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A Histopathologic Survey of *Galago* in Captivity*

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Summary. A histopathological survey was performed on necropsy material derived from 33 animals of the genus *Galago* over a four year period. Light, immunofluorescence, and electron microscopic techniques were used in this study. The principal lesions found were calcific atherosclerosis, focal myocarditis, hepatitis, fatty hepatic change, hemosiderosis of liver and spleen, and glomerulonephritis. The glomerulonephritis was found in 26 animals and included four morphologically distinct types. Possible etiologic and hereditary factors and the interrelationship of the various lesions are discussed.

Introduction

A high incidence of histopathological alterations of the kidney and in particular a variety of proliferative glomerulonephritis, in galagos necropsied at the Duke University Primate Facility led to this retrospective survey of all the histological lesions in these animals. The lack of knowledge about diseases which affect galagos in wild and captive populations is unfortunate since these small prosimian primates are becoming popular as laboratory animals. This is particularly unfortunate in behavioral studies utilizing the animals, since physical or organic disease can subtly or obviously affect animal behavior.

Materials and Methods

The colony of animals which serves as a nucleus for this study was started at Yale University in 1960 by Professor J. Buettner-Janusch. The animals were originally used for genetic and behavior studies (Buettner-Janusch and Hill, 1965; Buettner-Janusch, 1962; Andrew, 1964). The colony was moved to Duke University in 1965 where the animals were first housed in a converted goat barn under very poor conditions. Temperature and humidity controls were nonexistent and morbidity and mortality rates among the animals were very high.

In March, 1968 the animals were moved to a new building, the Primate Facility where consistant professional veterinary care was then available. The animals are presently used for research in genetics, anatomy, behavior, and hematology and are housed in large hexagonal rooms which are 16 feet in diameter with 18 foot high ceilings. The rooms are equipped with perches, artificial trees and resting shelves in an attempt to simulate a semi-natural environment. The temperature is maintained at 24° C and 40–60% relative humidity. The animals are fed a variety of fresh fruits and vegetables and commercial monkey chow. The omnivorous galagos also receive canned dog food, raw liver, and hard-boiled eggs.

The species or subspecies represented in this necropsy study include *Galago crassicaudatus crassicaudatus*, *G. c. argentatus*, *G. senegalensis*, and *G. demidovii*.

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Collection of Tissues for Histopathologic Examination. Blocks of tissue were fixed in 10% formalin or Zenker fixative in preparation for later routine light microscopic examination. In addition, in five cases (see Table 3) a portion of kidney was fixed in cold 4% glutaraldehyde buffered at pH 7.0 with sodium cacodylate in preparation for later electron microscopic study and another portion frozen at −70° C in a matrix of gelatin for later immunohistochemical analysis.

Light Microscopy. After fixation in formalin or Zenker fixative, the blocks of tissue were embedded in paraffin according to standard procedure. Paraffin blocks of most tissues were sectioned at 5–7 microns, but blocks of kidney were sectioned at 3 microns. Hematoxylin and eosin (H & E) was used as a routine stain for all tissues. Unfixed, frozen sections of aortas with atherosclerosis were also stained with oil-red-O for demonstration of lipids. Sections of kidney were additionally stained by the periodic acid-Schiff reaction (PAS), periodic acid-methenamine silver-Masson stain (PAMM), and Van Giesson (VG) connective tissue stain.

Electron Microscopy. The small fragments of kidney fixed in 4% glutaraldehyde were post-fixed in osmium tetroxide, stained en bloc with uranyl acetate, embedded in epon, sectioned with a Porter-Blum ultramicrotome, and stained on collodion-carbon coated copper grids (200 mesh) with lead citrate and uranyl-magnesium acetate. The stained specimens were examined and photographed with an Hitachi HS-7 or HS-8 electron microscope.

Immunofluorescence Microscopy. Specimens of tissue, frozen at −70° C in a matrix of gelatin (Burkholder *et al.*, 1961) were sectioned in an International Harris cryostat microtome at −20° C. The 4 micron thick sections were acetone "fixed" on glass slides and washed in phosphate buffered (0.02 M, pH 7.3) physiologic saline (PBS) prior to immunohistochemical treatment. The antisera used for the fluorescent-antibody studies were anti-galago 7 S immunoglobulins and anti-galago C3 (third component of complement) prepared in rabbits. Galago 7 S immunoglobulins and C3 were obtained by DEAE cellulose chromatography of pooled sera from several normal and sick galagos. The galago C3 was further purified by preparatory pevicon block electrophoresis followed by rechromatography on CM-cellulose by techniques previously reported for purification of guinea pig complement components (Burkholder, 1970). The sodium sulfate precipitated gamma-globulin fraction of these antisera was conjugated with optimal amounts of crystalline fluorescein isothiocyanate by methods modified from those of Marshall *et al.* (1958).

Clinical Chemistries and Laboratory Analyses. Certain clinical analyses were made for selected animals on samples taken during illness or at necropsy. Tests were performed in the laboratories of the Primate Facility (hematocrit, hemoglobin, urinalysis, blood glucose, and BUN), or in the central clinical chemistry laboratories of Duke Hospital (BUN, total serum protein, or serum albumin).

Results

Pertinent historical information is presented in summary form in Table 1 where the individual animals are listed by species. Multiple references are made to "fungal dermatitis" and "arthritis". The fungal dermatitis was manifested clinically as multifocal, moist, inflamed, alopectic areas. In some instances, the lesions fluoresced under UV light. The clinical impression was not supported by cultures, but mycelia or yeast forms were noted in sections of skin taken from three animals at necropsy. The arthritis was seen clinically as swelling of the knee joints. The onset was rapid and apparently quite painful. The swellings were often warm to the touch. The acute phase of the arthritis lasted as long as two weeks. The joints became fused in a mid-flexed position and the animals involved became chronically lame.

Several animals in this study were closely related and many had living parents, offspring, or siblings. Detailed pedigrees of the animals have been presented elsewhere (Buettner-Janusch and Wiggins, 1970).

The results of necropsy examinations on 33 animals are summarized in Tables 2 and 3.

