4.1 AN OVERVIEW OF SELECTED DISEASES OF AFRICAN PRIMATES

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An indication of high, medium or low concern is provided next to each disease, based on either published data or anecdotal evidence. Disease is of higher concern if it has relatively high mortality/ morbidity, if it is Zoonotic and/ or if it would have as yet unknown consequences, especially for release programmes.

VIRUSES

SIMIAN VARICELLA VIRUS (Moderate Concern)

Etiology: Cercopithicine herpes virus 6, 7 and 9. Group of closely-related herpesviruses including Delta herpesvirus, Medical Lake macaque virus, Liverpool vervet monkey virus, and others. All are antigenically related to human varicella-zoster.

Transmission: Respiratory. Latency is common and the origin of some outbreaks is unexplained.

Clinical: Affects patas, African green monkeys, macaques, chimps and gorillas. Herpetic rash, depression, respiratory difficulty.

Diagnosis: Usually based on clinical signs. Virus isolation, and PCR

Pathology: Vesicles on skin, oral mucous membranes, and esophagus; focal necrosis in lung, liver, spleen, lymph nodes, adrenal, bone marrow, intestinal tract. Multinucleated giant cells and intranuclear inclusion bodies. Becomes latent in ganglia.

HERPES SIMPLEX VIRUS (Low Concern)

Etiology: Herpes simplex virus (type 1 and 2)

Transmission: Latent or active infection in many humans, which are the natural reservoir. Human to monkey and monkey to monkey transmission from active lesions.

Clinical: Lesions may be local or generalized. Oral vesicles and ulcers, conjunctivitis, encephalitis, death. Chimpanzees, gorillas, and gibbons can be infected, but usually remains confined to skin, oral cavity, external genitalia, and conjunctiva.

Diagnosis: Usually based on clinical signs. Virus isolation, electron microscopy –or florescent antibody can confirm. Commercial kits available.

Pathology: Oral, lingual, labial, or genital vesicles & ulcers. Conjunctivitis, keratitis. Multinucleated giant cells and intranuclear inclusion bodies.

AFRICAN MONKEY HERPES VIRUS (Low Concern)

Etiology: Simian Agent 8 (SA8) (a.k.a. *Herpesvirus papionis*)

Transmission: Saliva and other bodily fluids.

Clinical: Usually asymptomatic in baboons. Genital and oral vesicles and pustules with genital lesions becoming more severe. Latency and recrudescence can occur. Has not been described in great apes.

Diagnosis: As for HSV 1 and 2.

Pathology: As for HSV 1 and 2. Multinucleated giant cells and intranuclear inclusion bodies.

CYTOMEGALOVIRUS (Moderate concern)

Etiology: Betaherpesvirus

Transmission: Horizontal (shed in urine, saliva, blood), transplacental, highly species-specific and may become latent in glandular tissue

Clinical: Usually asymptomatic. Chimpanzees and gorillas have been infected with clinical signs of diarrhea, anorexia and lethargy. Widespread latent infections in macaques, with most seroconverting during the first year of life. Disease produced only in fetuses and immunodeficient individuals. CNS and respiratory tract signs. CMV is a common opportunistic infection in SIV and SRV infected macaques.

Diagnosis: Usually based on clinical signs. Confirmed based on histopathology of discrete small foci of rounded cells, fluorescent antibody or enzyme immunoassay.

Pathology: In immunodeficient animals, generalized infections with necrotizing meningitis and neuritis, interstitial pneumonia, arteritis, enterocolitis, orchitis, and focal necrosis in liver and spleen. Characteristic large basophilic intranuclear inclusion bodies and granular eosinophilic cytoplasmic inclusion bodies in mesenchymal cells (not surface epithelium like other herpesviruses).

EPSTEIN-BARR VIRUS (Moderate concern)

Etiology: Nonhuman primate EBV-related Herpesviruses

Transmission: Prolonged contact with saliva

Clinical: Most infections are asymptomatic and latent. Specific chimpanzee, gorilla and orangutan types. In immunodeficient animals, EBV has been associated with lymphoma and with squamous epithelial proliferative lesions. Most humans are subclinical carriers

of the human type.

Diagnosis: Serology

Pathology: Extranodal B-cell lymphoma or squamous cell proliferations resembling oral hairy leukoplakia on oral, genital, and cutaneous surfaces in immunodeficient animals. Intranuclear inclusions are present in epithelial lesions.

ENCEPHALOMYOCARDITIS VIRUS (High Concern)

Etiology: Encephalomyocarditis virus (Family: Picornaviridae, Genus: Cardiovirus)

Transmission: Oral, other routes suspected. Probable rodent reservoir with contamination of food and surfaces.

Clinical: Sudden death. Causes myocarditis in nonhuman primates, pigs, elephants, some others. EMCV is probably not a significant human pathogen, although some people are seropositive.

Diagnosis: Virus isolation especially in acute cases and serology.

Pathology: Pericardial effusion, pale areas in myocardium. Myofiber necrosis with inflammation and edema. Secondary lesions of acute heart failure. Extensive myocardial scarring in animals that survive acute infection. Some strains of EMCV cause necrosis of the exocrine pancreas in some species.

MONKEYPOX (Moderate concern)

Etiology: Orthopoxvirus immunologically related to smallpox and vaccinia

Transmission: Zoonotic disease of monkeys and humans in tropical rain forests of western and central Africa. Spread via aerosols, biting and other contact. Animal reservoir unknown, but possibly squirrels and probably not monkeys. Occurs sporadically.

Clinical: Vaccine is protective, but hasn't been used since 1980. Disease in children resembles discrete ordinary smallpox, except lymphadenopathy occurs commonly in monkeypox. Human to human transmission has occurred. In monkeys (red tail monkey, Allen's swamp monkey, Lesser white-nosed monkey, red colobus), disease may be mild to fatal. Usually see 1 to 4 mm diameter cutaneous papules that become pustules and then crust over and drops off, leaving small scars. In more severe disease, facial edema, dyspnea, oral ulcers, and lymphadenopathy.

Diagnosis: Virus isolation, Electron microscopy (vesicular fluid superior to swabs, and serology.

Pathology: Hyperplasia and necrosis of epidermis, with swelling of keratinocytes and

large eosinophilic intracytoplasmic inclusions. Visceral lesions can occur.

