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Natural Pathology of the Captive Chimpanzee (*Pan troglodytes*): A 35 Year Review

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Abstract

Background—We present the spontaneous pathological lesions identified as a result of necropsy or biopsy for 245 chimpanzees (*Pan troglodytes*) over a 35-year period.

Methods—A review of the pathology database was performed for all diagnoses on chimpanzees from 1980 to 2014. All morphologic diagnoses, associated system, organ, etiology, and demographic information were reviewed and analyzed.

Results—Cardiomyopathy was the most frequent lesion observed followed by hemosiderosis, hyperplasia, nematodiasis, edema, and hemorrhage. The most frequently affected systems were the gastrointestinal, cardiovascular, urogenital, respiratory, and lymphatic/hematopoietic systems. The most common etiology was undetermined, followed by degenerative, physiologic, neoplastic, parasitic, and bacterial.

Conclusions—Perinatal and infant animals were mostly affected by physiologic etiologies and chimpanzee-induced trauma. Bacterial and physiologic etiologies were more common in juvenile animals. Degenerative and physiologic (and neoplastic in geriatric animals) etiologies predominated in adult, middle aged, and geriatric chimpanzees.

Keywords

Chimpanzee; Pathology; Lesions; Cardiomyopathy; Geriatric; Ageing; Primates

Introduction

Surveys of spontaneous pathological lesions of chimpanzees have been rarely reported [1–3]. Except for a few short surveys of lesions and causes of mortality [1–6], an extensive documentation of chimpanzee lesions is lacking. Most of the published studies are in the form of case series that include pathology findings related to body systems (central nervous [7–18], cardiovascular [19–30], respiratory [31–34], gastrointestinal [35–38], urinary [39–43], and integumentary [44–61]), etiologies (parasitic [62–64], degenerative [5, 65], and

neoplastic [66–83]), and individual case reports [84–86]. An extensive survey of the pathological lesions is lacking in literature.

Recently captive chimpanzees were classified as an endangered species, and thus, their use in research has essentially ceased [87]. Additionally, due to the NIH moratorium on chimpanzee breeding since 1995, the captive population is getting older, and at times it becomes increasingly difficult to distinguish pathological lesions from normal ageing associated changes [3]. As the captive population ages, an in-depth knowledge of the natural pathology of this species is required so that veterinarians can continue to provide high quality medical care to these animals. Further, given the close phylogenetic resemblance to humans, a survey of chimpanzee pathology is required for better understanding of several common age associated disorders in humans.

We document the spontaneous pathological lesions identified as a result of necropsy or biopsy for 245 chimpanzees, at the Southwest National Primate Research Center at the Texas Biomedical Research Institute, San Antonio, Texas, over a 35-year period (1980 to 2014). To the best of our knowledge, this is the most comprehensive documentation of lesions in captive chimpanzees and provides an extensive summary of natural age associated changes as well as pathological lesions in captive chimpanzees.

Materials & Methods

Colony

The chimpanzee colony was originally formed in 1967 at the Texas Biomedical Research Institute's Southwest National Primate Research Center as a breeding colony. In 1995, the National Institute of Health (NIH) enacted a moratorium on breeding NIH-owned chimpanzees. Due to the moratorium, there are few young chimpanzees in our colony and the population is aging. The chimpanzees were used in biomedical research involving Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Human Immunodeficiency Virus (HIV), as well as research with monoclonal antibody therapies. Chimpanzees were socially housed with free choice of indoor and outdoor areas and enrichment, which included toys and climbing structures. They were fed a standard monkey chow (Teklad®, PMI Nutrition International, LLC, Brentwood, MO 63144) with additional fruits, grains, and vegetables as enrichment. All animal care and procedures were approved by the Texas Biomedical Research Institute Animal Care and Use Committee. The Texas Biomedical Research Institute is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International.

Cases

Chimpanzees that died naturally or were humanely euthanized were necropsied and tissues were collected for histologic evaluation as required for diagnosis. Tissues were fixed in 10% neutral buffered formalin, conventionally processed, embedded in paraffin, cut at 5µm, and stained with hematoxylin and eosin or other stains. When indicated, individual tissues were frozen in liquid nitrogen and stored at –80°F, fixed in 2% glutaraldehyde for electron microscopy, placed in normal saline or transport medium for cytogenetic evaluation,

cultured for bacteria and viruses, or frozen in Optimal Cutting Temperature Compound (Tissue-Tek®) compound for frozen sectioning. Further evaluation using immunohistochemistry was performed as required. Board-certified veterinary pathologists performed the necropsies and histologic evaluation, and results were filed in an internal database. Complex lesions or those of unknown etiology were reviewed by three to five other board-certified veterinary pathologists. If deemed necessary, cases were referred to the Armed Forces Institute of Pathology, the Joint Pathology Center, or other pathologists with expertise in the field. Biopsy specimens were handled as stated for necropsy tissues. Biopsies represented 5% of diagnoses and were almost exclusively from the skin, oral cavity, or lymph node.

Records

A series of SQL queries were used to search the pathology database for all diagnoses from chimpanzees from 1980 to 2014 was performed. All morphologic diagnoses, and the associated system, organ, and etiology were retrieved, as well as the animals' date of birth and death, age at death, and sex. Excluded were animals that were on experimental protocols with the exception of the chimpanzees with chronic HBV, HCV, and HIV infection. The HBV, HCV, and HIV status of each animal was retrieved from a separate database used to track the animals viral status with regard to detectable persistent viremia or no detectable viremia. Historical exposure data were not used due to complexity in interpretation of older data and the unlikely relevance. All original or computerized medical records, gross necropsy reports, histopathology reports and related laboratory results were retrieved.

Data Analysis

Animals were categorized by sex and separated into age groups to categorize lesions. The age groups were defined as perinatal (< 1 day old), infant (>1 day to 4 years), juvenile (>4 years to 12 years), adult (>12 years to 23 years), middle age (>23 years to 35 years), and geriatric (>35 years). Chimpanzees were considered infants until they were weaned at approximately 4 years of age, and transitioned from juvenile to adult when they reach sexual maturity at approximately 12 years of age [88]. Middle age was defined as the latter half of the interval between the start of adulthood and the start of geriatric age. The lower limit of geriatric age was chosen to be 85% of total expected lifespan [88] and to coincide with a prior survey of geriatric reproductive tract lesions in chimpanzees [3].

Specific criteria were developed to categorize the findings: (1) stillborn animals were considered as separate cases from the dam, included in the urogenital system, and were given the age of zero; (2) localized hemorrhage was counted within the affected organ; (3) lesions that affected multiple organs or the body as a whole, such as disseminated hemorrhage, lymphosarcoma, or amyloidosis were categorized as multisystem; (4) adenomyosis and endometriosis were included with the category of neoplasia; (5) all papillomas were considered to be neoplastic (it is possible that some or all may have been viral induced, but this could not be ascertained from the records); and (6) cardiomyopathy, defined as the presence of multifocal to coalescing areas of fibrosis, necrosis, mineralization, and inflammation, was characterized as a degenerative disease.

