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Natural Mortality and Cause of Death Analysis of the Captive Chimpanzee (*Pan troglodytes*): A 35 Year Review

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Abstract

Background—We present the spontaneous causes of mortality for 137 chimpanzees (*Pan troglodytes*) over a 35 year period.

Methods—A records review of the pathology database was performed and a primary cause of mortality was determined for each chimpanzee.

Results—The most common causes of mortality were: cardiomyopathy (40% of all mortalities); stillbirth/abortion; acute myocardial necrosis; chimpanzee-induced trauma; amyloidosis; and pneumonia. Five morphologic diagnoses accounted for 61% of mortalities: cardiomyopathy; hemorrhage; acute myocardial necrosis; amyloidosis; and pneumonia. The most common etiologies were degenerative, undetermined, bacterial, traumatic, and neoplastic. The cardiovascular system was most frequently involved, followed by the gastrointestinal, respiratory, and multi-systemic diseases.

Conclusions—Degenerative diseases were the primary etiological cause of mortality of the adult captive chimpanzee population. Chimpanzee-induced trauma was the major etiological cause of mortality among the perinatal and infant population. This information should be a useful resource for veterinarians and researchers working with chimpanzees.

Keywords

Chimpanzee; Mortality; Lesions; Pathology

1. Introduction

Captive chimpanzees are now considered to be an endangered species, and thus, their use in research has essentially ceased [1]. Due to the moratorium on breeding NIH owned chimpanzees that was enacted in 1995, the captive population is becoming more aged [2]. As the captive population ages, increased knowledge of the natural pathology of this species is required so that veterinarians can continue to provide high quality medical care to these

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animals. Also, information about the natural pathology in chimpanzees provides crucial insights into the comparative pathology in humans, as well evolutionary aspects of certain disease pathology.

Although chimpanzees have long been used in human biomedical research, there is scant literature available regarding the natural pathology and primary cause of mortality in captive chimpanzees. Some data on specific diseases and causes of death in chimpanzees is available in the form of individual case reports and small case series; however, a comprehensive study of spontaneous causes of mortality in captive chimpanzees has not been published. Published studies of spontaneous causes of death include: cardiac disease [3–7], amyloidosis [8], nephrotic syndrome [9], diabetes mellitus [10], Chagas disease (*Trypanosoma cruzi*) [11], cerebral vascular lesions [12, 13], and neoplasia including leiomyoma [14], hepatocellular carcinoma [15], myelolipoma [15], and gastrointestinal stromal tumors [16, 17], among others [18].

In a relatively detailed study at by Hubbard *et al* [19], the authors documented the most prevalent/important disease problems in 181 chimpanzees that died/necropsied between 1967 to 1989 at the Southwest Foundation for Biomedical Research [19]. However, the above study documented only the most important diseases based upon available information, and identified the major causes of death as respiratory, cardiovascular, central nervous system, chimpanzee-induced trauma, and reproductive [19]. In the same study, the major causes of death from 1982 to 1989 (data from computerized records) were cardiovascular, chimpanzee-induced trauma, and respiratory [19]. There have been two published studies of group mortality involving free ranging East African Chimpanzees (*Pan troglodytes schwinfurthii*) [20, 21]. A 2011 study in Gombe National Park, Tanzania, Africa examined 11 chimpanzees over a six year period and reported necropsy and histopathology findings [20]. Although the sample size was relatively small (n = 11); trauma was identified as the primary cause of death, and cardiac lesions were commonly noted [20]. A 2013 study in Kibale National Park, Uganda, Africa included survival curves and mortality rates based on age and sex, however, the cause of death was not addressed [22].

We report a comprehensive documentation of spontaneous causes of mortality (primary cause of death or reason for euthanasia) for 137 chimpanzees (*Pan troglodytes*) that died naturally or were humanely euthanized 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 published documentation of chimpanzee mortality, and should be an extremely helpful source of information for veterinarians, care givers, and researchers working with chimpanzees.

2. Materials & Methods

2.1 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. 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 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.

2.2 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 −80ºF, 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.

2.3 Records

A computer search of the pathology database for all chimpanzee necropsies 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 hepatitis and HIV infection. The HCV, HBV, 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.