YABA POX (Low concern)

Etiology: Unclassified poxvirus closely related to swinepox

Transmission: Mosquitoe vector.

Clinical: Natural infections have occurred in macaques and baboons. Humans are also susceptible. Rapidly growing subcutaneous nodules up to 4 cm diameter on head and limbs. These spontaneously slough and heal in 6 to 12 weeks.

Diagnosis: Tissue culture, immunohistochemistry and serology

Pathology: Unlike other poxviruses, Yaba pox infects histiocytes rather than epithelial cells. Yaba pox virus induces subcutaneous proliferation of round to polygonal histiocytes which often contain eosinophilic cytoplasmic inclusions. Usually described as benign histiocytomas. Similar to lumpy skin disease of cattle.

MOLLUSCUM CONTAGIOSUM (Low concern)

Etiology: poxvirus unrelated to smallpox

Transmission: Unknown

Clinical: Humans, chimpanzees and macaques. Smooth-surfaced, hemispheric, waxy, umbilicated epithelial papules, 3-8 mm diameter, anywhere on skin, but especially eyelid and groin.

Diagnosis: Tissue culture or serology

Pathology: Marked acanthosis with large basophilic intracytoplasmic inclusion bodies that become more prominent towards the skin surface.

MEASLES (High concern)

Etiology: Human measles virus (Paramyxoviridae: Morbillivirus)

Transmission: Respiratory. Human reservoir. Measles is not a natural disease of macaques, but is acquired through contact with humans.

Clinical: Affects apes, macaques, baboons, African green monkeys, colobus, . May be subclinical or cause maculopapular rash, conjunctivitis, facial erythema, respiratory difficulty, diarrhea. Causes temporary immunosuppression.

Diagnosis: Tissue culture or serology

Pathology: Focal necrosis on oral mucous membranes, interstitial pneumonia, syncytial cells in skin, lymph nodes, lung. Intranuclear and intracytoplasmic inclusion bodies.

ADENOVIRUS (Moderate concern)

Etiology: Adenovirus (> 80 species)

Transmission: Spread through respiratory, fecal-oral and direct contact modes.

Clinical: Usually asymptomatic. Conjunctivitis and respiratory infections, diarrhea, pancreatitis. Severe infections in immunodeficient animals. Chimpanzees appear more susceptible to disease than other great ape species.

Diagnosis: Virus isolation or serology (complement fixation). Electron microscopy not that reliable.

Pathology: Frequently isolated from intestine and lung of healthy animals. Necrotizing alveolitis and bronchiolitis, pneumonia, necrotizing pancreatitis, enteritis. Intranuclear inclusions vary from small and eosinophilic to large, basophilic, and "smudgy".

RESPIRATORY SYNCYTIAL VIRUS (Moderate concern)

Etiology: RSV - Family: Paramyxoviridae

Transmission: Aerosols.

Clinical: Chimpanzees affected with clinical signs of coughing, sneezing, mucopurulent nasal discharge.

Diagnosis: Tissue culture (syncytial cell formation) and serology

Pathology: Bronchopneumonia with synctial cell formation**.**

HUMAN METAPNEUMOVIRUS (High concern)

Etiology: In the Paramyxoviridae family closely related to RSV

Transmission: Aerosols, possibly fecal-oral as virus can be found in feces several days after resolution of clinical signs.

Clinical: Chimpanzees affected with clinical signs ranging from mild coughing, sneezing, to thick mucopurulent nasal discharge, lethary, dyspnea abortion and death. Gorillas appear to be largely asymptomatic. Also reported in macaques.

Diagnosis: Tissue culture, PCR (fecal and respiratory secretions), and serology

Pathology: Bronchointerstitial pneumonia**.**

POLIOMYELITIS (Moderate concern)

Etiology: Poliovirus. Enterovirus in the Family Picornaviridae.

Transmission: Fecal-oral with many asymptomatic carriers.

Clinical: Chimpanzees, bonobos, gorillas and colobus are susceptible. Symptoms range from fever, diarrhea nuchal rigidity to paralytic disease.

Diagnosis: Tissue culture, PCR, immunofluorescence and serology

Pathology: Non-purulent myeloencephalitis. Extensive loss of ganglia cells and marked glial cell proliferation with preferential sites in the spinal cord, cerebella nuclei and diencephalon.

PAPILLOMAVIRUS (Low concern)

Etiology: Papillomavirus

Transmission: Direct skin contact

Clinical: Papillomas on skin, oral or genital mucosa.

Diagnosis: Papillomavirus antigens can be demonstrated by immunohistochemistry and virions by electron microscopy.

Pathology: Focal hyperkeratosis, parakeratosis, acanthosis.

FOCAL EPITHELIAL HYPERPLASIA OF CHIMPANZEES (Low concern)

Etiology: Papovavirus

Transmission: Direct contact

Clinical: Circumscribed soft elevations of the oral mucosa of lips, tongue, gingiva. This is usually a benign condition that may persist for years or may spontaneously regress.

Diagnosis: Papovavirus like particles can be demonstrated in nuclei of epithelial cells. PCR and transmission electron microscopy.

Pathology: Focal acanthosis with koilocytosis, mild chronic inflammation.

SV40 (Low concern)

Etiology: Papovavirus (Polyomavirus subgroup)

Transmission: Respiratory. Virus is shed in urine.

Clinical: Usually none. Widespread latent infection in wild and captive macaques. In immunodeficient animals can cause CNS and respiratory signs.

Diagnosis: PCR

Pathology: Usually none. In immunocompromised animals, interstitial pneumonia, renal tubular necrosis, encephalitis, demyelination (progressive multifocal leukoencephalopathy). PML probably represents a reactivated latent infection, whereas pneumonia, nephritis, and meningeoencepLesions in brain may have typical distribution of PML or may be around ventricles (particularly in brainstem) and in superficial cortex. Astrocytes and oligodendrocytes are infected. Large basophilic intranuclear inclusions in lung, oligodendroglia, renal tubular epithelium.

YELLOW FEVER (Low concern)

Etiology: Arbovirus (Flaviviridae)

Transmission: Via mosquitoes (numerous *Aedes* species)

Clinical: Usually none in old world monkeys. The exception is Galago (*Galago crassicaudatus*) with mortality rates up to 50% in laboratory infected animals

Diagnosis: Virus isolation, serology, RT-PCR

Pathology: Fatty liver degeneration, extensive hepatocellular necrosis, and hemorrhagic diathesis.