Statistical tests

The R language and environment for statistical computing was used within the RStudio [89] for all analyses [90]. The R packages stringi [91], RODBC [92], readxl [93], dplyr [94], and XLConnect [95] were used. Fisher's exact test for two-by-two tables was used to test for independence of the animals' age, sex, viral status, and observed morphology at necropsy. Fisher's exact tests that could not produce a p-value of 0.05 or less when all animals with the specified morphology were not performed. The Bonferroni-Holm [96] correction was used in assessing the fit to the null hypothesis (no effect of attribute: sex, age, or viral status). Since some of these morphologies and thus the tests are correlated, this is a conservative adjustment.

Results

A total of 1362 diagnoses from 245 chimpanzees (123 male, 16.5 ± 13.7 years; 113 female, 19.6 ± 17.8 years; and 9 animals of unknown sex, 0 years) were identified during the 35-year period. The population demographics are shown in Table 1. There were 34 chimpanzees chronically infected with HCV (3 juvenile, 6 adult, 24 middle age, and 1 geriatric), 8 chronically infected with HBV (1 adult, 2 middle age, and 5 geriatric), and 16 chronically infected with HIV (2 juvenile, 2 adult, 11 middle age, and 1 geriatric). The numbers above include four middle age male chimpanzees that were chronically infected with both HCV and HIV. Also included above were one middle age male and one geriatric female chimpanzee each chronically infected with both HBV and HIV.

Table 2 presents the morphologic diagnoses in order by frequency of occurrence (total number and percentage of diagnoses), and lists the numbers and percentages of male, female or unknown gender, and the numbers of chimpanzees in each age group for each diagnosis. The ten most common morphologic diagnoses accounted for 36.9% of all lesions: cardiomyopathy (n = 67, 4.9%); hemosiderosis (n = 66, 4.8%); hyperplasia (n = 64, 4.7%); nematodiasis (n = 55, 4.0%); edema (n = 50, 3.7%); hemorrhage (n = 46, 3.4%); fibrosis (n = 45, 3.3%); pneumonia (n = 41, 3.0%); congestion (n = 35, 2.6%); and nephritis (n = 34, 2.5%).

Table 3 presents the etiologies in order by frequency of occurrence (total number and percentage of diagnoses) and lists the numbers and percentages of male, female or unknown gender, and the percentages of chimpanzees in each age group for each etiology. The most common etiologies were: undetermined (n = 525, 38.5%); degenerative (n = 281, 20.6%); physiologic (n = 209, 15.3%); neoplastic (n = 100, 7.3%); parasitic (n = 72, 5.3%), and bacterial (n = 55, 4.0%). Excluding lesions of undetermined etiology, lesions seen in perinatal animals were exclusively physiologic (n = 10, 15.4%), traumatic (n = 10, 15.4%), or congenital (n = 5, 7.7%). Lesions of infant chimpanzees were varied, but most often traumatic (n = 10, 13.7%), bacterial (n = 6, 8.2%), parasitic (n = 5, 6.8%), physiologic (n = 4, 5.5%), and viral (n = 3, 4.1%). Juvenile chimpanzees most often had lesions resulting from bacterial (n = 15, 19.2%), physiologic (n = 11, 14.1%), neoplastic (n = 8, 10.3%; all papillomas), or parasitic (n = 6, 7.7%) causes. Adult lesions were the most varied and commonly due to degenerative (n = 50, 17.4%), physiologic (n = 49, 17.0%), bacterial (n = 17, 5.9%), parasitic (n = 16, 5.6%), mycotic (n = 13, 4.5%), traumatic (n = 13, 4.5%), or

neoplastic (n = 10, 3.5%) etiologies. Degenerative, physiologic, neoplastic and parasitic lesions predominated in middle aged and geriatric chimpanzees, accounting for majority of all lesions in both age groups.

Table 4 presents the body systems and organs with lesions in order by frequency of occurrence (total number and percentage of diagnoses), lists the percentages attributable to each organ within the system, lists the numbers of male, female or unknown gender, and numbers of chimpanzees in each age group. Lesions were most often observed in the gastrointestinal (350 of 1362, 25.7%), cardiovascular (297, 21.8%), urogenital (215, 15.8%), respiratory (158, 11.6%), and lymphatic/hematopoietic (128, 9.4%) systems, followed by the integumentary (54, 4.0%), endocrine (53, 3.9%), nervous (43, 3.2%), musculoskeletal (31, 2.3%), multi-systemic lesions (20, 1.5%), and lesions involving the special senses (13, 1.0).

Table 5 presents the relative risk assessment using chi-square goodness of fit analyses between morphologies and gender. In the chimpanzees for which we had adequate sex data, there were 1349 morphology records providing 322 morphology - sex comparisons. Only 124 had enough observations to possibly have a significant test at the 0.05 level of significance. The Bonferroni corrected p-value was 3.9e-05 (0.05/124). Those with a relative risk greater than 1 are more likely to exhibit the morphology and those with a relative risk less than 1 are less likely to exhibit the morphology than those of the other sex. Cardiomyopathy and leiomyoma were significantly associated with gender. Male chimpanzees had much higher risk of developing cardiomyopathy. Female chimpanzees had much higher risk of developing leiomyoma; this was a result of the majority of leiomyomas occurring in the myometrium.

Table 6 presents the correlation analyses and risk factor analyses between morphologic diagnoses and age groups. In the chimpanzees for which we had adequate age data, there were 1333 morphology records providing 972 morphology - age comparisons. However, only 657 had enough observations to possibly have a significant test at the 0.05 level of significance. The Bonferroni corrected p-value was 5.82e-05 (0.05/657). Those with a relative risk greater than 1 are more likely to exhibit the morphology and those with a relative risk less than 1 are less likely to exhibit the morphology than those in other age groups. Hemorrhage was significantly associated with perinatal and infant chimpanzees. Pneumonia was significantly associated with infant animals. Papilloma and hemosiderosis were significantly associated with juvenile and middle age chimpanzees respectively.

Persistent HBV, HCV, and HIV viremia

Statistical analyses using Chi-square Goodness of fit test did not reveal any significant association between persistent HBV, HCV, and HIV viremia status of the chimpanzees and any morphologic diagnosis.

Gastrointestinal system

Gastrointestinal system lesions were most often seen in middle aged (178 of 350, 50.9%), geriatric (n = 69, 19.7%), and adult (n = 67, 19.1%) chimpanzees, with an approximately 1:1 male to female ratio. The organs most often affected were the liver (n = 113, 32.3%), colon (n = 66, 18.9%), cecum (n = 22, 6.3%), pancreas (n = 22, 6.3%), small intestine (n = 19,

5.4%), gall bladder (n = 18, 5.1%), and peritoneal cavity (n = 18, 5.1%). Nematodiasis (n = 55, 15.7%) was the most frequent morphologic diagnosis, followed by colitis (n = 27, 7.7%), hepatitis (n = 23, 6.6%), peritonitis (n = 15, 4.3%), hepatopathy (n = 15, 4.3%), hemosiderosis (n = 15, 4.3%), fibrosis (n = 14, 4.0%), and hyperplasia (n = 14, 4.0%). Gastrointestinal lesions were mostly considered to be of undetermined (n = 139, 39.7%), parasitic (n = 69, 19.7%), degenerative (n = 31, 8.9%), physiologic (n = 30, 8.6%), or neoplastic (n = 26, 7.4%) etiology.

