals as a means of preventing secondary infections.

**Trichinella spiralis**

Trichinellosis due to *Trichinella spiralis* is possible in guinea pigs, but rare, especially in laboratory animals that seldom come in contact with infected material (raw or undercooked meat) (Sebesteny, 1976). Enteritis could develop in infected animals if *T. spiralis* organisms migrate through the intestinal wall.

**Trematodes**

**Fasciola**

**BACKGROUND** Infection in present laboratory-housed guinea pigs is rare, but when *Fasciola* organisms are noted it is often in conjunction with recent diet supplementation of a leafy vegetable carrying encysted trematodes (Baker, 2007; Fox, 2002).

**ETIOLOGY** Two *Fasciola* species are noted in guinea pigs, *Fasciola hepatica* and *Fasciola gigantica* (Baker, 2007). *F. gigantica* is slightly larger in size than *F. hepatica*, although *F. gigantica* rarely reach patency in guinea pigs.
**PATHOGENESIS** Guineas pigs ingest encysted *Fasciola* metacercariae on vegetation (Baker, 2007; Fox, 2002). Once ingested, metacercariae hatch in the small intestine and migrate through the wall to the peritoneal cavity and the liver. Juvenile flukes develop in the liver and, once mature, burrow in the bile ducts. Eggs are shed and enter the gut, where they pass in the feces. A snail intermediate host is necessary for maturation from cercariae to infectious metacercariae. Metacercariae encyst on leafy vegetation.

**CLINICAL MANIFESTATIONS** Emaciation and anemia have been associated with *Fasciola* infection (Sebesteny, 1976). Posterior paresis was noted in animals that developed cysts in the lumbar musculature after aberrant fluke migration (Baker, 2007).

**PATHOLOGY** Hepatic congestion and hemorrhage, especially around portal vessels, central veins and sinusoids is possible (Baker, 2007). Fibronecrotic tracks and granulomas may also be observed in the liver. Other pathology due to fluke infection is often the result of aberrant migration, resulting in cysts in areas such as the kidney, the peritoneal cavity and the pelvic cavity. Cysts often contain coffee-brown-colored material.

**DIAGNOSIS** *Fasciola* spp. can be observed on fecal flotation (Baker, 2007).

**PREVENTION AND THERAPY** Prevention is best achieved by limiting the amount of leafy vegetation supplemented in a guinea pig’s diet; if supplemented, do not feed vegetation from fluke-endemic locations. *Fasciola* in ruminants is treated with albendazole and clorsulon (Baker, 2007).

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III. GUINEA PIGS

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