SIMIAN HEMORRHAGIC FEVER VIRUS (Moderate concern in species affected)

Etiology: Togaviridae, Arterivirus

Transmission: Simian Hemorrhagic Fever Virus is endemic in some wild Patas monkeys (*Erythrocebus patas*) and possibly other African species (African green monkeys, baboons), which remain persistently viremic, but asymptomatic for life. Animals may be viremic without antibody production. Transmission from Patas to macaques in laboratory settings appears to require parenteral exposure to blood or body fluids. The virus spreads much more readily among macaques by contact or aerosol.

Clinical: None in African primates. The virus causes explosive epidemics with nearly 100% mortality in captive macaques. Clinical signs in macaques include fever, anorexia, depression, facial edema, epistaxis, cutaneous and subcutaneous hemorrhage. Severely elevated LDH, disseminated intravascular coagulation, thrombocytopenia.

Any epizootic of hemorrhagic disease should be reported to the special pathogens

branch, Centers for Disease Control, Atlanta, GA.

Diagnosis: Virus isolation, indirect immunofluorescence, serology

Pathology: None in African primates. In Macaques gross lesions are variable, may be absent, and are seen only in the final stage of disease. Petechial hemorrhage on mucosal and serosal surfaces, hemorrhage and necrosis of the mucosa of the proximal duodenum, splenomegaly, splenic lymphoid follicles ringed with a zone of bright red hemorrhage. Microscopic changes consist of lymphoid necrosis, vasculitis, hemorrhage, and intravascular fibrin deposition (DIC). Large amounts of fibrin are present in splenic cords. Lymphohistiocytic meningoencephalitis occasionally present. Hepatic necrosis with Councilman's bodies is not a feature of simian hemorrhagic fever, unlike other hemorrhagic fevers. Additionally, in SHF aspartate aminotransferase>alanine aminotransferase, while the reverse is true in the other hemorrhagic fevers.

HEPATITIS A VIRUS (Low concern)

Etiology: Picornaviridae (Hepatovirus or Enterovirus)

Transmission: fecal-oral

Clinical: Infects humans, chimpanzees, African green monkeys. Seroconversion and elevation of transaminases are usually the only clinical evidence of infection. Some HAV isolates may be unique to nonhuman primates. Zoonotic potential. A vaccine (Havrix) is available and should be required for all humans working with chimpanzees.

Diagnosis: Virus isolation is not practical. Serology (ELISA, CF, RIA)

Pathology: Periportal and parenchymal mononuclear inflammation, slight focal hepatocellular degeneration and necrosis with acidophilic bodies, Kupfer cell hyperplasia. Chimpanzee pathology shows evidence of bile duct hyperplasia and bile duct epithelial cell necrosis.

HEPATITIS B VIRUS (Moderate concern)

Etiology: Orthohepadnavirus

Transmission: Infected blood, saliva, semen. Parenteral inoculation or intimate contact required.

Clinical: Infects humans, chimpanzee, gibbon, gorilla, possibly cynomolgus monkey, orangutans and long tailed macaques. Usually no clinical signs other than seroconversion and elevated transaminases. But in advanced cases can cause fibrosis and tumour development.

Diagnosis: Serology or PCR

Pathology: Chronic periportal inflammation with focal hepatocyte necrosis.

HEPATITIS C VIRUS (Low concern)

Etiology: Flaviviridae

Transmission: Parenteral or sexual contact

Clinical: Only humans and chimpanzees susceptible. Can cause an acute or chronic hepatitis with chronic cases in chimpanzees leading to icterus, lethargy, inappetance and vomiting.

Diagnosis: Serology or PCR

Pathology: Chronic active hepatitis, cirrhosis or hepatocellular carcinoma

STLV-I (Moderate concern in species affected)

Etiology: Retroviridae subfamily oncovirinae: Type C

Transmission: Parenteral or sexual contact

Clinical: Old world monkeys and apes including baboons, African green monkeys, Patas monkeys, various macaques, and chimps, bonobos and gorilla. Although most infected animals remain latently infected and asymptomatic for life, STLV-I has been associated with lymphoma/leukemia in baboons, African green monkeys, and macaques. Causes Non-Hodgkin's lymphomas.

Diagnosis: Viral isolation, PCR.

Pathology: STLV-I typically infects CD4+ T-cells in macaques and CD8+ T-cells in African monkeys, but some infected T-cell lines express neither marker. STLV-I appears to be nonpathogenic in Asian primates.

NONHUMAN PRIMATE LENTIVIRUSES:

SIV_{mac}	*Macaca mulatta* (Rhesus)
SIV_{smm}	*Cercocebus torquatus atys* (Sooty mangabey)
SIV_{mne}	*Macaca nemestrina* (Pigtailed macaque)
$SIV_{agm/gri}$, $SIV_{agm/tan}$, $SIV_{agm/ver}$	*Cercopithecus sp.* (African green monkey)
SIV_{mnd}	*Papio sphinx* (Mandrill)
SIV_{stm}	*Macaca arctoides* (Stump-tailed macaque)
SIV_{cyn}	*Macaca fascicularis* (Cynomolgus monkey)
SIV_{cpz}	*Pan troglodytes* (Chimpanzee)
SIV_{WCM}	*Cercocebus torquatus lunulatus* (White-crowned mangabey)
SIV_{SYK}	*Cercopithecus mitis* (Sykes monkey)

SIV_{HU} *Cercocebus Macaca Homo*

SIMIAN IMMUNODEFICIENCY VIRUSES (SIV) (High concern)

Etiology: Retroviridae subfamily oncovirinae: Type C

Transmission: Direct contact (bite, sexual) and through maternal milk to offspring

Clinical: Documented in African green monkeys, vervets, grivets, tantalus monkeys, Sykes monkeys, mandrills and anubis, sooty, red capped, and white crowned mangabeys, and chimpanzee. Weight loss, diarrhea, and anemia/thrombocytopenia are common clinical findings. **Zoonotic**

Diagnosis: RT-PCR, serology, electron microscopy

Pathology: Infected animals lose lymphoid tissues which becomes depleted and opportunistic infections occur. The most common infections are: CMV, *Candida, M. avium/intracellularae*, *Cryptosporidium, Pneumocystis, Trichomonas, Plasmodium*, adenovirus, rhEBV, and SV40. Lesions thought to be directly caused by SIV include lymphoid hyperplasia, lymphoid depletion, retroviral pneumonia, retroviral encephalitis, giant cell disease, aseptic thrombosis, and glomerulosclerosis. Many lesions are dependent on the secondary infections.