Despite surveillance and regular deworming, nematodiasis was observed in all age groups but perinatal, was primarily due to *Enterobius* spp., and was present in an approximately 3:2 male to female ratio. Hepatitis occurred in an approximately 3:2 male to female ratio, predominantly seen in adult, middle aged, and geriatric animals. Peritonitis was only seen in middle aged (10 of 15, 66.6%) or adult (n = 5, 33.3%) animals. The most common neoplasms were oral papilloma (n = 7; 5 juveniles) and hepatocellular carcinoma (n = 5, 1 adult, 3 middle aged, and 1 geriatric). Of the five animals with a diagnosis of hepatocellular carcinoma, three were chronically infected with HCV, one was chronically infected with HBV, and one had no data concerning viral status.

Cardiovascular system

Cardiovascular system lesions were almost exclusively seen in middle aged (143 of 297, 48.1%), adult (n = 75, 25.3%), and geriatric (n = 67, 22.6%) chimpanzees, with an approximately 3:2 male to female ratio. The organs most often affected were the heart (n = 173, 58.2%), artery (n = 31, 10.4%), peritoneal cavity (n = 18, 6.1%), thoracic cavity (n = 17, 5.7%), pericardial sac (n = 14, 4.7%), and aorta (n = 13, 4.4%). The most common diagnoses were: cardiomyopathy (n = 67, 22.6%), arteriosclerosis/atherosclerosis (n = 28, 9.4%), fibrosis (n = 21, 7.1%), myocarditis (n = 21, 7.1%), endocardiosis (n = 19, 6.4%), ascites (n = 18, 6.1%), hydrothorax (n = 17, 5.7%), infarct (n = 16, 5.4%), and hydropericardium (n = 16, 5.4%). Cardiovascular lesions were nearly all considered to be of degenerative (n = 148, 49.8%), undetermined, (n = 78, 26.3%), or physiologic (n = 59, 19.9%) etiology. Although most lesions in the cardiovascular system were more common in males, there were some exceptions. Arteriosclerosis/atherosclerosis, infarct, and thrombus were each observed in an approximately 1:2 male to female ratio. Seven of sixteen infarcts occurred in the brain and were characterized as cerebrovascular accidents (stroke); these occurred in five female (4 geriatric; 1 middle aged) and 2 male (1 geriatric; 1 adult) chimpanzees. Myocarditis, necrosis, and degeneration were seen equally in males and females. With the exception of one infant with pulmonary lesions, arteriosclerosis/atherosclerosis was exclusively observed in middle age and geriatric animals.

Urogenital system

Urogenital system lesions were seen most often in middle aged (94 of 215, 43.7%), geriatric (n = 41, 19.1%), perinatal (n = 37, 17.2%), and adult (n = 31, 14.4%) chimpanzees, with an approximately 1:2 male to female ratio. Lesions of the urogenital system were subdivided into four major areas: lesions of the urinary tract (n = 102, 47.4%), female reproductive tract (n = 66, 30.7%), male reproductive tract (n = 18, 8.4%), and stillbirths (n = 29, 13.5%).

Urinary tract lesions were mostly seen in middle aged (49 of 102, 48.0%), adult (n = 21, 20.6%), and geriatric (n = 14, 13.7%) chimpanzees, with an approximately equal male to female ratio. The kidney was the primary focus of majority of urinary tract lesions (80 of 102, 78.4%), predominantly nephritis (34 of 80, 42.5%), and glomerulonephritis (n = 15, 18.8%).

Lesions of the female reproductive tract were almost exclusively seen in middle aged (36 of 66, 54.5%), geriatric (n = 21, 31.8%), and adult (n = 7, 10.6%) chimpanzees. The most common lesions were leiomyoma (n = 20, 30.3%), cyst (n = 11, 16.7%; 7 ovarian, 2 oviductal, and 2 uterine), adenomyosis (n = 8, 12.1%), and uterine polyp (n = 5, 7.6%). Although most lesions in the urogenital system were of undetermined etiology (112 of 215, 52.1%), the exception was lesions of the female reproductive tract where 39 of 66 (59.1%) were neoplastic. Neoplasms included 20 leiomyomas (19 uterine and one oviductal), eight cases of adenomyosis, five uterine polyps, four ovarian tumors (2 granulosa cell tumors, 1 Brenner tumor, and one teratoma), a vaginal papilloma, and one case of uterine endometriosis.

Lesions of the male reproductive tract were restricted to middle aged (9 of 18, 50.0%), geriatric (n = 6, 33.3%), and adult (n = 3, 16.7%) chimpanzees. The most common lesions were prostatitis (n = 6, 33.3%) and testicular atrophy (n = 3, 16.7%). The gender of stillbirths appeared roughly even (M=12; F=10); however, as seven (24.1%) stillbirths were of unrecorded sex, the true ratio remains uncertain.

Respiratory system

Respiratory system lesions were seen across all age groups, but most commonly in middle aged (65 of 158, 41.1%) and adult (n = 36, 22.8%) chimpanzees, with an approximately 1:1 male to female ratio. The organs most often affected were the lung (n = 126, 79.7%) and air sac (n = 14, 8.9%). The most common diagnoses were pneumonia (n = 41, 25.9%), edema (n = 23, 14.6%), hemosiderosis (n = 18, 11.4%), congestion (n = 14, 8.9%), hemorrhage (n = 14, 8.9%), air sacculitis (n = 10, 6.3%), and atelectasis (n = 9, 5.7%). Males were overrepresented in lesions involving the air sac and diagnoses of air sacculitis (M:F ratio of 10:4 and 7:3 respectively). Respiratory lesions were most often of undetermined (n = 61, 38.6%), physiologic (n = 52, 32.9%), or bacterial (n = 18, 11.4%) etiology.

Infectious agents were often encountered in respiratory lesions. There were ten cases of confirmed bacterial pneumonia, all involving adult or younger animals; cultures were obtained in seven. *Streptococcus pneumoniae* was isolated in five of the cases; *Staphylococcus hemolyticus* and *Micrococcus* spp. were each identified in one animal. There were five instances of confirmed bacterial airsacculitis, all in male animals ranging from juvenile to middle age. Cultures were obtained in four animals and a total of six organisms were isolated: *Streptococcus pneumoniae*, *Micrococcus* spp., *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Viridans group streptococci*. There were five animals with mycotic pneumonia; four due to *Coccidioides immitis* and one middle aged diabetic female with *Pneumocystis carinii*. Two infants had adenoviral pneumonia; one had concurrent *Streptococcus pneumoniae* infection (included in

the above culture results). Pneumonia associated with *Strongyloides* spp. larvae was observed in one adult female chimpanzee.

Lymphatic/Hematopoietic system

Lymphatic and hematopoietic system lesions were most often seen in middle aged (44 of 128, 34.4%) and adult (n = 39, 30.5%) chimpanzees, in an equal number of males and females. The lymph node (n = 74, 57.8%) and spleen (n = 36, 28.1%) were most often affected. The most common diagnoses in the lymph nodes were hyperplasia (20 of 74, 27.0%), lymphadenitis (n = 13, 17.6%), hemosiderosis (n = 11, 14.9%), amyloidosis (n = 4, 5.4%), atrophy (n = 4, 5.4%), and edema (n = 4, 5.4%). The most common diagnoses in the spleen were hemosiderosis (11 of 36, 30.6%), splenitis (n = 6, 16.7%), congestion (n = 5, 13.9%), and amyloidosis (n = 4, 11.1%). Lymphatic and hematopoietic lesions were most often of undetermined (n = 58, 45.3%), physiologic (n = 32, 25.0%), or degenerative (n = 17, 13.3%), mycotic (n = 8, 6.3%), or bacterial (n = 7, 5.5%) etiology. The eight mycotic lesions were four cases each of lymphadenitis and splenitis due to disseminated *Coccidioides immitis*. Only one of the bacterial lesions was cultured; it was a case of *Streptococcus pneumoniae* lymphadenitis in an infant female. Lymphadenitis associated with *Strongyloides* spp. larvae was observed in the chimpanzee with parasitic pneumonia.