Table 1. *Summaries of clinical histories*

Animal No., sex	Date introduced into colony	Date of birth	Date of death	Clinical summary
Galago crassicaudatus crassicaudatus				
004, m	—	4/62	3/68	Chronic anal fissure, death due to rectal perforation.
007, m	9/59	—	8/66	No clinical information.
008, f	—	7/62	12/67	8/66: fungal dermatitis. 3/67: metritis. 6/67: arthritis in left knee, normal blood picture.
011, m	—	10/64	6/69	8/66: fungal dermatitis. 2/67: arthritis in both knees. 2/68: keratitis. 6/68: conjunctivitis.
012, m	—	5/65	12/68	1/67: fungal dermatitis. 9/67: arthritis in right knee. 1/68: proteinuria, hematuria, keratitis. 6/68: edema in region of face and neck, anemia. 12/68: terminal elevated blood urea nitrogen, low blood sugar, anemia.
016, f	—	5/66	8/69	8/66: bite wounds on tail, amputation of tail. 1/67: Pneumonia, developed right sided vestibular damage resulting in permanent head tilt.
256, f	5/69	—	6/69	Sudden death attributed to infected bite wounds.
404, f	—	9/66	7/68	12/66: coccidial infection. 5/67: elevated white blood count, anemia. 7/68: bite wound on tail, severe anemia.
417, m	—	9/68	6/69	Severe bite wounds, blood loss and shock apparent cause of death.
Galago crassicaudatus argentatus				
101,f	9/61	—	8/66	6/66: fungal dermatitis. 8/66: anemia.
105, m	—	10/61	3/69	6/66: Fungal dermatitis. 11/66: upper respiratory infection. 10/67: tail wound. 3/69: sudden onset of dyspnea, treated initially for pneumonia, suspected tumor, died during diagnostic radiography.
108, m	—	6/65	5/69	6/66: fungal dermatitis. 5/67: coccidial infection, arthritis, proteinuria. 11/67: icterus, anemia, hematuria, neutrophilia. 5/69: anemia, elevated blood urea nitrogen.
107,f	—	5/64	9/66	6/66: fungal dermatitis.
110, m	—	4/66	5/67	6/66: fungal dermatitis. 5/67: Pneumonia.
701, m	4/66	—	9/68	6/66: fungal dermatitis. 8/66: anemia, proteinuria. 8/68: upper respiratory infection, proteinuria, hematuria.

Table 1 (continued)

Animal No., sex	Date introduced into colony	Date of birth	Date of death	Clinical summary
704, f	4/66	—	6/69	6/66: fungal dermatitis. 9/66: anemia. 10/67: upper respiratory infection. 12/68: recurrent anemia until. 6/69: elevated blood urea nitrogen, euthanized.
705, f	4/66	—	8/66	6/66: fungal dermatitis.
706, m	4/66	—	2/69	6/66: fungal dermatitis. 4/67: arthritis. 6/67: anemia 11/67: upper respiratory infection 12/68–2/69: chronic anemia
707, f	4/66	—	6/69	6/66: Fungal dermatitis 9/66: anemia 3/67: keratitis 12/68: anemia
712, m	4/66	—	8/66	6/66: fungal dermatitis. 8/66: proteinuria
709, m	4/66	—	3/70	6/66: fungal dermatitis 8/66: proteinuria 4/67: ringworm 8/68: proteinuria 3/70: anemia, normal blood urea nitrogen
710, f	4/66	—	8/66	8/66: moderate anemia
713, m	4/66	—	8/66	6/66: fungal dermatitis 8/66: anemia, proteinuria
Galago senegalesis				
301, m	—	11/61	10/68	2/67: respiratory infection, ringworm 4/68: infected bite wounds on arms
306, f	—	—	10/68	No clinical information
310, f	6/67	—	1/69	4/68: bite wounds on left arm, amputation at elbow
312, m	—	8/67	9/68	6/68: flaccid paralysis of rigth leg 9/68: severe diarrhea
311, f	4/67	—	3/68	No clinical information
000, m	—	5/68	5/69	No clinical information
Galago demidovii				
1002, f	5/67	—	3/68	No clinical information
1003, m	5/67	—	9/68	5/68: ataxia 6/68 found comatose, terminal neutrophilia
1005, m	5/67	—	10/68	No clinical information
1009, m	10/67	—	3/68	No clinical information

Table 2. *Incidence of more commonly*

Animal Number	Genitourinary							Cardiovascular			Respiratory		
	Kidney							Heart		Aorta	Lung		
	Stalk glomerulonephritis	Stalk-lobular glomerulonephritis	Diffuse glomerulonephritis	Progressive-sclerotic glomerulonephritis	"Membranous" glomerulonephropathy	Cystic alteration	Interstitial foam Cells	Focal carditis	Focal fibrosis	Atherosclerosis	Bronchopneumonia	Hemorrhage, focal	Edema/congestion
Galago crassicaudatus crassicaudatus													
004	+								+				
007	±											+	
008					+			+			+	+	
011				+						+			
012				+									
016											+		+
256													
404	+												
417	+												
Totals 9 animals	4	0	0	2	1	0	0	1	1	1	2	2	1
Galago crassicaudatus argentatus													
101	+												
105	+												
107	+												
108				+						+			
110			+								+		
701		+				+			+				+
704		+				+		±					+
705			+										+
706				+		±	+			+			
707				+						+			+
709				+						+			
710	+										+	+	+
712	±										+		
713	+											+	+
Totals 14 animals	6	2	2	4	0	3	1	1	1	4	3	2	6
Galago senegalensis													
301			+									+	
306													
310					+								
311													
312			+										
000	+							+					
Totals 6 animals	1	0	2	0	1	0	0	1	0	0	0	1	0