MARBURG (High concern)

Etiology: Filoviridae, Mononegavirales

Transmission: Aerosols and contact

Clinical: In monkeys clinical signs develop within 2-6 days and include fever, anorexia, weight loss, petechial rash, leucopenia, thrombocytopenia, elevated aminotransferase, urea and creatinine levels. **Zoonotic.**

Diagnosis: Virus isolation, IHC, TEM, serology

Pathology: Feulgen stain positive inclusion bodies in hepatocytes. Hemorrhage in lung, liver, spleen and focal necrosis in all organs.

EBOLA (High concern)

Etiology: Filoviridae, Mononegavirales

Transmission: Aerosols, contact and eating infected meat

Clinical: In chimpanzees, gorillas and monkeys clinical signs develop within 3-9 days and include fever, anorexia, weight loss, nasal discharge, hemorrhagic rash, diarrhea, thrombocytopenia, elevated LDH. **Zoonotic.**

Diagnosis: Virus isolation, PCR, TEM, serology

Pathology: Amphophilic cytoplasm inclusion bodies, fibrin deposition in splenic cords, lymphoid depletion in splenic white pulp, interstitial pneumonia and bronchiolar/alveolar necrosis, adrenal cortical necrosis, splenomegaly and petechial hemorrhage in many organs.

BACTERIAL

TUBERCULOSIS (High concern). Refer to section 4.3.

Etiology: *Mycobacterium tuberculosis, M. bovis*, *M. avium-intracellulare*

Transmission: Primarily through aerosols, occasionally nosocomial and rarely peroral

Clinical: Zoonotic and can infect all primates with chimpanzees and members of the Cercopithedidae family often, and rarely Prosimiae. In most cases there are no symptoms other than positive tuberculin skin reactions. In severely affected animals clinical signs include dry, soft chronic cough, lymphadenopathy, wasting, diarrhea, cutaneous ulcerations, hepato and splenomegaly.

Diagnosis: Difficult to confirm and no test is 100%. Screening tests include intradermal testing with mammalian and avian tuberculin injections, blood rapid tests, and x-rays. Culture from tracheal or gastric lavages and Multiantigen print immunoassay (MAPIA).

Treatment: None. Euthanasia recommended due to zoonotic and multi-drug resistance concerns.

Pathology: Focal granulomatous or miliary lesions in any organ are suggestive of tuberculosis, but lesions are most regularly are found in the lung, liver , lymph nodes and spleen.

LEPROSY (Moderate concern)

Etiology: *Mycobacterium leprae*

Transmission: Respiratory, and possibly through skin.

Clinical: Nodular thickening of skin and peripheral nerves. Paralytic deformity of hands and feet. Natural infections in chimpanzee and sooty mangabey (*Cercocebus torquatus atys*).

Diagnosis: This bacteria does not grow *in vitro*. Serology and special stains on tissues.

Treatment: None. Euthanasia recommended.

Pathology: Leprosy is a pathologically complex disease that has a spectrum of lesions that depend on the degree of cell mediated immunity the host is able to mount against *M. leprae*. Natural infections in nonhuman primates have taken the lepromatous form, indicating no CMI. Lesions occur predominantly in the skin and peripheral nerves, particularly in cooler areas (ears, tail, scrotum). Histiocytic infiltrate with variable numbers of lymphocytes and plasma cells in skin and nerves. Acid-fast bacilli demonstrable with Fite-Faraco acid fast stain. Nerve lesions are pathognomonic.

LEPTOSPIROSIS (Moderate concern)

Etiology: *Leptospira interrogans* subspecies

Transmission: Shed in urine and can survive in soil or alkaline water. Infection occurs via mucous membranes or cutaneous lesions.

Clinical: Most are asymptomatic with infection noted in African green monkeys, orangutans and bush babies based on presence of antibodies. Clinical signs observed range from edema, vomitus, melaena, jaundice, weakness, lethargy and fever.

Diagnosis: Dark field microscopy, silver impregnation, electron microscopy and serology.

Treatment: If active infection, tetracycline or doxycycline.

Pathology: Usually none in African primates. Icterus, hemorrhage (skin, lymph nodes, heart), liver necrosis, fatty degeneration and necrosis of renal tubules

SHIGELLOSIS (High concern)

Etiology: *Shigella flexneri, S. sonnei,* others are less common.

Transmission: fecal-oral.

Clinical: Variable. Asymptomatic carriers are common. May have soft stool, fluid diarrhea, or more commonly, the bloody mucoid diarrhea of classical dysentery. Monkeys with colitis due to *Shigella* will rapidly dehydrate and die unless treated promptly and vigorously. Shigella affects only primates. Clinical disease is often precipitated by stress.

Diagnosis: Culture

Treatment: Supportive care and antibiotics based on culture and sensitivity testing.

Pathology: The lesions of shigellosis are limited to the colon, may be focal or diffuse, and are characterized by edema, hemorrhage, erosion & ulceration, and pseudomembrane formation. Microscopically the lesion is purulent, necrotizing colitis, often with crypt abscesses. *Shigella* occasionally causes periodontitis in monkeys.

SALMONELLA (High concern if clinical)

Etiology: *Salmonella enteritidis, S. typhimurium* (>1800 *Salmonella* spp.)

Transmission: fecal-oral, rodent feces most common source.

Clinical: All non-human primates, but especially Old World species. Can carry asymptomatically. Sporadic or epizootic. Watery to bloody, mucoid diarrhea. Occasionally vomiting, abortion and osteomyelitis. May become moribund and die.

Diagnosis: Culture, enzyme immunoassays, immunofluorescence.

Treatment: Supportive care usually results in recovery. If antibiotics are prescribed they should be based on culture and sensitivity testing.

Pathology: Necrotizing, suppurative enterocolitis. May become septicemic resulting in pyogranulomas in liver and other organs. Resembles shigellosis, but *Shigella* does not become septicemic and does not affect the small intestine.