Integumentary system

Integumentary system lesions almost exclusively involved the skin and subcutis (51 of 54), with the exception of three lesions involving the mammary gland (one case each of fibrosis, hyperplasia, and mastitis in female chimpanzees). Integumentary system lesions were most often of undetermined (22 of 54, 40.7%), neoplastic (n = 14, 25.9%), or traumatic (n = 7, 13.0%) etiology. Of the lesions involving the skin and subcutis, most were seen in middle aged (22 of 51, 41.2%), adult (n = 15, 27.5%), and juvenile (n = 10, 19.6%) chimpanzees, with an approximately equal male to female ratio. The most common diagnoses were dermatitis (n = 19, 37.3%), papilloma (n = 9, 17.6%), hyperplasia (n = 6, 11.8%), and lipoma (n = 5, 9.8%). Dermatitis was seen almost twice as often in males than in females. Papilloma and hyperplasia were seen approximately four times more often in females than males. All the hyperplasia diagnoses occurred in female chimpanzees; six of the seven were adult or older. Lipomas were observed in middle age and geriatric animals; four of the five were in females. There were four bacterial lesions: two cases of cellulitis (*Staphylococcus aureus* was cultured from one); one abscess; and one case of dermatitis resulting from *Mycobacterium leprae*.

Endocrine system

Endocrine system lesions were almost exclusively seen in middle aged (32 of 53, 60.4%), geriatric (n = 10, 18.9%), and adult (n = 8, 15.1%) chimpanzees, with slightly more lesions in females than males. Endocrine lesions were predominantly of degenerative (n = 16, 30.2%), undetermined (n = 13, 24.5%), neoplastic (n = 11, 20.8%), or physiologic (n = 8, 15.1%) etiology. The organs most often affected were the pituitary (n = 24, 45.3%), adrenal gland (n = 15, 28.3%), and thyroid (n = 9, 17.0%). The most common diagnoses were hyperplasia (n = 13, 24.5%), cyst (n = 10, 18.9%), adenoma (n = 9, 17.0%), and amyloidosis (n = 6, 11.3%). Hyperplasia was observed in adult to aged chimpanzees and most often

involved the pituitary gland (n=8); other sites included the adrenal gland (n = 2), thyroid (n = 2), and islets of Langerhans (n = 1). Cysts were generally observed in middle aged animals and involved the pituitary (n = 8) or thyroid (n=2). Adenomas were seen in middle aged and geriatric chimpanzees and involved the pituitary (n = 5), thyroid (n = 3), and adrenal gland (n = 1). Amyloid was identified in the adrenal gland (n = 4), islets of Langerhans (n = 1), and thyroid (n = 1), primarily in middle aged animals.

Nervous system

Nervous system lesions were most often seen in middle aged (16 of 43, 37.2%), infant (n = 10, 23.3%), and perinatal (n = 7, 16.3%) chimpanzees, with a 4:3 male to female ratio. Nervous system lesions were mostly considered to be of undetermined (n = 21, 48.8%), traumatic (n = 9, 20.9%), or degenerative (n = 7, 16.3%) etiology. The brain (n = 29, 67.4%) and meninges (n = 7, 16.3%) accounted for the majority of lesions. The most common diagnoses were: hemorrhage (n = 11, 25.6%), meningitis/meningoencephalitis/encephalitis (n = 7, 16.3%), and mineralization (n = 6, 14.0%). Meningitis/meningoencephalitis/encephalitis was generally observed in infant and juvenile animals; six of the seven were male. A bacterial etiology was identified in three: two cases of *Staphylococcus hemolyticus* and one of *Klebsiella pneumoniae*. Chimpanzee-induced trauma accounted for nine of the eleven incidences of hemorrhage, was restricted to perinatal and infant chimpanzees, and generally attributed to poor mothering skills.

Musculoskeletal system

Musculoskeletal system lesions mostly seen in middle aged (12 of 31, 38.7%), adult (n = 7, 22.6%), and geriatric (n = 7, 22.6%) chimpanzees, with slightly more males than females. The organs most often affected were the skeletal muscle (n = 14, 45.2%), bone (n = 7, 22.6%), and joint (n = 6, 19.4%). There was a wide variety of lesions, the most common were arthritis, (n = 5, 16.1%), degeneration, (n = 4, 12.9%), and myositis, (n = 3, 9.7%). Most musculoskeletal lesions were considered to be of undetermined (n = 12, 38.7%), degenerative (n = 11, 35.5%), or traumatic (n = 4, 12.9%) etiology.

Multisystem disease

Multisystem system lesions were most often seen in middle aged (8 of 20, 40.0%), adult (n = 5, 25.0%), and geriatric (n = 4, 20.0%) chimpanzees, with an approximately 2:1 male to female ratio. The most commonly diagnosed lesions that affected the whole body included amyloidosis (5 of 20, 25%) which was considered degenerative in etiology and hemorrhage (n = 5, 25%), usually related to trauma.

Special Senses

Lesions involving the special senses were almost exclusively seen in and geriatric (6 of 13, 46.2%) and middle aged (n = 4, 30.8%) chimpanzees, with an approximately equal male to female ratio. The affected organs were the eye (n = 7, 53.8%) and conjunctiva (n = 6, 46.2%); ocular lesions were more common in males and conjunctival lesions were more common in females. Conjunctivitis (n = 5, 38.5%) and cataract (n = 3, 23.1%) were the most frequent diagnoses. The majority of findings were of undetermined (n = 6, 46.2%) or

degenerative (n = 5, 38.5%) etiology. There was also a squamous cell carcinoma of the sclera and a case of traumatic panophthalmitis.

Discussion

We report 1,362 spontaneous pathology lesions observed at necropsy or biopsy for 245 chimpanzees (*Pan troglodytes*) over a 35-year period (1980 to 2014). Cardiomyopathy was the most frequent lesion observed, followed by hemosiderosis, hyperplasia, nematodiasis, edema, hemorrhage, fibrosis, pneumonia, congestion, nephritis, necrosis, and stillborn. The most frequently affected systems were the gastrointestinal, cardiovascular, urogenital, respiratory, and lymphatic/hematopoietic systems. The most common etiology was undetermined, followed by degenerative, physiologic, neoplastic, parasitic, and bacterial. Distribution of etiology (excluding undetermined) by age group indicated that chimpanzee-induced trauma was predominantly observed in perinatal and infant chimpanzees, generally attributed to poor mothering skills. Juvenile chimpanzees most often had lesions of bacterial, physiologic, or neoplastic (all papillomas) etiology. Lesions of adult chimpanzees varied the most in etiology, but were often due to degenerative and physiologic etiologies. Degenerative, physiologic, and neoplastic etiologies predominated in middle aged and geriatric chimpanzees which is consistent with previous observation [4].