occurring lesions in each galago

Gastrointestinal								Endocrine		Hematopoietic					Miscellaneous		
Liver										Spleen							
"Hepatitis"	Hemosiderosis	Adenoma	Congestion	Fatty Change	Cholelithiasis	Peptic ulcer	Peritonitis	Adrenalitis	Decreased spermatogenesis	Reticuloendothelial hyperplasia	Lymphoid hyperplasia	Lymphoid hypoplasia	Hemosiderosis	Hypercellularity, bone marrow	Infections (skin)[a]	Arthritis[a]	"Keratitis"[a]
+										+					+		
	+		+	+									+		Cl	Cl	
+	+			+					+	+			+	+	Cl		+
+	+			+	+					+					Cl	+	Cl
	+			+						+							
			+	+							+				+		
+						+		+		+					+		
+											+						
			+			+				+		+	+				
5	4	0	3	5	1	2	0	1	1	6	2	1	4	1	6	2	2
															Cl		
	+			+				±		+			+		Cl		
										+			+		+		
	+			+	+					+			+		Cl	+	
							+		+	+			+		Cl		
+									+			+	+		Cl		+
		+			+					+			+		Cl		
F[b]			+								+				+		
									+	+		+		+	Cl	+	±
				+						+	+			±	Cl		+
±							+			+					Cl		
			+											+	+		
			+	+					+			+		+	Cl		
+									+		+				+		
3	2	1	3	4	2	0	2	1	5	8	3	4	6	4	14	2	3
			+					+				+			+		
								+			+						
±								+			+		+				
			+							+		+					
			+			+		+							+		
+			+	+			+						+				
2	0	0	4	1	0	1	1	4	0	1	2	2	2	0	2	0	0

Table 2

Animal Number	Genitourinary							Cardiovascular			Respiratory		
	Kidney							Heart		Aorta	Lung		
	Stalk glomerulonephritis	Stalk-lobular glomerulonephritis	Diffuse glomerulonephritis	Progressive-sclerotic glomerulonephritis	"Membranous" glomerulonephropathy	Cystic alteration	Interstitial foam Cells	Focal carditis	Focal fibrosis	Atherosclerosis	Bronchopneumonia	Hemorrhage, focal	Edema/congestion
Galago demidovii													
1002							[c]	+					
1003					+								
1005													+
1009							[d]						
Totals 4 animals	0	0	0	0	1	0	0	1	0	0	0	0	1
Totals 33 animals	11	2	4	6	3	3	1	4	2	5	5	5	8

[a] Cl refers to a clinical manifestation observed at some time but not seen postmortem.

[b] F refers to a single focus of chronic inflammatory infiltrate and fibrosis in an area associate with a liver fluke.

[c] Acute tubular necrosis.

[d] Cytomegalic inclusions.

+ indicates that a lesion was present, ± indicates a very mild incidence of a particular lesion.

Cardiovascular System. The most striking alteration of the cardiovascular system was calcific atherosclerosis confined to the ascending portion and arch of the thoracic aorta (Figs. 1–3). This disease occurred almost exclusively among *G. c. argentatus* with one exception (Table 2). Furthermore, each animal with this atherosclerotic lesion also had the more severe, chronic form of glomerulonephritis (see Table 2). Four males and one female were afflicted with the atherosclerosis. The atherosclerosis spared the leaflets of the aortic valves and seemed to arise sharply just above the sinuses of Valsalva (Fig. 1). Almost as sharply, the process stopped in the arch of the aorta near the subclavian artery. Microscopically, in addition to lipid-laden endothelial and histiocytic cells in the atherosclerotic plaques, calcium deposits, which also could be appreciated by palpation and x-ray examination of the specimens (Figs. 2–3), were present. No atherosclerosis of the coronary, cerebral, or other major arterial systems was noted in these or other necropsied galagos.

Most of the animals had no alterations of the heart or major vessels; however, one animal from each species had mild, very isolated focal inflammation of the myocardium. This consisted of a few neutrophilic leukocytes and mononuclear

(continued)

Gastrointestinal								Endocrine		Hematopoietic					Miscellaneous		
Liver										Spleen							
"Hepatitis"	Hemosiderosis	Adenoma	Congestion	Fatty Change	Cholelthiasis	Peptic ulcer	Peritonitis	Adrenalitis	Decreased spermatogenesis	Reticuloendothelial hyperplasia	Lymphoid hyperplasia	Lymphoid hypoplasia	Hemosiderosis	Hypercellularity, bone marrow	Infections (skin)[a]	Arthritis[a]	"Keratitis"[a]
±			+ +	±						+ +		+	+				
1	0	0	2	1	0	0	0	0	0	2	0	2	0	0	0	0	0
11	6	1	12	11	3	3	3	6	6	17	7	9	12	5	22	4	5

cells with minimal extent of local necrosis of myofibers (Fig. 4). In some instances the inflammation was subepicardial, in others subendocardial (as in Fig. 4), and in general no consistent pattern of localization was obvious. The two cases with minimal focal fibrosis of the myocardium probably were examples of healed previous carditis.

Respiratory System. In the majority of animals, only minor or no alterations were noted in the lungs, and in at least half of the animals the lungs were normal. Five animals had focal or, less often, generalized bronchopneumonia. Two of these animals had associated pulmonary hemorrhage, and two other animals also had several small foci of pulmonary hemorrhage. Edema and congestion of the lungs occurred fairly frequently, particularly in *G. c. argentatus*. Focal atelectasis of the lung was a rather rare finding and may in some instances have been the result of the post-mortem collapse incurred in handling the lung tissue.