A primary cause of mortality (PCM: cause of death or reason for euthanasia) was determined for each chimpanzee. Specific criteria were developed to determine the PCM: (1) stillborn animals were considered as separate cases from the dam and were given the age of zero; (2) animals that had a PCM of hemorrhage were categorized by the affected organ; and (3) lesions that affected multiple organs or the body as a whole, such as disseminated hemorrhage, lymphosarcoma, or amyloidosis were categorized as multisystem; and (4) cardiomyopathy, defined as the presence of multifocal to coalescing areas of fibrosis, disorganization of cardiac myofibers in the areas of fibrosis, irregular size and nucleation of

individual cardiac myofibers, and variable necrosis, mineralization, and inflammation [4–6, 23], was characterized as a degenerative disease.

2.4 Data Analysis

Animals were categorized by sex and separated into age groups to categorize PCM by life stages. 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 [24]. Middle age was defined as the latter half of the interval between the start of adulthood and the start of geriatric age [24]. The lower limit of geriatric age was chosen to be 85% of total expected lifespan [24, 25] and to coincide with a prior survey of geriatric reproductive tract lesions in chimpanzees [26].

3. Results

A total of 208 chimpanzees (M=113; F=85; Undetermined (U)=10) that died of natural causes or were humanely euthanized were identified. A PCM could not be determined due to missing or incomplete records for 42 chimpanzees (M=20, F=19, U=3). A total of 29 stillbirths/abortions (M=12, F=10, U=7) were identified, however records were generally incomplete or missing and it was not possible to definitively determine the age of gestation or the underlying cause of the stillbirth/abortion for most cases. A PCM was only determined for eight; three were associated with placenta abrupta, two with dystocia, one with an unspecified congenital heart defect, one with a cleft palate, and one with a suppurative pyelonephritis involving the fetus. Neither the 29 stillbirth/abortion cases nor the 42 cases with missing or incomplete records are included in the mortality evaluations or tables that follow.

A PCM could be determined for 137 (M=81, F=56) chimpanzees that died naturally or were humanely euthanized over the 35 year period. The population demographics are shown in Table 1. There were 27 chimpanzees chronically infected with HCV (5 adult, 21 middle age, and 1geriatric), 5 chronically infected with HBV (all geriatric), and 8 chronically infected with HIV (7 middle age, and 1geriatric). The numbers above include 3 middle age male chimpanzees that were chronically infected with both HCV and HIV.

Table 2 presents the morphologic diagnoses resulting in mortality in order by frequency of occurrence (total number and percentage of deaths), lists the numbers and percentages of males and females, and lists the numbers of chimpanzees in each age group. The five most common morphologic diagnoses accounted for 62% of all mortalities: cardiomyopathy (n = 55, 40.1%); hemorrhage (n = 10, 7.3%); acute myocardial necrosis (n = 7, 5.1%); amyloidosis (n = 7, 5.1%); and pneumonia (n = 5, 3.6%).

Table 3 presents the etiologies resulting in mortality in order by frequency of occurrence (total number and percentage of deaths) and lists the numbers of male or female, and the numbers of chimpanzees in each age group for each etiology. The most common etiologies were: degenerative (n = 68, 49.6%); undetermined (n = 28, 20.04%); bacterial (n = 12,

8.8%); traumatic (n = 8, 5.8%); and neoplastic (n = 7, 5.1%). Trauma related PCM was almost exclusively seen in perinatal and infant animals. Bacterial related PCM was seen across all age groups, but was the most frequent PCM in juveniles. PCM in adult, middle age, and geriatric chimpanzees most often resulted from degenerative etiologies. PCM resulting from bacterial and mycotic etiologies were most often seen in adults and juveniles (bacterial); PCM resulting from physiologic and neoplastic etiologies were most often seen in middle aged chimpanzees.

Table 4 presents the body systems and organs with lesions resulting in mortality in order by frequency of occurrence (total number and percentage of deaths), lists the percentages attributable to each organ within the system, lists the numbers of male or female, and lists the numbers of chimpanzees in each age group. The cardiovascular system was most frequently involved (n = 70, 51.1%), followed by the gastrointestinal (n = 19, 13.9%), respiratory (n = 13, 9.5%), multi-systemic diseases (n = 12, 8.8%), urogenital (n = 10, 7.3%), nervous (n = 7, 5.1%), musculoskeletal (n = 3, 2.2%), integumentary (n = 2, 1.5%), and endocrine (n = 1, 0.7%).