Cardiovascular disease, specifically, cardiomyopathy (also known as cardiac fibrosis or interstitial myocardial fibrosis), is reported to be the primary cause of mortality in captive chimpanzees in several previous publications and was the most common morphologic diagnosis in this study [4, 19, 21, 22, 97, 98]. The high incidence of cardiomyopathy in chimpanzees could suggest a genetic component, and warrants further investigation of this pathology relative to genealogy. Hemosiderosis, edema, hemorrhage, ascites, hydrothorax, and hydropericardium were often interpreted as sequela of cardiac insufficiency due to cardiomyopathy [97]. Renal lesions were most common in middle aged to geriatric groups, and the two primary diagnoses were nephritis and glomerulonephritis, which is consistent with previous literature [6].

The gastrointestinal system was the most affected system, with the liver accounting for almost one third of gastrointestinal system diagnoses. Etiologically, most of the gastrointestinal lesions were undetermined, followed by parasitic, degenerative, physiologic, and neoplastic. The three primary liver lesions were hemosiderosis, hepatitis, and hepatopathy. Although several chimpanzees in this study group were chronically infected with HBV, HCV, and HIV, we did not find any statistical correlation between virus status and liver diseases. This is not an unexpected finding given that chimpanzees infected with these virus rarely develop clinically significant disease [99–101]. Despite extensive control measures, nematodiasis (pinworms; *Enterobius* spp.) remains prevalent in our colony and other captive colonies [102, 103].

Excluding lesions of undetermined etiology, lesions of degenerative etiology were the most frequently encountered, as would be expected from an aging population. The most common degenerative lesions were cardiomyopathy, amyloidosis, and arteriosclerosis/atherosclerosis. Lesions of neoplastic etiology mostly affected the urogenital (females), gastrointestinal, and

integumentary systems. The most common uterine lesions were leiomyoma and adenomyosis, occurring in a slightly greater than 2:1 ratio. This is different from baboons where adenomyosis is much more common than leiomyoma [104], and in humans where leiomyomas (fibroids) are much more prevalent than adenomyosis [105, 106]. This difference should be considered, when evaluating a uterine mass in a chimpanzee, as imaging alone may be insufficient for a definitive diagnosis [107]. Neoplasms of the gastrointestinal system were comprised of mostly oral papillomas and hepatocellular carcinomas. A viral etiology for either of these two lesions could not be confirmed. However, the exclusive occurrence of papillomas within the juvenile age group does suggest a viral etiology for this lesion. Although, a statistical correlation could not be demonstrated due to the few animals with hepatocellular carcinoma and large number of animals with unknown viral status, this data does suggest the need to identify and regularly monitor chronically infected chimpanzees. Lesions of bacterial etiology most commonly affected the respiratory, gastrointestinal, and urogenital systems, and were most common in juvenile animals which is consistent with previous literature [4].

This dataset provides significant insights into the natural pathology of captive chimpanzees. While some data regarding specific aspects of captive and wild chimpanzee pathology have been reported before [2, 3, 97, 108], this publication provides an exhaustive account of all lesions across all age groups over a significantly long period of time (35-years). It is our hope that the information presented in this publication should serve as a reference for the veterinarians, care givers, and investigators working with chimpanzees.

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Table 1

Total number of animals by age-group, sex, and viral status. Chronic viral status refers to persistent viremia based on detection of viral genome by quantitative PCR. Undetermined viral status means the animal died prior to viral testing.

Age Group	Total	Male	Female	Unknown	HCV			HBV			HIV		
					Chronic	Negative	Undetermined	Chronic	Negative	Undetermined	Chronic	Negative	Undetermined
Perinatal	36	15	12	9		1	18			36			36
Infant	19	9	10				36			18			19
Juvenile	30	15	15		3	16	11		21	9	2	16	12
Adult	54	34	20		6	24	24	1	27	26	2	19	33
Middle Age	80	42	38		24	31	25	2	46	32	11	27	42
Geriatric	26	8	18		1	13	12	5	7	14	1	8	17
Total	245	123	113	9	34	85	126	8	102	135	16	70	159

Table 2

Morphologic diagnoses by sex and age-group in descending order of occurrence.

Morphologic diagnosis	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric	References
	n	%	n	%	n	%	n	%							
Cardiomyopathy	67	4.9	51	7.4	16	2.4		0.0				21	35	11	[19–23, 67]
Hemosiderosis	66	4.8	27	3.9	39	5.9		0.0			2	12	49	3	
Hyperplasia	64	4.7	27	3.9	37	5.6		0.0		3	9	17	24	11	[37, 70, 109, 110]
Nematodiasis	55	4.0	32	4.6	23	3.5		0.0		3	6	10	28	8	[52–55, 57]
Edema	50	3.7	29	4.2	21	3.2		0.0	1	2	3	13	26	5	[111, 112]
Hemorrhage	46	3.4	25	3.6	20	3.0	1	7.7	11	10	3	13	8	1	[9, 10, 13, 42, 53, 54]
Fibrosis	45	3.3	24	3.5	21	3.2		0.0		2	1	7	25	10	[20, 21, 113]
Pneumonia	41	3.0	21	3.0	20	3.0		0.0	1	10	6	12	10	2	[32, 114, 115]
Congestion	35	2.6	22	3.2	13	2.0		0.0	8	2		8	14	3	[116]
Nephritis	34	2.5	15	2.2	19	2.9		0.0		5		6	17	6	[40]
Necrosis	30	2.2	15	2.2	14	2.1	1	7.7	1	3	3	3	13	7	[10, 34, 42, 62, 117–123]
Stillborn	29	2.1	12	1.7	10	1.5	7	53.8	29						[124]
Arteriosclerosis/Atherosclerosis	28	2.1	11	1.6	17	2.6		0.0		1			14	13	[29, 125]
Anylodosis	27	2.0	17	2.5	10	1.5		0.0				7	17	3	[5]
Colitis	27	2.0	11	1.6	16	2.4		0.0		2	1	5	12	7	[54]
Cyst	27	2.0	6	0.9	21	3.2		0.0				5	15	7	[14, 126]
Ascites	23	1.7	14	2.0	9	1.4		0.0				6	11	6	[83, 127]
Hepatitis	23	1.7	15	2.2	8	1.2		0.0		1	2	6	9	5	[117, 118, 128–131]
Leiomyoma	23	1.7	1	0.1	22	3.3		0.0				2	11	10	[66–69]
Atrophy	21	1.5	15	2.2	6	0.9		0.0				6	12	3	[3, 132]
Myocarditis	21	1.5	11	1.6	10	1.5		0.0		1	1	6	10	3	[62, 133]
Degeneration	19	1.4	12	1.7	7	1.1		0.0				7	9	3	[3, 134, 135]
Dermatitis	19	1.4	12	1.7	7	1.1		0.0			5	8	4	2	
Endocardiosis	19	1.4	13	1.9	6	0.9		0.0			2	5	7	5	
Hydrothorax	18	1.3	11	1.6	6	0.9	1	7.7	1			5	8	4	