CAMPYLOBACTERIOSIS (Moderate concern if clinical)

Etiology: *Campylobacter. jejuni, C. coli*

Transmission: Oral via contaminated food or water

Clinical: Asymptomatic carriers are common. Diseased monkeys have fluid, sometimes bloody diarrhea and dehydration. *Campylobacter* has been associated with abortions in primates.

Diagnosis: Isolation requires special media and atmosphere, PCR or serology.

Treatment: Usually supportive care. If antibiotics are required they should be selected based on culture and sensitivity testing as multi-drug resistance is common. Erythromycin, Tetracycline and Quinolones commonly used.

Pathology: Small intestine and colon reddened, roughened, edematous. Histology in colon can be similar to shigellosis, but is usually much less severe and can also affect small intestine. Colonic mucosa sometimes hyperplastic. Can demonstrate spiral bacteria with silver stains.

HELICOBACTERIOSIS (Low concern)

Etiology: *Helicobacter pylori*

Transmission: Oral (oral-oral or fecal-oral) and possibly via waterborne infections

Clinical: Asymptomatic usually. Clinical signs range from intermittent vomiting and diarrhea.

Diagnosis: Can see organism with HE, but Giemsa or silver stains will more readily demonstrate slightly curved, rod-shaped, gull-wing, or loosely-coiled organisms, 1-4 μm long, associated with gastric epithelium in antral mucosa. Best to culture biopsy rather than swab, are urease positive. Can use rapid urease test rather than culture.

Treatment: Antibiotics and anti-ulcer medications.

Pathology: Seldom grossly apparent, but sometimes focal reddening or erosions of gastric mucosa. Mononuclear inflammatory cell infiltrate in lamina propria of stomach, superficial erosions, epithelial hyperplasia.

STREPTOCOCCUS PNEUMONIAE (DIPLOCOCCUS) (Moderate concern)

Etiology: *Streptococcus (Diplococcus) pneumoniae.*

Transmission: Aerosols

Clinical: Tends to occur in small focal outbreaks. Often found dead, but may have signs of pneumonia, meningitis, arthritis, depression, dehydration, paralysis, tremors or seizures.

Diagnosis: Culture, PCR

Treatment: Antibiotics (penicillin, cephalosporin and macrolide resistance is common) based on culture and sensitivity testing.

Pathology: Fibrinopurulent serositis affecting meninges, pleura, peritoneum, and/or joints. Often severe fibrinopurulent pneumonia. Sometimes only septicemia, especially if splenectomized. Numerous thrombi and infarcts - can result in permanent CNS damage if survive. Diplococci easy to see on gram stained smear of exudates.

YERSINIOSIS (High concern if clinical)

Etiology: *Yersinia pseudotuberculosis, Y. enterocolitica.*

Transmission: Wild birds and rodents are reservoir hosts. Transmission by ingestion of feed/water contaminated by feces of infected animals.

Clinical: Disease of all non-human primates. Affected primates are often found dead but sometimes show diarrhea, depression, and dehydration. *Yersinia* is occasionally associated with abortions and stillbirths.

Diagnosis: Culture, PCR, serology

Treatment: Supportive care. If antibiotics are required they should be selected based on culture and sensitivity testing as multi-drug resistance is common.

Pathology: The infection begins as a focal necrotizing enteritis and mesenteric lymphadenitis, which rapidly becomes septicemic resulting in necropurulent hepatitis, splenitis, and myelitis. Large colonies of gram negative bacteria in necrotic centers are nearly diagnostic.

LISTERIOSIS (Moderate concern)

Etiology: *Listeria monocytogenes*

Transmission: *Listeria* is widespread in the environment. Oral from contaminated food and transplacental transmission.

Clinical: Disease occurs in stillborn and neonatal infants. Abortion, intrauterine death, neonatal sepsis, meningoencephalitis in infants. Mother usually clinically normal.

Diagnosis: Culture, serology

Treatment: Antibiotics (Ampicillin, penicillin, tetracycline, erythromycin) based on culture and sensitivity.

Pathology: Purulent placentitis (hematogenous pattern), purulent meningo-encephalitis, intrauterine pneumonia, focal necrosis in liver and other organs, gram-positive rods in tissues.

BORDETELLOSIS (Low concern)

Etiology: *Bordetella bronchiseptica*

Transmission: Respiratory

Clinical: Asymptomatic carriers. Mucopurulent nasal discharge, dyspnea, and sometimes peracute death.

Diagnosis: Culture, serology

Treatment: Antibiotics (Polymyxin B, Tetracycline, Gentamycin, Kanamycin) based on culture and sensitivity.

Pathology: Fibrinopurulent hemorrhagic bronchopneumonia. Fibroplasia around bronchioles.

TETANUS (Moderate concern)

Etiology: *Clostridium tetani*.

Transmission: *C. tetani* is a soil organism and an obligate anaerobe that contaminates skin wounds or bites

Clinical: Begins in upper limbs, then lower. Deliberate stiff gait, trismus, extensor rigidity, opisthotonos and death. Usually fatal in l-10 days due to respiratory paralysis and exhaustion. Tetanus is a non-immunizing disease - multiple episodes are possible. Antibody is not usually detectable in affected animals.

Diagnosis: Usually based on clinical signs as culture is extremely difficult

Treatment: Hyperimmuneserum, Penicillin, Tetracyclines

Pathology: None. Must be diagnosed clinically.

STAPHYLOCOCCUS (Moderate concern)

Etiology: *Staphylococcus aureus*

Transmission: *Staphylococcus* is commonly carried asymptomatically in the nose and throat but occasionally infects breaks in the skin and invades the bloodstream.

Clinical: Pustular dermatitis in young animals. Breaks in skin become infected resulting in cellulitis, abscesses, and lymphadenitis. Bacteremia often develops, leading to visceral abscesses, endocarditis, and septic shock. Vegetative valvulitis may cause septic emboli and infarcts in various organs. Indwelling catheters are a common source of infection. The source of infection is usually clinically obvious.

Diagnosis: Culture

Treatment: Antibiotics based on culture and sensitivity testing.

Pathology: Cellulitis, abscesses filled with thick creamy pus, fibrinous pericarditis, vegetative valvulitis, thrombosis and infarction. Histologic lesions consist of fibrinopurulent exudate with masses of gram-positive cocci. Monkeys sometimes develop secondary immune complex glomerulonephritis.