Gastrointestinal System. A wide variety of minor and major alterations of the gastrointestinal system were noted, and most of these were referable to the hepatic system. Focal, mild or extensive fatty change of hepatic parenchymal cells, usually centrolobular in distribution was present in 11 animals. Most commonly affected were *G. c. argentatus* and *G. c. crassicaudatus*. Focal or extensive hepatitis (Fig. 5) with or without necrosis of parenchymal cells occurred independent of the fatty change in eight animals and in association with fatty change in three animals. The inflammation, which was random in its histological distribution, consisted mainly of small round mononuclear cells (lymphoid cells) and variable numbers of polymorphonuclear leukocytes. Some animals of each species were affected by

Table 3. *Immunofluorescence and electron microscopic findings in five galagos with glomerulonephritis*

Animal Number	Immunofluorescence (glomeruli)			Electron microscopy (glomeruli)			
	Galago γ-globulin	Galago C3	Pattern of localized antibody	Deposits		Collagen fibers	Thickened membrane
				Subepithelial	Subendothelial		
Galago crassicaudatus argentatus							
108	+	+	Local, heavy homogeneous or granular; subendothelial	+	+ Loose granular	+	0
110	0	0		0	0	0	+
707	+	+	Very local, limited solid homogeneous or granular; subendothelial	0	+ Loose granular	+	±
709	+	+	Local, limited granular; subendothelial	0	+ Loose granular	+	0
Galago crassicaudatus crassicaudatus							
011	+	+	Extensive, local heavy homogenous or granular, subendothelial	0	+ Dense homogeneous and loose granular	+	0

this hepatitis. One *G. c. crassicaudatus* (No. 004) with mild hepatitis also had chronic cholangitis. Two animals (No. 012 and 701) had mild portal fibrosis, but it was not possible to determine histologically whether this "cirrhosis" bore any relationship to possible previous hepatitis. One animal had a liver fluke (No. 705) with associated local chronic inflammation and fibrosis of the liver. Centrolobular vascular congestion of the liver occurred in 12 cases, some of which also had congestion of the lungs which probably represents terminal congestive heart failure. Hemosiderosis of the liver was present in four *G. c. crassicaudatus* and in two *G. c. argentatus*, and this bore an inconsistent relationship to hemosiderosis of the spleen (see Hematopoietic System) and possibly to the anemia so common in these animals. Other more incidental findings in the liver were a hepatic adenoma (Figs. 8–9) seen in animal No. 704, and cholelithiasis seen in one *G. c. crassicaudatus*. Acute ulcer of the stomach or of the duodenum was present in three animals, non-specific enteritis in two other animals, and peritonitis of unspecified cause in three additional animals.

Genitourinary System. A number of histologic alterations were noted in the kidneys of these animals. Four types of proliferative glomerulonephritis were observed as described in extensive detail elsewhere (Burkholder and Bergeron, 1970). In four animals it was a mild or moderate type. In eleven animals it con-

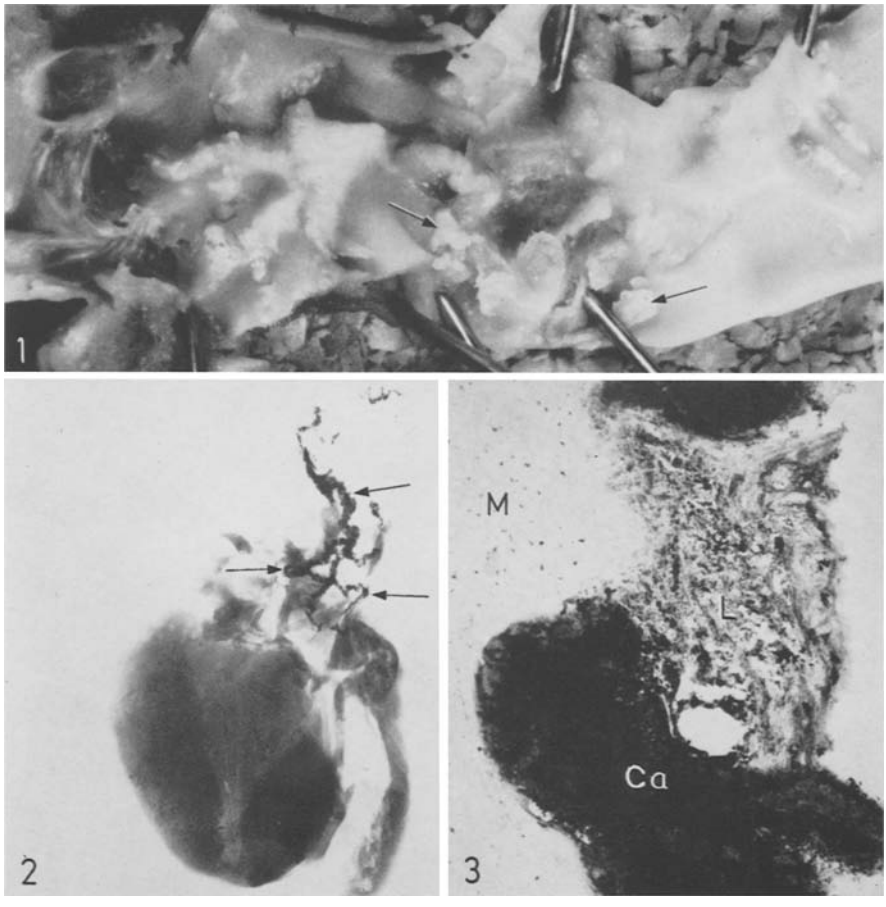


Fig. 1. Ascending aorta from animal number 108 with calcific atherosclerosis shows hard, granular calcific and atheromatous lesions beginning at the aortic (*A*) sinuses of Valsalva and extending through the arch of the aorta. (Gross photograph)

Fig. 2. Heart and ascending aorta from animal No. 108 showing x-ray dense deposits of calcium (arrows) following the course of the aorta. (Positive of roentgenogram of the gross)

Fig. 3. Deposits of lipid (*L*) within histiocytes of the aortic intima of animal No. 108, with nearby nodules of calcium; aortic media (*M*). (Oil-red-O fat stain, × 91)

sisted of a mild glomerular mesangial lesion and in two animals a more marked mesangial lesion with lobular accentuation of glomerular tufts. In six animals a progressive-sclerotic form of glomerulonephritis was observed. In addition, three animals had a "membranous" thickening of glomerular capillary walls.