3.1 Cardiovascular system

Lesions involving the cardiovascular system accounted for half of all PCM, accounting for 70 of 137 (51.1%) deaths. Cardiovascular-related deaths were typically seen in middle aged (35 of 70, 50.0%), adult (20 of 70, 28.6%), and geriatric (14 of 70, 20.0%) animals; males were overrepresented (50 of 70, 71.4%). Cardiovascular related mortality could be subdivided into lesions that affected the heart (63 of 70, 90.0%) and lesions that affected the vasculature (7 of 70, 10.0%).

Chronic cardiomyopathy accounted for nearly all heart related mortality (55/63, 87.3%), and accounted for the overrepresentation by male animals with a 4:1 male to female ratio. Gross lesions associated with chronic cardiomyopathy included hydropericardium (n = 25, 45.5%), hydrothorax (n = 22, 40.0%), scrotal edema (n = 17, 30.9%) and ascites (n = 10, 18.2%). Affected hearts were generally enlarged (n = 20, 36.4%), pale (n = 17, 30.9%), rounded (n = 8, 14.5%), hemorrhagic (n = 4, 7.3%), and thick- or thin-walled (n = 3 each, 5.5%). The liver was frequently enlarged (n = 15, 27.3%) or occasionally small (n = 3, 5.5%). Histologic findings included hemosiderosis in the lung (n = 32, 58.2%), liver (n = 21, 38.2%), and spleen (n = 10, 18.2%), as well as pulmonary edema (n = 25, 45.5%), and hepatic fibrosis (n = 15, 27.3%). Five (9.1%) animals had no additional findings other than the histologic lesions of cardiomyopathy; three of these were specifically noted to be instances of “sudden death”. There were seven (M=4; F=3) cases of acute myocardial necrosis. A thrombus was identified in the coronary artery of one of these animals. One animal was described to have a microangiopathy, characterized by thickening of the walls of small vessels. No vascular lesions were described in the other five animals. There was one case of myocarditis due to *Trypanosoma cruzi* involving an adult male.

Mortality arising from vascular lesions was almost exclusively seen in female animals (M=1; F=6). Four of these presented clinically as cerebrovascular accidents (stroke), including three geriatric animals with cerebral, cerebellar, or brainstem infarcts secondary to atherosclerosis, and a middle age female chimpanzee with vasculitis and thrombosis of a

cerebral artery. The remaining mortalities resulting from vascular lesions were, a middle age female chimpanzee with thrombosis of the mesenteric artery, an adult female chimpanzee with thrombosis of the pulmonary artery, and a geriatric female chimpanzee with thrombosis of the left atrium.

3.2 Gastrointestinal system

Gastrointestinal-related deaths accounted for 19 of 137 (13.9%) PCM and were mostly seen in middle aged (8 of 19, 42.1%), geriatric (n = 5 of 19, 26.3%), and adult (n = 5 of 19, 26.3%) animals, with females outnumbering males (M=8; F=11). Lesions of the intestinal tract accounted for roughly half of gastrointestinal-related PCM (10 of 19, 52.6%), and included three cases of intussusception (all involving the ileum), three of enteritis, three of colitis, and one animal with a duodenal trichobezoar. Hepatic lesions accounted for roughly 1/3 of gastrointestinal-related PCM (6 of 19, 31.6%) and were due to four cases of hepatocellular carcinoma, one case of hepatic amyloidosis, and one hematoma of the liver. Of the four animals with a PCM of hepatocellular carcinoma, three were chronically infected with HCV and the other was chronically infected with HBV. A statistical correlation could not be demonstrated due to the few animals with hepatocellular carcinoma and large number of animals with unknown viral status. However, this data does suggest the need to identify and regularly monitor chronically infected chimpanzees. Other gastrointestinal-related mortality was due to a combination of cholecystitis and cholelithiasis associated with *Escherichia coli* in a geriatric female, a case of sialadenitis, leading to cellulitis and neurologic involvement in a middle age female, and diffuse pancreatic necrosis in an infant male.