Morphologic diagnosis	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile		Adult		Middle Age	Geriatric	References
	n	%	n	%	n	%	n	%			n	%	n	%	n	n	
Mineralization	17	1.2	13	1.9	4	0.6		0.0					2		15		[9, 10]
Papilloma	17	1.2	4	0.6	13	2.0		0.0			8		2		6	1	
Hydropericardium	16	1.2	10	1.5	6	0.9		0.0			1		5		8	2	
Infarct	16	1.2	5	0.7	11	1.7		0.0					2		4	10	[8]
Glomerulonephritis	15	1.1	9	1.3	6	0.9		0.0					3		11	1	[42, 43]
Hepatopathy	15	1.1	9	1.3	6	0.9		0.0					3		12		[136, 137]
Peritonitis	15	1.1	6	0.9	9	1.4		0.0					4		10	1	[138]
Lymphadenitis	13	1.0	7	1.0	6	0.9		0.0		4	1		6		2		[139]
Adenoma	12	0.9	3	0.4	9	1.4		0.0					1		7	4	[73]
Protozoiasis	12	0.9	8	1.2	4	0.6		0.0					2		7	3	[62]
Esophagitis	11	0.8	3	0.4	8	1.2		0.0		1	1				7	2	[1]
Typhlitis	11	0.8	6	0.9	5	0.8		0.0					1		7	3	[51]
Air sacculitis	10	0.7	7	1.0	3	0.5		0.0			2		2		5	1	[34, 140]
Carcinoma	10	0.7	3	0.4	7	1.1		0.0					1		4	5	[58, 70, 80, 141–143]
Enteritis	10	0.7	4	0.6	6	0.9		0.0		1			1		5	3	[53, 139]
Thrombus	10	0.7	3	0.4	7	1.1		0.0					5		3	2	
Atelectasis	9	0.7	5	0.7	4	0.6		0.0	3	1			1		4		
Lipidosis	9	0.7	3	0.4	6	0.9		0.0		2	1		1		3	2	
Adenomyosis	8	0.6		0.0	8	1.2		0.0					1		2	5	[3, 82]
Polyp	8	0.6	2	0.3	6	0.9		0.0					1		5	2	[55, 76–78]
Inflammation	7	0.5	3	0.4	4	0.6		0.0		2	1				4		[3, 18, 35, 120, 135, 144]
Meningitis/Meningoencephalitis/Encephalitis	7	0.5	6	0.9	1	0.2		0.0		4	2				1		[1, 11, 15, 73]
Steatosis	7	0.5	3	0.4	4	0.6		0.0					2		5		
Cardiomegaly	6	0.4	6	0.9		0.0		0.0					3		1	2	[20, 25, 27]
Cholecystitis	6	0.4	1	0.1	5	0.8		0.0							2	4	
Hypoplasia	6	0.4	3	0.4	3	0.5		0.0	2				1		2	1	
Prostatitis	6	0.4	6	0.9		0.0		0.0					1		2	3	[3]
Splenitis	6	0.4	4	0.6	2	0.3		0.0		1			3		1	1	

Morphologic diagnosis	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric	References
	n	%	n	%	n	%	n	%							
Ulcer	6	0.4	3	0.4	3	0.5		0.0			1	3	1	1	[26, 41, 42]
Arthritis	5	0.4	1	0.1	4	0.6		0.0				1	1	3	[65, 108]
Conjunctivitis	5	0.4	1	0.1	4	0.6		0.0		1		1	1	2	[64, 145]
Cystitis	5	0.4	3	0.4	2	0.3		0.0				3	1	1	
Depletion	5	0.4	2	0.3	3	0.5		0.0		2	1	2			[2, 146, 147]
Lipoma	5	0.4	1	0.1	4	0.6		0.0					3	2	[70, 148]
Nephrocalcinosis	5	0.4	4	0.6	1	0.2		0.0				3	2		
Regeneration	5	0.4	5	0.7		0.0		0.0				1	4		[149–151]
Tracheitis	5	0.4	2	0.3	3	0.5		0.0				1	4		
Glomerulosclerosis	4	0.3	2	0.3	2	0.3		0.0					2	2	[97]
Pancreatitis	4	0.3		0.0	4	0.6		0.0					1	3	
Pleuritis	4	0.3	1	0.1	3	0.5		0.0		2		1	1		
Rhinitis	4	0.3	3	0.4	1	0.2		0.0			1	1		2	[78, 152]
Tonsillitis	4	0.3	1	0.1	3	0.5		0.0		2	1		1		
Urethritis	4	0.3	3	0.4	1	0.2		0.0				3	1		[145, 153, 154]
Arteritis	3	0.2	2	0.3	1	0.2		0.0					3		
Cataract	3	0.2	2	0.3	1	0.2		0.0					1	2	
Cholelithiasis	3	0.2	1	0.1	2	0.3		0.0						3	[53]
Dehydration	3	0.2	2	0.3	1	0.2		0.0			1	2			
Endocarditis	3	0.2	1	0.1	2	0.3		0.0				2	1		[26]
Hematoma	3	0.2	2	0.3	1	0.2		0.0				1	2		
Hydrocephalus	3	0.2	2	0.3	1	0.2		0.0	1				2		[11]
Intussusception	3	0.2	3	0.4		0.0		0.0				2	1		
Lymphosarcoma	3	0.2		0.0	3	0.5		0.0						3	[83, 155]
Metritis	3	0.2		0.0	3	0.5		0.0			1		2		
Myositis	3	0.2	1	0.1	2	0.3		0.0				1	2		
Obese	3	0.2	1	0.1	2	0.3		0.0					2	1	
Pyelonephritis	3	0.2		0.0	3	0.5		0.0	1			2			

Morphologic diagnosis	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile		Adult	Middle Age		Geriatric	References
	n	%	n	%	n	%	n	%			n	%		n	%		
Vasculitis	3	0.2	2	0.3	1	0.2		0.0		1			1	1		n	
Cellulitis	2	0.1	2	0.3		0.0		0.0					1	1			
Cholangiohepatitis	2	0.1	1	0.1	1	0.2		0.0						1		1	
Concretions	2	0.1	2	0.3		0.0		0.0						1		1	
Dilatation	2	0.1	1	0.1	1	0.2		0.0		1				1			[156, 157]
Dystrophy	2	0.1	1	0.1	1	0.2		0.0						2			
Epicarditis	2	0.1	1	0.1	1	0.2		0.0			1			1			
Erythrophagocytosis	2	0.1	1	0.1	1	0.2		0.0			1			1			
Extramedullary hematopoiesis	2	0.1		0.0	2	0.3		0.0						2			
Gastritis	2	0.1	1	0.1	1	0.2		0.0						1		1	[158]
Glossitis	2	0.1	1	0.1	1	0.2		0.0						1		1	
Granuloma	2	0.1	1	0.1	1	0.2		0.0		1				1			[2, 64]
Granulosa cell tumor	2	0.1		0.0	2	0.3		0.0						2			[3]
Histiocytosis	2	0.1	2	0.3		0.0		0.0					1	1			
Hydrocele	2	0.1	2	0.3		0.0		0.0						1		1	
Hypertrophy	2	0.1	1	0.1	1	0.2		0.0					1	1			[3, 27, 34, 81, 159]
Nephrosis	2	0.1	1	0.1	1	0.2		0.0			2						[68, 160]
Placenta abrupta	2	0.1	2	0.3		0.0		0.0	2								
Placentitis	2	0.1		0.0		0.0	2	15.4	2								
Pneumothorax	2	0.1		0.0	2	0.3		0.0			1			1			
Proctitis	2	0.1		0.0	2	0.3		0.0						2			
Sialadenitis	2	0.1		0.0	2	0.3		0.0						2			
Splenomegaly	2	0.1	2	0.3		0.0		0.0					2				[161]
Spondylosis	2	0.1		0.0	2	0.3		0.0								2	[104]
Telangiectasis	2	0.1	2	0.3		0.0		0.0						2			[13]
Trichobezoar	2	0.1	1	0.1	1	0.2		0.0					1			1	[38]
Urolithiasis	2	0.1	2	0.3		0.0		0.0						2			
Abscess	1	0.1		0.0	1	0.2		0.0						1			[162–165]