Those animals with the most severe progressive-sclerotic form of glomerulonephritis were four *G. c. argentatus* and two *G. c. crassicaudatus*. The glomerular lesions in these six animals consisted of diffuse endocapillary cellularity (endothelial and mesangial cells) with widening of mesangial areas by argyrophilic basement membrane matrix and by Masson-positive (green), Van Gieson-positive

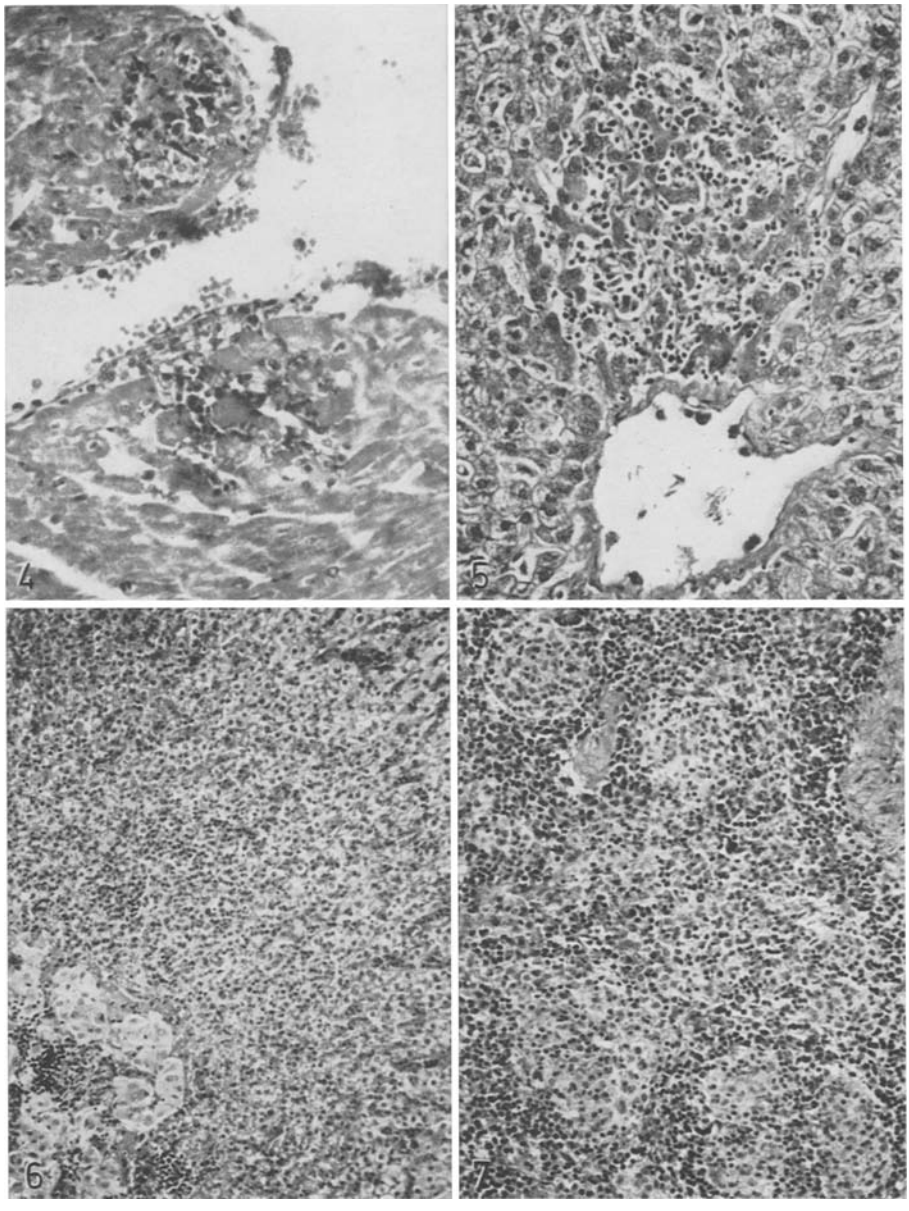


Fig. 4. Focal myocarditis in animal No. 008; there is focal necrosis of myofibers and infiltration by a few chronic inflammatory cells within the areas of necrosis and in the nearby endocardium. (H & E stain, × 190)

Fig. 5. Liver from animal No. 713 with focal hepatitis, a small area of infiltration with chronic inflammatory cells and "dropping out" or atrophy of a few hepatic parenchymal cells near a central lobular vein. (H& E stain, × 160)

Fig. 6. Adrenal gland from animal No. 256 with adrenalitis, showing infiltration by predominantly chronic inflammatory cells in the medulla (lower left) and cortex. (H & E stain, × 96)

Fig. 7. Spleen from animal No. 012 with reticuloendothelial and some lymphoid hyperplasia. (H & E stain, × 150)

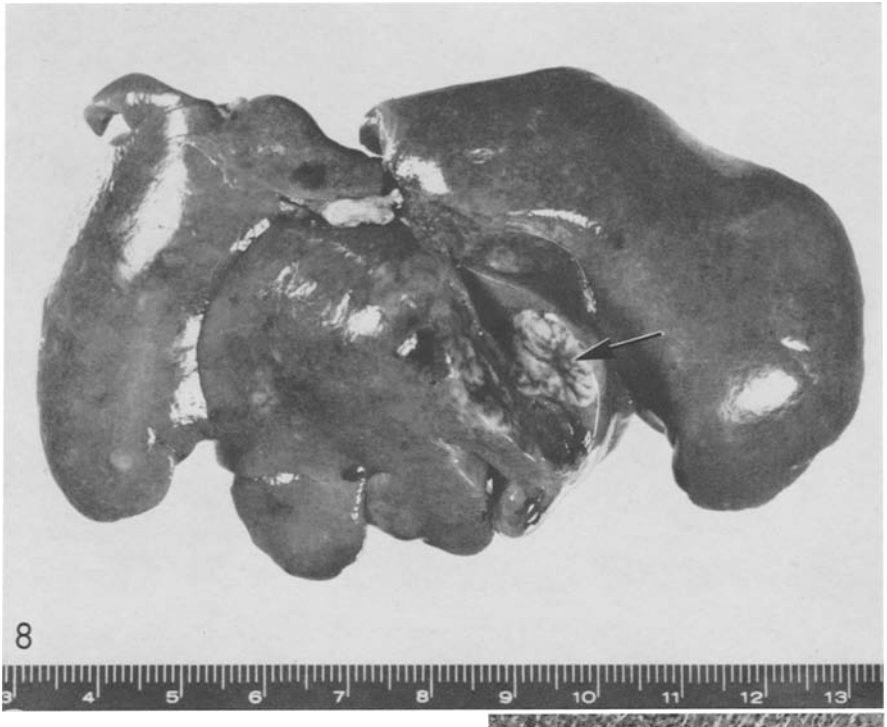


Fig. 8. Liver from animal No. 704 with several "tumor" nodules, one of which has been bisected (scale in cm). (Gross photograph)