KLEBSIELLA (Moderate concern)

Etiology: *Klebsiella pneumoniae*

Transmission: Respiratory. Carried in nose and throat. Often seen in chimpanzees

Clinical: Nasal discharge, air sacculitis, bronchopneumonia, meningitis, arthritis, cystitis

Diagnosis: Culture

Treatment: Supportive care. Bacteria is resistant to most antibiotics and therefore if antibiotics are prescribed they should be selected based on culture and sensitivity testing.

Pathology: Fibrinopurulent pneumonia and serositis, septicemia. Abundant gram-negative bacteria with prominent capsules in exudate. Exudate sometimes has a gelatinous consistency.

ESCHERICHIA COLI (High concern for highly pathogenic strains)

Etiology: *E. coli* (serotypes 0119:B14, 055:B5, 026:B6)

Transmission: Fecal-oral

Clinical: All non-human primates. Occurs as sporadic cases but often a peracute disease. Pneumonia, meningitis, diarrhea, lethargy and dehydration.

Diagnosis: Culture

Treatment: Aggressive antibiotic therapy and prophylactic antibiotics to exposed individuals. Vaccination is ineffective.

Pathology: Fibrinopurulent pneumonia and serositis, pyelonephritis, hemorrhagic gastroenteritis.

MELOIDOSIS (Moderate concern)

Etiology: *Pseudomonas (*aka *Burkholderia) pseudomallei* (A saprophyte with worldwide distribution)

Transmission: Most cases are due to contamination from bites or other wounds. Occasionally inhalation and ingestion have been reported with a prolonged incubation period (3 months to 10 years!)

Clinical: All non-human primates. Infection can involve any organ system and therefore clinical signs are based on the organs infected. Most commonly infected are lung, liver and bone.

Diagnosis: Culture, PCR and serology

Treatment: Usually unsuccessful due to multi-drug resistance and ability to quickly acquire resistance during the course of treatment.

Pathology: Yellowish coloration of the subcutaneous tissues, white, milky subcutaneous abscesses. Acute necrotizing-glaucomatous inflammation containing giant macrophages with phagocytes leukocytes and intracellular bacteria.

FUNGAL DISEASES

DERMATOMYCOSIS (Moderate concern)

Etiology: *Trichophyton rubrum* and *Microsporum canis*

Transmission: Contact with an animal or fomite

Clinical: Circular lesions on the skin with alopecia.

Diagnosis: Culture and direct microscopic examination of hairs with characteristic hyphae or arthrospores

Treatment: Systemic anti-fungals (ketoconazole, itrarconazole, lefuronon, griseofulvin, terbinafine)

Pathology: Folliculitis, alopecia and clusters of arthrospores in keratinized tissues.

CANDIDIASIS (Moderate concern)

Etiology: *Candida albicans*

Transmission: Ubiquitous organism. Opportunistic infection of immuno-compromised animals.

Clinical: Occurs in debilitated animals or animals on long-term antibiotics. Dysphagia, white pseudomembrane on oral mucous membranes.

Diagnosis: Culture**.** Organism can be seen on HE, but best studied with PAS or GMS stains

Treatment: Nystatin, ketoconazole, itraconazole, use with probiotics.

Pathology: White pseudomembrane on oral and esophageal mucous membranes. Underlying tissue may be ulcerated. Septate pseudohyphae and oval budding blastospores in superficial epithelium. Rarely invade past basement membrane.

PNEUMOCYSTIS (Moderate concern)

Etiology: *Pneumocystis carinii* (Unculturable fungus between ascomycetes and basidiomycetes)

Transmission: Aerosol

Clinical: Often asymptomatic. Horizontally acquired or reactivated latent infections in immunodeficient animals. Fever, dyspnea, cough, anorexia and weight loss.

Diagnosis: Histopathology (Methenamine-silver staining), IHC, PCR

Treatment: Trimethoprim-sulfa

Pathology: Lesions usually restricted to lung, but generalized infections have been described in severely immunodeficient humans. Foamy eosinophilic intra-alveolar exudate mixed with alveolar macrophages, interstitial lymphocytic infiltration, hypertrophy of alveolar lining cells. Organisms in exudate and along alveolar walls. Cysts demonstrable with GMS stain.

HISTOPLASMOSIS (Low concern)

Etiology: *Histoplasma capsulatum* var *capsulatum*, *Histoplasma capsulatum* var *duboisii* (African histoplasmosis)

Transmission: Inhalation of spores of *H capsulatum* from soil rich in bird or bat excreta. *H. duboisii* may be spread by dermal contact and may have a long incubation period.

Clinical: *H. capsulatum*: Infection is usually latent. Clinical disease can occur with heavy exposure, resulting in influenza-like disease, with pre-existing lung lesions, or disseminated disease can result from immunodeficiency. Rare in monkeys.
H. duboisii. Reported only from Africa in humans and baboons. Affects skin, lymph node, and bone.

Diagnosis: Sometimes with fine-needle aspirates. Tissue biopsies with PAS, methenamine silver or Gridley's fungal stains.

Treatment: Itraconazole, ketoconazole or in difficult cases amphotericin B.

Pathology: Granulomatous inflammation in affected organs, histiocytes packed with yeast form of organism. *H. capsulatum* 2-4μ, *H. duboisii* 7-15μ.

CRYPTOCOCCOSIS (Low concern)

Etiology: *Cryptococcus neoformans*

Transmission: Inhalation

Clinical: CNS and ocular abnormalities usually.

Diagnosis: Cytology with gram stain (retains crystal violet and capsule stains lightly red), culture and serology.

Treatment: Fluconazole, itraconazole, amphotericin B.

Pathology: Gelatinous nodules or cystic areas, especially on meninges, grossly. Sparse granulomatous inflammation surrounding abundant yeasts. Organism is 5-10μ, has

single buds, and is surrounded by a thick mucin positive capsule.

PARASITES (see also sections 3.10, 3.11)

GIARDIA (Moderate concern)

Etiology: *Giardia intestinalis*

Transmission: Fecal-oral, contaminated water

Clinical: Diarrhea (small intestinal), vomiting

Diagnosis: Characteristic trophozoites or cysts in feces, fluorescent antibody, fecal antigen

Treatment: Isolation and treatment of infected animals with metronidazole

Pathology: Presence of organisms on epithelial surface of small intestine. Organisms most common in middle of jejunum. Mucosa may be normal or have nonspecific villus atrophy and inflammation of lamina propria.