3.3 Respiratory system

Respiratory-related deaths accounted for 13 of 137 (9.5%) deaths and were seen in all but geriatric animals, with females outnumbering males (M=5; F=8). The most common PCM (4 of 13, 30.8%) was pneumonia. Three were due to *Streptococcus pneumoniae*, all in young animals: one perinatal, two infants, and one juvenile. There was one case of pneumonia due to adenovirus with *Streptococcus pneumoniae* in an infant. Acute pulmonary hemorrhage and edema (4 of 13, 30.8%) was also a common PCM. Two of these involved infants, and were likely related to poor mothering; another case was in a juvenile, associated with rhabdomyolysis. The other occurred in a middle aged female. There were 2 deaths due to airsacculitis. One involved a juvenile; both *Streptococcus pneumoniae* and *Micrococcus* spp. were cultured. The other was in an adult; both *Staphylococcus aureus* and *Pseudomonas aeruginosa* were cultured. One animal died of hypoxia resulting from severe nasal myxoid polyps; the animal failed to recover following sedation. There was one case of atelectasis, and one of pneumothorax.

3.4 Multisystem disease

Multi-systemic lesions accounted for 12 of 137 (8.8%) PCM and were generally seen in adult (7 of 12, 58.3%) and middle aged (3 of 12, 25.0%) animals, with a 2:1 male:female ratio (M=8; F=4). Disseminated amyloidosis and disseminated coccidioidomycosis were seen in four (33.3%) animals each. Although amyloidosis most often presented as a multisystem disease, there were also three cases of mortality arising from amyloidosis

restricted to the liver, kidney, or islets of Langerhans; these cases are included in their respective systems. There were two cases of disseminated hemorrhage; one attributed to trauma in an adult male and one attributed to poor maternal care in a perinatal male. There was one case each of hemolytic anemia in an adult animal and of disseminated lymphosarcoma in a geriatric animal.

3.5 Urogenital system

PCM resulting from urogenital lesions accounted for 10 of 137 (7.3%) deaths and were generally seen in middle aged (7 of 10, 70.0%) animals, with a 1:2 male:female ratio (M=3; F=7). Renal lesions (9 of 10, 90.0%) accounted for almost all these cases. Glomerulonephritis was the most common (4 of 9, 44.4%) lesion and the three male animals that died of urogenital lesions were all middle aged males with glomerulonephritis. Pyelonephritis (n = 2, 22.2%) was seen in adult females and associated with *Escherichia coli*. One middle aged female had nephritis, another had renal amyloidosis, and one infant died as a result of septicemia resulting from omphalitis. Non-renal PCM were a middle aged female euthanized for an inoperable uterine leiomyoma and a case of septicemia arising from the umbilicus in an infant female.

3.6 Nervous system

PCM related to the nervous system accounted for 7 of 137 (5.1%) deaths and were generally seen in perinatal (3 of 7, 42.9%) and juvenile (2 of 7, 28.6%) animals; males and females were generally equally represented (M=3; F=4). Hemorrhages were the most frequent lesion (4 of 7, 57.1%). Three of these were in perinatal animals and attributed to trauma resulting from poor mothering. The other was a middle aged female with hemorrhages secondary to seizures. Meningoencephalitis (3 of 7, 42.9%) was generally observed in younger animals: two juvenile and one infant. *Klebsiella pneumoniae* and *Staphylococcus haemolyticus* were each cultured once.

3.7 Musculoskeletal system

Musculoskeletal system PCM accounted for 3 of 137 (2.2%) deaths. Included were a fracture (site not specified) in an infant male, a large organizing hematoma associated with necrotic bone involving the forearm of an adult male, and a case of osteomyelitis due to Beta-*Streptococcus* and *Escherichia coli* that resulted in a fracture in a geriatric female.

3.8 Integumentary system

PCM due to integumentary lesions were reported in just two middle aged male animals. One had cellulitis caused by *Staphylococcus aureus*, resulting in septicemia, and the other had severe dermatitis that was refractory to treatment from which both *Staphylococcus aureus* and *Escherichia coli* were cultured.