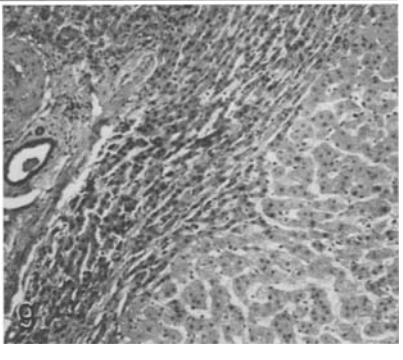
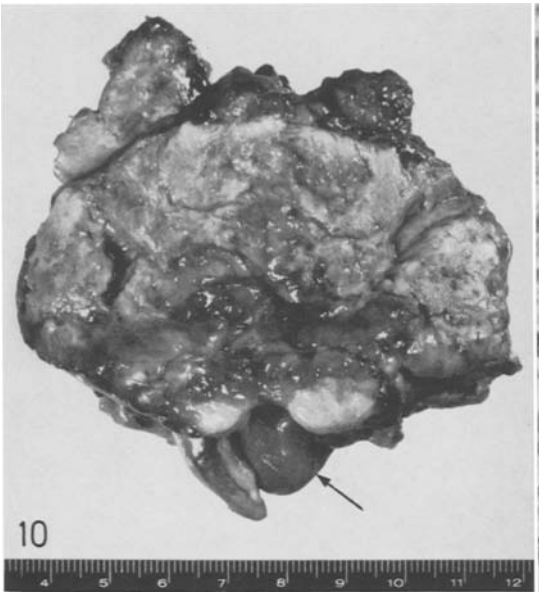


Fig. 9. The cells in the hepatic tumor, illustrated in Fig. 8, are large, polygonal hepatic parenchymal cells (lower right) with good differentiation and no mitotic figures. The tumor nodule compresses the hepatic cells of the adjacent liver. (H & E stain, × 73)

(red) "conntecive tissue" material (Figs. 12, 15). In addition, peripheral portions of glomerular capillary walls were greatly thickened by finely or coarsely fibrillar connective tissue-like material and/or amorphous deposits which stained dark red or gray-green with PAMM stain. This mesangial and mural capillary thickening greatly narrowed glomerular capillary lumens. By immunofluorescence microscopy, deposits of host antibody-globulins and a component of host complement (C3) were present in many of the greatly thickened peripheral portions of glomerular capillary walls in three of the four *G. c. argentatus* and in the one *G. c. crassicaudatus* studied by this technique (Figs. 13, 16; Table 3). This localized host globulin could be dissociated from its complexes in the tissues by rinsing sections of kidney in acid buffer (pH 3.4). Phase-fluorescence microscopic examination



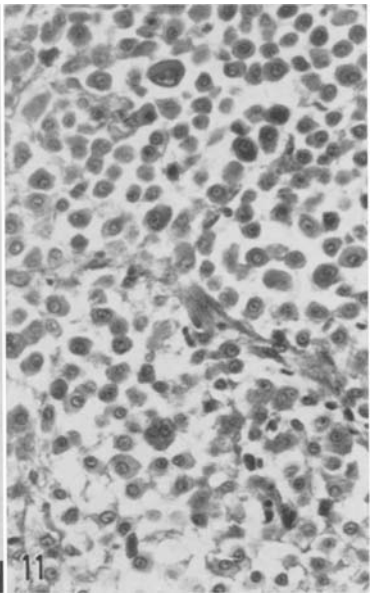


Fig. 10. Mediastinal tumor in animal No. 105 is a fleshy, solid and focally necrotic mass partially enveloping the heart (arrow points to posterior wall of the heart) and invading one lung (scale in cm). (Gross photograph)

Fig. 11. The cells comprising the tumor, illustrated in Fig. 10, are round cells with usually one eccentric nucleus, few mitotic figures, and an occasional multinucleate form. A delicate reticular stroma is present. (H & E stain, × 220)

revealed these globulin deposits to lie immediately beneath the glomerular capillary basement membrane. Ultrastructurally, dense homogeneous or loose coarsely granular electron dense deposits were seen beneath the glomerular capillary basement membrane. These deposits correspond in distribution with the immunofluorescent deposits of globulins described above for four of the five cases examined by fluorescence and electron microscopy (Figs. 14, 17; Table 3). Many collagen fibers, including some rather large forms were identified by electron microscopy in the glomerular capillary deposits and mesangial regions (Figs. 14, 17). In one animal (No. 108), several subepithelial, hump-like deposits (Figs. 17, 18) with substructural "crystalline" lattice (Fig. 18) were identified in one of three glomeruli examined.

Thirteen animals, nine *G. c. argentatus* and four *G. c. crassicaudatus* had stalk proliferative glomerulonephritis (Table 2). In this form of glomerular disease, the glomerular mesangial regions were slightly to moderately thickened in 11 animals and in zanimals greatly thickened with lobular accentuation by increase in mesangial basement membrane matrix and mesangial cells. The one animal examined by immuno-fluorescence and electron microscopy (No. 110, see Table 3) had no deposits of immunoglobulins and no electron dense deposits or collagen in glomerular capillary walls.