Morphologic diagnosis	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric	References
	n	%	n	%	n	%	n	%							
	1	0.1	1	0.1		0.0		0.0					1		[139]
Adenitis	1	0.1	1	0.1		0.0		0.0						1	
Anthracosis	1	0.1	1	0.1		0.0		0.0							
Arteriopathy	1	0.1	1	0.1		0.0		0.0					1		[9]
Brenner tumor	1	0.1		0.0	1	0.2		0.0					1		
Bronchitis	1	0.1		0.0	1	0.2		0.0					1		[59]
Choristoma	1	0.1		0.0	1	0.2		0.0					1		
Choroiditis	1	0.1	1	0.1		0.0		0.0	1						
Cleft	1	0.1	1	0.1		0.0		0.0	1						[151, 166–168]
Defect	1	0.1		0.0		0.0	1	7.7	1						
Detached retina	1	0.1	1	0.1		0.0		0.0						1	
Dicidua	1	0.1		0.0	1	0.2		0.0			1				
Endometriosis	1	0.1		0.0	1	0.2		0.0						1	[82]
Foreign body	1	0.1		0.0	1	0.2		0.0					1		[41, 169–171]
Fracture	1	0.1	1	0.1		0.0		0.0		1					[172, 173]
Gastrointestinal stromal tumor	1	0.1		0.0	1	0.2		0.0						1	[71, 72]
Gingivitis	1	0.1		0.0	1	0.2		0.0				1			[1, 26]
Goiter	1	0.1		0.0	1	0.2		0.0					1		
Hemangioma	1	0.1	1	0.1		0.0		0.0					1		
Hepatomegaly	1	0.1		0.0	1	0.2		0.0					1		[5, 59]
Hydronephrosis	1	0.1	1	0.1		0.0		0.0				1			[68, 160]
Hyperkeratosis	1	0.1	1	0.1		0.0		0.0			1				
Icterus	1	0.1		0.0	1	0.2		0.0					1		
Lipofuscinosis	1	0.1		0.0	1	0.2		0.0						1	
Lymphadenopathy	1	0.1		0.0	1	0.2		0.0					1		[174]
Mastitis	1	0.1		0.0	1	0.2		0.0				1			
Myelopathy	1	0.1	1	0.1		0.0		0.0						1	
Myxoma	1	0.1	1	0.1		0.0		0.0				1			[76]
Nephropathy	1	0.1		0.0	1	0.2		0.0						1	

Morphologic diagnosis	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile		Adult	Middle Age		Geriatric	References
	n	%	n	%	n	%	n	%			n	%		n	%		
Neuropathy	1	0.1	1	0.1		0.0		0.0					1			n	[162]
Omphalitis	1	0.1		0.0	1	0.2		0.0		1							
Osteomyelitis	1	0.1		0.0	1	0.2		0.0								1	[33]
Osteopenia	1	0.1		0.0	1	0.2		0.0			1						[108]
Panophthalmitis	1	0.1		0.0	1	0.2		0.0			1						
Parakeratosis	1	0.1	1	0.1		0.0		0.0			1						
Periarteritis nodosa	1	0.1	1	0.1		0.0		0.0						1			
Pheochromocytoma	1	0.1	1	0.1		0.0		0.0						1			
Scoliosis	1	0.1	1	0.1		0.0		0.0								1	
Septicemia	1	0.1		0.0	1	0.2		0.0								1	[21]
Spermatidic giant cells	1	0.1	1	0.1		0.0		0.0						1			
Spongiosis	1	0.1		0.0	1	0.2		0.0					1				
Squamous cell carcinoma	1	0.1	1	0.1		0.0		0.0								1	
Steatitis	1	0.1	1	0.1		0.0		0.0					1				
Teratoma	1	0.1		0.0	1	0.2		0.0						1			
Vacuolization	1	0.1		0.0	1	0.2		0.0						1			[120]
Vaginitis	1	0.1		0.0	1	0.2		0.0						1			[3]
Total	1362	100.0	689	100.0	660	100.0	13	100.0	65	73	78		288	618		240	

Table 3

Percentage of lesions in each age group by etiology.

Etiology	Total		Male		Female		Unknown		Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric
	n	%	n	%	n	%	n	%	%	%	%	%	%	%
Undetermined	525	38.5	237	34.4	278	42.1	10	76.9	60.0	58.9	37.2	37.5	39.5	25.8
Degenerative	281	20.6	179	26.0	102	15.5		0.0	0.0	1.4	2.6	17.4	23.6	34.2
Physiologic	209	15.3	114	16.5	95	14.4		0.0	15.4	5.5	14.1	17.0	17.3	11.7
Neoplastic	100	7.3	20	2.9	80	12.1		0.0	0.0	0.0	10.3	3.5	7.4	15.0
Parasitic	72	5.3	40	5.8	32	4.8		0.0	0.0	6.8	7.7	5.6	5.5	4.6
Bacterial	55	4.0	29	4.2	26	3.9		0.0	1.5	8.2	19.2	5.9	1.8	2.1
Traumatic	39	2.9	26	3.8	13	2.0		0.0	15.4	13.7	2.6	4.5	0.3	0.8
Mycotic	23	1.7	12	1.7	11	1.7		0.0	0.0	1.4	0.0	4.5	1.1	0.8
Protozoal	16	1.2	11	1.6	5	0.8		0.0	0.0	0.0	2.6	1.0	1.3	1.3
Viral	15	1.1	11	1.6	4	0.6		0.0	0.0	4.1	1.3	1.0	1.1	0.4
Physical	11	0.8	4	0.6	7	1.1		0.0	0.0	0.0	2.6	0.7	0.3	2.1
Congenital	11	0.8	4	0.6	4	0.6	3	23.1	7.7	0.0	0.0	0.3	0.5	0.8
Foreign Body	5	0.4	2	0.3	3	0.5		0.0	0.0	0.0	0.0	1.0	0.2	0.4
Total	1362	100.0	689	100.0	660	100.0	13	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Table 4

Chimpanzee lesions by system and organ in descending order of occurrence.