3.9 Endocrine system

There was one case of endocrine related PCM due to pancreatic islet cell amyloidosis that led to end-stage diabetes in a middle aged female.

4. Discussion

We document the primary causes of natural mortality (cause of death or reason for euthanasia) for 137 chimpanzees (*Pan troglodytes*) that died naturally or were humanely euthanized over a 35 year period (1980 to 2014). The most common causes of mortality were cardiomyopathy (40% of all mortalities), stillbirth/abortion, acute myocardial necrosis, chimpanzee induced trauma, amyloidosis, and pneumonia. The five most common morphologic diagnoses which accounted for 61% of all mortalities were cardiomyopathy, hemorrhage, acute myocardial necrosis, amyloidosis, and pneumonia. PCM most often involved the cardiovascular (51%), gastrointestinal (14%), and respiratory (9%) systems, multisystem disease (9%), or the urogenital (7%) system. Degenerative diseases were the most common identified etiological cause of mortality (50%), followed by diseases of undetermined etiology (20%), bacterial (9%), traumatic (6%), and neoplastic (5%).

A previous study of chimpanzee mortality at this facility by Hubbard *et al* showed mortality was most often related to lesions involving the reproductive, cardiovascular, and respiratory systems, and chimpanzee-induced trauma [19]. Although our results are similar in several respects (cardiomyopathy, respiratory disease (particularly *Streptococcus pneumoniae* infection), stillbirth/abortion, and chimpanzee-induced trauma (in young animals) remain significant causes of mortality), there are also differences. Mortality from degenerative diseases were much more common in the current study, accounting for 50% of mortality; which is likely a reflection of the older age of the animals within the colony. Gastrointestinal system related mortality was second to cardiovascular system mortality in the present study, where it was rare in the Hubbard *et al* study [19].

Lesions of the cardiovascular system accounted for over 50% of all mortality, which is consistent with previous reports of heart disease as the #1 cause of mortality among captive chimpanzee populations [5, 6, 19, 23, 27, 28]. The majority of the cardiovascular cases in this report were classified as cardiomyopathy, a poorly understood entity, characterized by interstitial myocardial fibrosis. Chimpanzee cardiomyopathy is more common in males and manifests clinically as cardiac arrhythmias, sudden death, or chronic heart failure [3, 5, 6, 19, 23, 25, 27, 29]. The gastrointestinal system was the second most common affected system (14%), including four cases of hepatocellular carcinoma, and three cases each of intussusception, enteritis, and colitis.

Degenerative disease (50%) was the most common etiological cause of mortality in this study, which is consistent with the demographic profile of our cases (over 86% adult, middle age, or geriatric). Approximately 20% of cases had no identified primary etiological cause of mortality. Bacterial disease (9 %) was the second most common identified etiologic cause of mortality followed by trauma (6%) and neoplastic (5%). In a previous study of wild chimpanzee by Terio et al, 11 chimpanzees were examined over a six year period in Gombe National Park, Tanzania, Africa [20]. Conspecific trauma was identified as the primary cause of death in adult animals [20]. Although chimpanzee-induced trauma was also observed in our study, it was only common in very young (perinatal and infant) animals and generally attributed to poor mothering skills. This difference may result from the efforts of behavioral staff to identify compatible animals when selecting for group housing [30].

Overall, the results from this study indicate that cardiovascular system is the most commonly affected organ system in captive chimpanzee mortality, with majority of cases being affected by cardiomyopathy. Degenerative diseases were the primary etiological cause of mortality of the adult captive chimpanzee population, and chimpanzee-induced trauma was the major etiological cause of mortality among the perinatal and infant population. This information should be a useful resource for veterinarians, care givers, and researchers working with chimpanzees.

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Table 1

Total number of animals with a primary cause of mortality (PCM) by age-group, sex, and viral status.

Age Group	Total	Male	Female	HCV			HBV			HIV		
				Chronic	Negative	Undetermined	Chronic	Negative	Undetermined	Chronic	Negative	Undetermined
Perinatal	5	2	3	0	0	5	0	0	5	0	0	5
Infant	8	3	5	0	0	8	0	0	8	0	0	8
Juvenile	6	6	0	0	3	3	0	3	3	0	2	4
Adult	37	26	11	5	13	19	0	16	21		10	27
Middle Age	60	38	22	21	23	16	0	37	23	7	22	31
Geriatric	21	6	15	1	12	8	5	6	10	1	7	13
Total	137	81	56	27	51	59	5	62	70	8	41	85

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Table 2

Primary causes of mortality by sex and age-group.