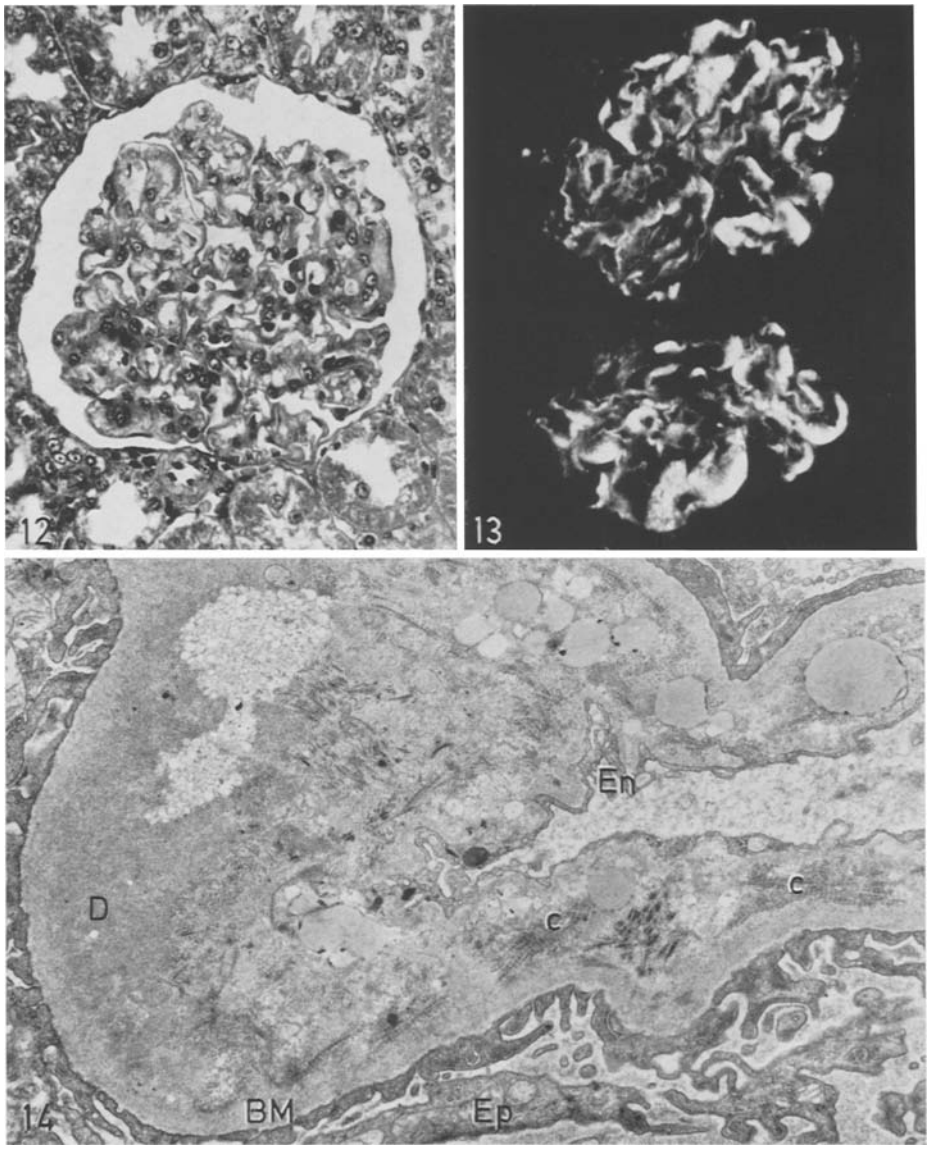


Fig. 12. Glomerulus in the kidney from animal No. 011 with glomerulonephritis showing thickening of mesangium and peripheral capillary walls, increased cellularity, and marked narrowing of capillary lumens. (H & E stain, × 200)

Fig. 13. Two additional glomeruli from animal No. 011 showing localization of galago antibody-globulins in elongate globular masses along capillary walls. (Fluorescent anti-galago 7 S globulins, × 150)

Fig. 14. Capillary loop of another glomerulus from animal No. 011 showing large subendothelial electron dense deposit (*D*) lying adjacent to the capillary basement membrane (*BM*); granular material, vacuoles (lipid material) and collagen fibers (*c*) are intermixed with the deposit; endothelial cell (*En*), epithelial cell (*Ep*). (Electron micrograph, × 9000)