AMEBIC DYSENTERY (High concern)

Etiology: *Entamoeba histolytica*

Transmission: Fecal-oral

Clinical: Lethargy, weakness, dehydration, anorexia, vomiting, severe diarrhea with blood and mucus present

Diagnosis: Fecal smears, IF, RIA's

Treatment: Imidazole derivatives (Metroniadazole, etc.)

Pathology: Cecocolic necrotic areas with occasional sunken centers, chornic colitis and in chimpanzees pulmonary abscesses. Colobinae have ulcerative gastritis and hepatic abscesses

AMEBIC MENINGOENCEPHALITIS (Low concern)

Etiology: *Balamutharis mandrillaris*

Transmission: Unknown

Clinical: Cutaneous granulomas, limb paresis or paralysis, depression and weakness

Diagnosis: Isolation of the organism from brain/skin tissue. Methenamine silver or PAS staining.

Treatment: Clarithromycin, fluconazole, sulfadiazin, flurocytosine.

Pathology: Random multimodal encephalomalacia and cerebral hemorrhage. Nodular necrosis of the liver, kidney, lung and pancreas. Presence of trophozoites and cysts in the affected neuropil.

MALARIA (Moderate concern)

Etiology: *Plasmodium sp.*

Transmission: Mosquito bites

Clinical: Asymptomatic. Weakness due to anemia

Diagnosis: Blood smear identification of the organism in erythrocytes

Treatment: Not required in great apes due to mild disease

Pathology: Grossly, the lungs, liver, and spleen are gray and the blood thin. Histologically, tissue macrophages are filled with malarial pigment, and there are hemodsiderosis and parasitized RBC's. Intravascular clotting with thrombi and parasitized RBC's is common. Often there is pulmonary and cerebral edema.

BALANTIDIASIS (High concern – but species dependant)

Etiology: *Balantidium coli*

Transmission: Fecal-oral

Clinical: Weight loss, anorexia, weakness, watery diarrhea, tenesmus, rectal prolapse

Diagnosis: Fecal floatation

Treatment: Imidazole derivatives (Metronidazole), tetracycline or doxycycline

Pathology: Organisms are often found in the lumen of the colon of normal animals and in ulcerative lesions, mucosa, capillaries, lymphatics, and mesenteric lymph nodes of animals with colitis. Usually associated with some other pathogen. May be a primary pathogen in great apes.

STRONGYLOIDOSIS (High concern)

Etiology: *Strongyloides stercoralis, S. fulleborni, S. cebus*

Transmission: Fecal-oral (transmucosal) usually via soil, percutaneous and transplacental

Clinical: Diarrhea with or without blood and mucus, urticaria, anorexia, depression, listlessness, vomiting, emaciation, constipation, dyspnea, cough, death

Diagnosis: Fecal floatation with typical larvae (*S. stercoralis*) or eggs (*S. fulleborni, S. cebus*) in stool

Treatment: Benzimidazole, ivermectin, pyrantel pamoate or levamizole

Pathology: Multifocal or diffuse pulmonary hemorrhage, catarrhal to hemorrhagic-necrotic enter colitis. In hyper infections there is sub acute eosinophilic interstitial pneumonia, eosinophilic vasculitis and perivasculitis.

NODULAR WORM (High concern)

Etiology: *Oesophagostomum sp.*

Transmission: Fecal-oral

Clinical: Low burdens are usually well tolerated. Unthriftiness and debilitation with weight loss and diarrhea and death in heavy infestations.

Diagnosis: Fecal floatation with identification of eggs. Note: *Oesophagostomum sp.* are indistinguishable from certain strongyles (*Ternidens)* and hookworm eggs. PCR-RFLP

Treatment: Benzimidazole, ivermectin, pyrantel pamoate or levamizole

Pathology: 2-5mm diameter nodules in the sub mucosal layer of the large intestine. On cut surface the nodules are filled by a brown, creamy material and connected to the intestinal lumen by a small ulcer)

HOOKWORM (High Concern)

Etiology: *Ancylostoma duodenal, Necator americanus*

Transmission: Fecal-oral for both parasites plus cutaneous penetration for *Necator*

Clinical: Anemia, weakness, distended abdomen, dyspnea on exertion and general debilitation.

Diagnosis: Identification of eggs in feces which should be cultured for definitive diagnosis.

Treatment: Benzimidazole, ivermectin, pyrantel pamoate or levamizole

Pathology: Adults found attached to the small intestine at necropsy with intestinal hyperemia, ulceration and edema. The liver and other organs may be pale. *Necator* larvae can be found in the lungs and heart.

PINWORM (Moderate concern)

Etiology: *Enterobius sp. (E. vermicularis* is zoonotic), *Colobenterobius* sp., *Prostmayria* sp., *Lemuricola* sp.

Transmission: Fecal-oral

Clinical: Perianal pruritus that can lead to self mutilation, restlessness and increased aggression

Diagnosis: Observing the adult worms emerging from the anus or from a cellophane tape impression. Egg identification on fecal floatation

Treatment: Benzimidazole, ivermectin, pyrantel pamoate or levamizole

Pathology: Cecal/colonic/rectal mucosal hyperemia. Edematous thickening or fibrosis of the large intestinal wall.

WHIPWORM (Moderate concern)

Etiology: *Trichuris trichura*

Transmission: Fecal-oral

Clinical: Anorexia and diarrhea in severe infections

Diagnosis: Identification of eggs on fecal floatation

Treatment: Benzimidazole, ivermectin, pyrantel pamoate or levamizole

Pathology: Adults found with anterior end embedded in mucosa of cecum and proximal colon. Little host reaction. Heavy infestations rarely associated with intussusception.

HYDATID DISEASE (Low concern)

Etiology: *Echinococcus sp.*

Transmission: Fecal-oral (canid/feline feces)

Clinical: Abdominal distension, exophthalmia, localized subcutaneous swellings. Sudden death in pulmonary echinococcosis due to anaphylactic shock.

Diagnosis: Ultrasonography; aspiration of cyst and identification of scolices in aspirate

Treatment: Mebendazole, Albendazole

Pathology: Cyst formation in abdominal, thoracic or pelvis organs that contain viable scolices that are surrounded by a thick laminated membrane.