Morphologic diagnosis	Total		Male		Female		Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric	Reference
	n	%	n	%	n	%	n	n	n	n	n	n	
Cardiomyopathy	55	40.1	44	54.3	11	19.6	0	0	1	17	28	9	[3–7, 30]
Hemorrhage	10	7.3	5	6.2	5	8.9	4	2	1	1	2	0	[12, 31–35]
Acute myocardial necrosis	7	5.1	4	4.9	3	5.4	0	0	0	1	5	1	[11, 33, 35–43]
Amyloidosis	7	5.1	4	4.9	3	5.4	0	0	0	3	4	0	[8]
Pneumonia	5	3.6	1	1.2	4	7.1	1	2	1	1	0	0	[44–46]
Glomerulonephritis	4	2.9	3	3.7	1	1.8	0	0	0	0	4	0	[33, 47]
Carcinoma	4	2.9	1	1.2	3	5.4	0	0	0	0	3	1	[15, 48–52]
Coccidioidomycosis	4	2.9	3	3.7	1	1.8	0	0	0	3	1	0	[53]
Infarct	4	2.9	1	1.2	3	5.4	0	0	0	0	1	3	[54]
Colitis	3	2.2		0.0	3	5.4	0	0	0	2	0	1	[34]
Intussusception	3	2.2	3	3.7		0.0	0	0	0	2	1	0	
Thrombus	3	2.2		0.0	3	5.4	0	0	0	1	1	1	
Enteritis	3	2.2	2	2.5	1	1.8	0	0	0	0	2	1	[32, 55]
Meningoencephalitis	3	2.2	2	2.5	1	1.8	0	1	2	0	0	0	[56–59]
Air sacculitis	2	1.5	2	2.5		0.0	0	0	1	1	0	0	[40, 60]
Pyelonephritis	2	1.5		0.0	2	3.6	0	0	0	2	0	0	
Hematoma	2	1.5	1	1.2	1	1.8	0	0	0	1	1	0	
Omphalitis	1	0.7		0.0	1	1.8	0	1	0	0	0	0	
Atelectasis	1	0.7		0.0	1	1.8	0	0	0	0	1	0	
Cellulitis	1	0.7	1	1.2		0.0	0	0	0	0	1	0	
Leiomyoma	1	0.7		0.0	1	1.8	0	0	0	0	1	0	[30, 61–63]
Cholecystitis	1	0.7		0.0	1	1.8	0	0	0	0	0	1	
Lymphosarcoma	1	0.7		0.0	1	1.8	0	0	0	0	0	1	[64, 65]
Osteomyelitis	1	0.7		0.0	1	1.8	0	0	0	0	0	1	[66]
Pancreatic necrosis	1	0.7	1	1.2		0.0	0	1	0	0	0	0	
Fracture	1	0.7	1	1.2		0.0	0	1	0	0	0	0	[67, 68]

Morphologic diagnosis	Total		Male		Female		Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric	Reference
	n	%	n	%	n	%	n	n	n	n	n	n	
Pneumothorax	1	0.7		0.0	1	1.8	0	0	0	0	1	0	
Myocarditis	1	0.7	1	1.2		0.0	0	0	0	1	0	0	[11, 69]
Sialadenitis	1	0.7		0.0	1	1.8	0	0	0	0	1	0	
Trichobezoar	1	0.7		0.0	1	1.8	0	0	0	0	0	1	[70]
Dermatitis	1	0.7	1	1.2		0.0	0	0	0	0	1	0	
Nephritis	1	0.7		0.0	1	1.8	0	0	0	0	1	0	[71]
Chronic hemolytic anemia	1	0.7		0.0	1	1.8	0	0	0	1	0	0	
Total	137	100.0	81	100.0	56	100.0	5	8	6	37	60	21	

Table 3

Primary causes of mortality by etiology.