System/Organ	Total		System	Male	Female	Unknown	Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric
	n	%		n	n							
Gastrointestinal	350	25.7	100.0	170	180		2	14	20	67	178	69
Liver	113	8.3	32.3	58	55		1	4	3	25	65	15
Colon	66	4.8	18.9	35	31			5	4	15	29	13
Cecum	22	1.6	6.3	13	9				2	2	14	4
Pancreas	22	1.6	6.3	9	13			1		4	8	9
Small intestine	19	1.4	5.4	11	8			1		6	9	3
Gall bladder	18	1.3	5.1	8	10			1		1	7	9
Peritoneal cavity	18	1.3	5.1	7	11					5	12	1
Esophagus	12	0.9	3.4	3	9			1	1		8	2
Oral cavity	11	0.8	3.1	6	5		1		7	2	1	
Stomach	11	0.8	3.1	4	7				1	3	4	3
Appendix	8	0.6	2.3	3	5				1		6	1
Ileum	7	0.5	2.0	4	3					2	3	2
Duodenum	5	0.4	1.4	2	3						2	3
Salivary gland	5	0.4	1.4	2	3			1			4	
Rectum	4	0.3	1.1	1	3				1		2	1
Mesentery	3	0.2	0.9	1	2					1	2	
Tongue	3	0.2	0.9	1	2						1	2
Large intestine	2	0.1	0.6	2							1	1
Gingiva	1	0.1	0.3		1					1		
Cardiovascular	297	21.8	100.0	182	113	2	2	5	5	75	143	67
Heart	173	12.7	58.2	116	56	1	1	3	4	49	87	29
Artery	31	2.3	10.4	13	18					5	16	10
Peritoneal cavity	18	1.3	6.1	12	6					5	7	6
Thoracic cavity	17	1.2	5.7	11	5	1	1			5	7	4
Pericardial sac	14	1.0	4.7	9	5				1	5	6	2

System/Organ	Total		System %	Male		Female		Unknown	Perinatal		Infant	Juvenile		Adult	Middle Age		Geriatric	
	n	%		n	%	n	%		n	%		n	%	n	%	n	%	n
Aorta	13	1.0	4.4	6		7										9		4
Brain	7	0.5	2.4	2		5										1		6
Whole body	7	0.5	2.4	3		4										6		1
Kidney	4	0.3	1.3	2		2					1					1		2
Lung	4	0.3	1.3	3		1					1			2		1		
Rectum	2	0.1	0.7	1		1												2
Scrotum	2	0.1	0.7	2										2				
Adrenal	1	0.1	0.3			1												1
Cerebellum	1	0.1	0.3	1										1				
Colon	1	0.1	0.3			1										1		
Diaphragm	1	0.1	0.3	1												1		
Skin/Subcutis	1	0.1	0.3			1								1				
Urogenital	215	15.8	100.0	78		127		10	37		7	5	31			94		41
Kidney	80	5.9	37.2	37		43			3		6	3	15			40		13
Uterus	42	3.1	19.5			42						2	5			19		16
Whole body	30	2.2	14.0	12		11		7	29							1		
Ovary	16	1.2	7.4			16								1		12		3
Testicle	9	0.7	4.2	9										1		6		2
Prostate	8	0.6	3.7	8										1		3		4
Urinary bladder	7	0.5	3.3	4		3							3			3		1
Placenta	5	0.4	2.3	2				3	5									
Urethra	5	0.4	2.3	4		1								3		2		
Vagina	4	0.3	1.9			4								1		3		
Oviduct	3	0.2	1.4			3										2		1
Peritoneal cavity	3	0.2	1.4	1		2										3		
Cervix	1	0.1	0.5			1												1
Epididymis	1	0.1	0.5	1										1				
Umbilical cord	1	0.1	0.5			1					1							

System/Organ	Total		System %	Male		Female		Unknown	Perinatal		Infant	Juvenile		Adult	Middle Age		Geriatric	
	n	%		n	%	n	%		n	%	n	n	%	n	n	%	n	%
Respiratory	158	11.6	100.0	86	72				7	21		16	36	65	13			
Lung	126	9.3	79.7	70	56				7	19		12	30	48	10			
Air sac	14	1.0	8.9	10	4							2	2	9	1			
Nasal cavity	5	0.4	3.2	3	2							1	2		2			
Pleura	5	0.4	3.2	1	4					2			1	2				
Trachea	5	0.4	3.2	2	3								1	4				
Thoracic cavity	3	0.2	1.9		3							1		2				
Lymphatic/Hematopoietic	128	9.4	100.0	64	64				5	12		15	39	44	13			
Lymph node	74	5.4	57.8	34	40				1	9		12	23	22	7			
Spleen	36	2.6	28.1	22	14				2	1		2	14	13	4			
Bone marrow	7	0.5	5.5	5	2								1	4	2			
Thymus	7	0.5	5.5	2	5				2	1			1	3				
Tonsil	4	0.3	3.1	1	3					1		1		2				
Integumentary	54	4.0	100.0	24	30					1		10	15	22	6			
Skin/Subcutis	51	3.7	94.4	24	27					1		10	14	21	5			
Mammary gland	3	0.2	5.6		3								1	1	1			
Endocrine	53	3.9	100.0	24	29				2	1			8	32	10			
Pituitary	24	1.8	45.3	10	14								4	12	8			
Adrenal	15	1.1	28.3	9	6				2	1			4	7	1			
Thyroid	9	0.7	17.0	4	5									8	1			
Islets of Langerhans	3	0.2	5.7	1	2									3				
Parathyroid	1	0.1	1.9		1									1				
Whole body	1	0.1	1.9		1									1				
Nervous	43	3.2	100.0	24	18			1	7	10		2	4	16	4			
Brain	29	2.1	67.4	14	14			1	4	8		2	3	10	2			
Meninges	7	0.5	16.3	3	4				3	1				3				
Choroid plexus	3	0.2	7.0	3						1				2				
Spinal cord	3	0.2	7.0	3									1		2			

System/Organ	Total		System %	Male n	Female n	Unknown n	Perinatal n	Infant n	Juvenile n	Adult n	Middle Age n	Geriatric n
	n	%										
Nerve	1	0.1	2.3	1							1	
Musculoskeletal	31	2.3	100.0	17	14		2	1	2	7	12	7
Skeletal muscle	14	1.0	45.2	10	4				1	5	8	
Bone	7	0.5	22.6	3	4		1	1	1			4
Joint	6	0.4	19.4	2	4					1	2	3
Adipose tissue	1	0.1	3.2		1						1	
Diaphragm	1	0.1	3.2	1							1	
Head	1	0.1	3.2		1		1					
Mesentery	1	0.1	3.2	1						1		
Multisystem	20	1.5	100.0	14	6		1		2	5	8	4
Special senses	13	1.0	100.0	6	7			1	1	1	4	6
Eye	7	0.5	53.8	5	2				1		2	4
Conjunctiva	6	0.4	46.2	1	5			1		1	2	2
Total	1362			689	660	13	65	73	78	288	618	240

Table 5

Sex-morphology combinations with significant relative risks.

Morphology	Sex	P value	Risk
Cardiomyopathy	M	3.90E-05	2.99
Cardiomyopathy	F	3.90E-05	0.33
Leiomyoma	F	1.70E-06	22.97
Leiomyoma	M	1.70E-06	0.04

Table 6

Age-morphology combinations with significant relative risks.

Morphology	Age Group	P value	Risk
Congestion	Perinatal	1.80E-06	10.67
Hemorrhage	Perinatal	< 1.00E-07	12.38
Hemorrhage	Infant	5.82E-05	5.23
Pneumonia	Infant	2.94E-05	5.75
Papilloma	Juvenile	1.50E-06	14.30
Hemosiderosis	Middle Age	3.20E-06	3.33