LUNG MITE (Moderate concern)

Etiology: *Pneumonyssus sp.*

Transmission: Oro-nasal from mother to offspring

Clinical: Paroxysms of coughing or sneezing. Death from massive infestation in chimpanzees.

Diagnosis: Identification of the egg or larvae in bronchial wash, feces or at necropsy

Treatment: Ivermectin

Pathology: 1-2mm diameter yellowish-white nodules due to focal chronic endo and peribronchiolitis. Adult lung mites in bronchoiectatic caverns, per bronchiolar and per vascular macrophages filled with yellow-brown pigment.

SCABIES (Moderate concern)

Etiology: *Sarcoptes scabiei*

Transmission: Direct skin contact

Clinical: Intense pruritus, anorexia, weakness, weight loss, emaciation and localized to generalized alopecia

Diagnosis: Identification of the mite on deep skin scrapings

Treatment: Ivermectin

Pathology: Characteristic appearance of mites and eggs within the stratum corneum.

SCHISTOSOMIASIS (Moderate concern)

Etiology: *Schistosoma mansoni, S. hematobium*

Transmission: Direct skin contact

Clinical: Anemia, ascites, hepatomegaly, emaciation, anorexia and death.

Diagnosis: Identification of the eggs in fecal floatations. Serology.

Treatment: Praziquantel

Pathology: Periportal hepatic fibrosis, hepatomegaly, colonic mucosal erosions.

PERIODONTAL DISEASE (Low concern)

Etiology: Unknown, various bacteria including Shigella sp. occasionally, NOMA associated with SAIDS.

Clinical: Usually none. Animals often debilitated or immunosuppressed due to other causes. Associated with dental calculus.

Pathology: Lesions vary from slight reddening of gums to necrotizing ulcerative gingivitis. Gingival bleeding common. Interproximal craters with alveolar bone destruction in severe cases. Spirochetes can be demonstrated in gingival connective tissue by silver staining. *Shigella flexneri*, serotype 4 is commonly present. Gangrenous necrosis of bone and overlying soft tissues in NOMA (Cancrum oris) -associated with type D retrovirus infection has been reported in macaques.

FIBROUS GINGIVAL HYPERPLASIA (Low concern)

Etiology: Unknown. May be a sequela to chronic gingivitis. Possibly familial in macaques. Phenytoin may also produce gingival enlargement.

Clinical: Usually none.

Pathology: Mild to marked firm enlargement of the marginal and alveolar gingiva, including the
interdental papillae. The hyperplastic tissue is normal in color and may completely cover the teeth. Microscopically, the tissue is dense collagen with little inflammation.

ACUTE GASTRIC DILATATION (BLOAT) (High Concern)

Etiology: Thought to be multifactorial including food restriction, overeating, anesthesia. Usually occurs in caged monkeys. *Clostridium perfringens Type A* can be isolated in large numbers and may be responsible for gas production.

Clinical: Old world monkeys. Usually found dead with enlarged and firm abdomens.

Pathology: Stomach markedly distended with gas and brown watery fluid, intestine congested.
Subcutaneous emphysema occurs if the stomach ruptures. Affected monkeys die of respiratory
embarrassment, impaired venous return, and shock.

DIVERTICULOSIS (Moderate concern)

Etiology: Unknown. Possibly congenital or due to spastic contraction of the colon

Clinical: Usually none. Abdominal pain.

Pathology: Saccular protrusions along taenia coli, muscular hypertrophy. May become impacted and inflamed.

CARDIOMYOPATHY (High Concern)

Etiology: Unknown.

Clinical: Gorillas and chimpanzees: Common from middle age onward, associated with obesity. May cause no clinical signs or sudden death, especially during anesthesia.

Pathology: Cardiomegaly, myocardial hypertrophy, fibrosis, atrial thrombosis, saddle thrombus in aorta, ascites, pulmonary oedema. Myocardial fibrosis and hypertrophy in apes.

IRON STORAGE DISEASE (Low concern)

Etiology Excessive iron accumulation leading to pathological conditions

Clinical: Associated with concurrent diseases, aging, or wasting. Seen in gorillas. Liver most affected tissue. Also gut, spleen, kidney, heart and pancreas.

Pathology: Copper or bronze coloured swollen liver. Sometimes some scarring and cirrhotic appearance. Yellow/gold pigment in cytoplasm of hepatocytes, Kupffer cells, renal tubular epithelium splenic reticular cells, myocardiocytes, pancreatic acinar cells. In hemochromatosis, liver has bridging fibrosis, biliary hyperplasia, hepatocellular cytomegalic and karyomegalic change and necrosis.

ENDOMETRIOSIS (Moderate concern)

Etiology: Implantation of normal endometrial tissue in ectopic locations. Several theories as to how this occurs but none conclusive.

Clinical: Depends on site of implantation. Abdominal swelling, constipation, uremia.

Pathology: Multiple cysts which contain "chocolate brown" fluid, extensive fibrosis, hemosiderosis, and adhesions. The lower abdominal and pelvic organs are often adhered into a single mass. Can cause obstruction of intestine and ureters. Histologically, endometrial epithelium and stroma must be present to differentiate endometriosis from endometrial carcinoma. Dense fibrosis and hemosiderosis are usually present.

ARTHRITIS (Moderate concern)

Etiology: Associated with calcium pyrophosphate crystal deposition in joint.

Clinical: Enlarged joints, muscle contracture and wasting.

Pathology: Can affect any joint. Interphalangeal joints and knees most obviously affected. Reducedsynovial fluid, cartilage erosion and ulceration, synovial hyperplasia, neutrophilic infiltrates. Calcium pyrophosphate crystals can be observed in articular surfaces by SEM in many cases.

TRAUMA DUE TO FIGHTING (Moderate concern)

Etiology: Fight injuries in group housed animals, particularly in breeding season or when new animals are added to group.

Clinical: Lacerations, bruises, abrasions, punctures, etc. Injuries to underlying soft tissue are often more extensive than is apparent from the appearance of the skin lesions. Gangrene of distal extremities can develop due to extensive crushing and bacterial contamination.

Pathology: Extensive muscle necrosis, gangrene, myoglobinuric nephrosis, hyperkalemia.

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