Etiology	Total		Male	Female	Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric
	n	%	n	n	n	n	n	n	n	n
Undetermined etiology	51	37.2	23	28	0	3	0	14	28	6
Degenerative	42	30.7	33	9	0	0	0	13	19	10
Bacterial	12	8.8	7	5	1	1	4	3	2	1
Traumatic	8	5.8	5	3	4	3	0	1	0	0
Physiologic	7	5.1	5	2	0	0	1	0	5	1
Neoplastic	7	5.1	2	5	0	0	0	0	5	2
Mycotic	4	2.9	3	1	0	0	0	3	1	0
Protozoal	2	1.5	2	0	0	0	1	1	0	0
Physical	2	1.5	1	1	0	0	0	1	0	1
Viral	1	0.7	0	1	0	1	0	0	0	0
Foreign Body	1	0.7	0	1	0	0	0	1	0	0
Total	137	100.0	81	56	5	8	6	37	60	21

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Table 4

Primary causes of mortality by system and organ.

System/Organ	Total		System	Male	Female	Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric
	n	%	%	n	n	n	n	n	n	n	n
Cardiovascular (Total)	**70**	**51.1**	**100.0**	**50**	**20**	**0**	**0**	**1**	**20**	**35**	**14**
Heart	64	46.7	91.4	49	15	0	0	1	19	33	11
Brain	4	2.9	5.7	1	3	0	0	0	0	1	3
Artery	2	1.5	2.9	0	2	0	0	0	1	1	0
Gastrointestinal (Total)	**19**	**13.9**	**100.0**	**8**	**11**	**0**	**1**	**0**	**5**	**8**	**5**
Liver	6	4.4	31.6	2	4	0	0	0	1	4	1
Ileum	5	3.6	26.3	4	1	0	0	0	2	2	1
Colon	3	2.2	15.8	0	3	0	0	0	2	0	1
Salivary gland	1	0.7	5.3	0	1	0	0	0	0	1	0
Pancreas	1	0.7	5.3	1	0	0	1	0	0	0	0
Small intestine	1	0.7	5.3	1	0	0	0	0	0	1	0
Gall bladder	1	0.7	5.3	0	1	0	0	0	0	0	1
Duodenum	1	0.7	5.3	0	1	0	0	0	0	0	1
Respiratory (Total)	**13**	**9.5**	**100.0**	**5**	**8**	**1**	**4**	**3**	**2**	**3**	**0**
Lung	10	7.3	76.9	3	7	1	4	2	1	2	0
Air sac	2	1.5	15.4	2	0	0	0	1	1	0	0
Thoracic cavity	1	0.7	7.7	0	1	0	0	0	0	1	0
Multisystem (Total)	**12**	**8.8**	**100.0**	**8**	**4**	**1**	**0**	**0**	**7**	**3**	**1**
Urogenital (Total)	**10**	**7.3**	**100.0**	**3**	**7**	**0**	**1**	**0**	**2**	**7**	**0**
Kidney	8	5.8	80.0	3	5	0	0	0	2	6	0
Uterus	1	0.7	10.0	0	1	0	0	0	0	1	0
Umbilical cord	1	0.7	10.0	0	1	0	1	0	0	0	0
Central Nervous System (Total)	**7**	**5.1**	**100.0**	**3**	**4**	**3**	**1**	**2**	**0**	**1**	**0**
Brain	6	4.4	85.7	2	4	2	1	2	0	1	0
Meninges	1	0.7	14.3	1	0	1	0	0	0	0	0
Musculoskeletal (Total)	**3**	**2.2**	**100.0**	**2**	**1**	**0**	**1**	**0**	**1**	**0**	**1**

System/Organ	Total		System	Male	Female	Perinatal	Infant	Juvenile	Adult	Middle Age	Geriatric
	n	%	%	n	n	n	n	n	n	n	n
Bone	2	1.5	66.7	1	1	0	1	0	0	0	1
Arm	1	0.7	33.3	1	0	0	0	0	1	0	0
Integumentary (Skin)	**2**	**1.5**	**100.0**	**2**	**0**	**0**	**0**	**0**	**0**	**2**	**0**
Endocrine (Islets of Langerhans)	**1**	**0.7**	**100.0**	**0**	**1**	**0**	**0**	**0**	**0**	**1**	**0**