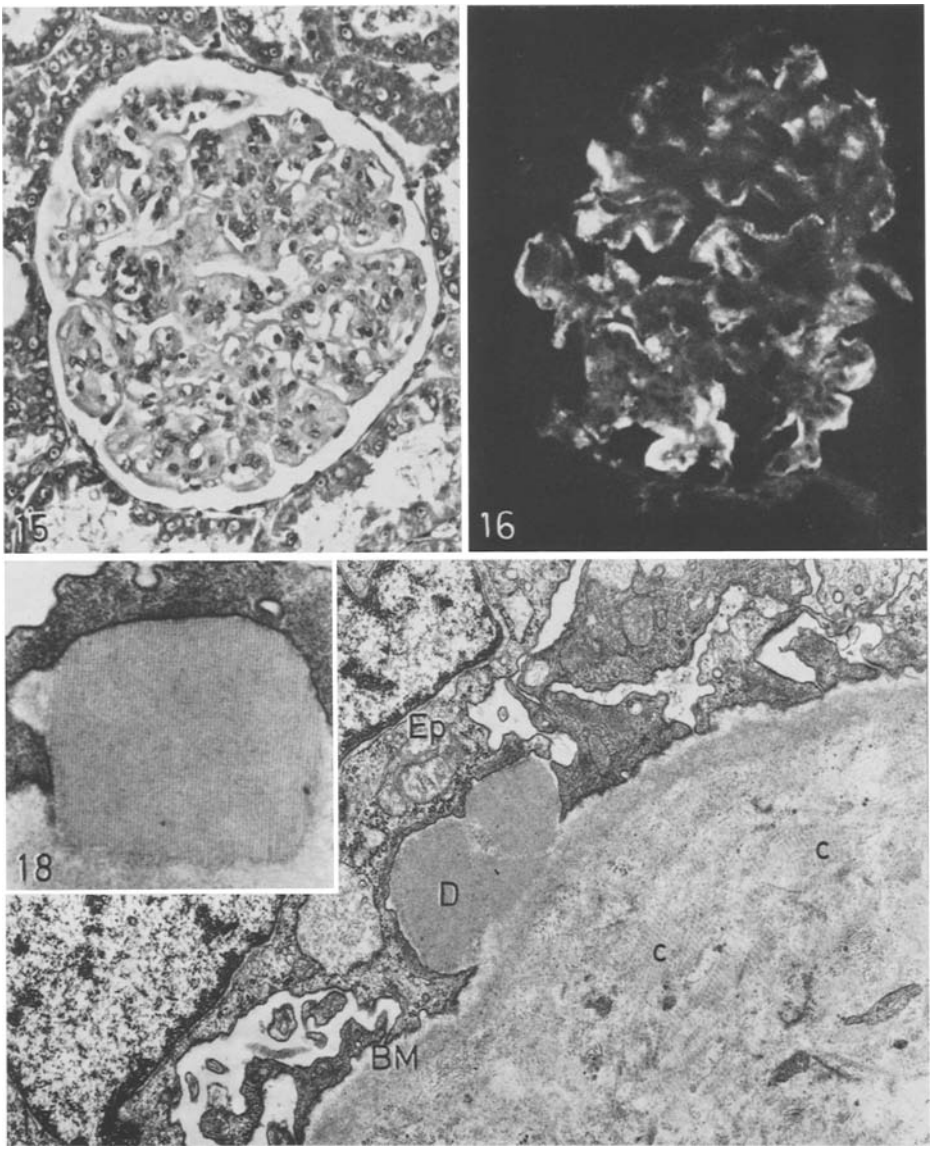


Fig. 15. A glomerulus in the kidney from animal No. 108; mesangial areas are thickened by increase of cells and membranous matrix with some compromise of capillary lumens, peripheral portion of glomerular capillary walls are locally thickened. (H & E stain, × 190)

Fig. 16. A second glomerulus from animal No. 108 showing local clumped granular and globular localization of galago antibody-globulins in capillary walls. (Fluorescent anti-galago 7 S globulins, × 175)

Fig. 17. Segment of capillary wall in another glomerulus from animal No. 108 with many large collagen fibers intermixed with granular and focally finely fibrillar subendothelial deposit; a subepithelial nodule (*D*), somewhat reminiscent of those seen in human hypersensitivity proliferative nephritis is present; capillary basement membrane (*BM*), epithelial cell (*Ep*) with loes of foot process slit pores overlying the electron dense "hump". (Electron micrograph, × 9200)

Fig. 18. This insert shows at higher magnification the "linen-like" crystalline substructure of a typical subepithelial "hump" elsewhere in the same tuft as Fig. 17. (Electron micrograph, × 38000)

Four animals had a diffuse proliferative glomerulonephritis characterized by a generalized mild to moderate increase in cellularity of glomerular tufts. Glomerular capillary lumina were narrowed but no neutrophilic leukocytes, subepithelial deposits, capillary thrombi, or sites of capillary necrosis were present.

Only three animals, each from a different species, had the diffuse membranous thickening of glomerular capillary walls and no other significant renal abnormalities. One *G. demidovii* had acute tubular necrosis and another had cytomegalic inclusion lesions in a rare proximal convoluted tubule.

Additional histologic features observed in other structures of the kidneys were cystic dilation of glomerular spaces and of some convoluted tubules which could be appreciated on gross inspection (three animals, Nos. 701, 704, 706), numerous collections of interstitial foam cells (one animal, No. 706), focal interstitial infiltrates consisting of lymphoid and plasma cells (seven animals, Nos. 704, 105, 301, 701, 706, 709, 1003), focal hydropic swelling of epithelial cells in proximal convoluted tubules (three animals, Nos. 007, 101, 312), and focal, interstitial, or tubular calcification (five animals, Nos. 012, 301, 310, 701, 705).

Endocrine System. The only endocrine organs observed to have histologic abnormalities were the adrenal glands and testes. Six animals, four of whom were *G. senegalensis*, had foci of chronic inflammatory cell infiltrates in the adrenal cortex and medulla (Fig. 6). Aspermatogenesis with foci of frank atrophy of seminiferous tubules was noted in six animals.

Hematopoietic System. The spleens of many animals displayed a variety of histologic alterations. The major observation was a nodular and/or diffuse increase in reticuloendothelial or histiocytic type cells (Fig. 7). In two animals with reticuloendothelial hyperplasia and in five others there was a marked lymphoid hyperplasia of the spleen. Nine other animals had lymphoid hypoplasia, and four of these were animals with concommitant reticuloendothelial hyperplasia. A common finding was hemosiderosis of the spleen which was observed in twelve animals five of whom also had hemosiderosis of the liver. In many animals, a few or many multinucleated giant cells were scattered randomly in the spleen.

Hypercellularity of the bone marrow (granulopoietic cells) was present in five cases. One of these had cutaneous infections and bronchopneumonia, one other had bronchopneumonia, and all five had some type of glomerulonephritis at the time of death.

Miscellaneous Findings. Eight animals had acute or chronic infected lesions of the skin at the time of death. It is of some interest that six of these animals had some form of glomerular disease; two of them had the more severe diffuse proliferative glomerulonephritis. Histologic examination revealed *Candida* in some of these wounds (Nos. 007, 710, 312) and *Candida* was cultured from an abscess in animal No. 110. Fifteen other animals also had clinical evidence of cutaneous infections at some time even though these were not present at necropsy.

Destructive, crepitating arthritis of one or both knee joints occurred in four animals. Histologically, it was felt that these joint changes were the result of trauma rather than a rheumatoid arthritic process.

A massive neoplasm in the mediastinum was seen in one animal (No. 105) (Figs. 10–11). This tumor invaded the pleural surface of one lung and, by its size, seriously hampered respiration. Microscopically the tumor was comprised of

undifferentiated round cells with abundant pale eosinophilic cytoplasm and eccentrically located nuclei (Fig. 11). No mitotic figures were seen, but occasional multinucleated cells were present. There were no metastases. The differential diagnosis was reticulum cell sarcoma, plasmacytoma, thymoma, or mediastinal tumor of undetermined origin. Since no satisfactory conclusion could be reached regarding this tumor, the last-listed diagnosis was recorded.

There were corneal "ulcers" noted at necropsy in three animals who were quite ill with glomerulonephritis. These lesions probably were the result of desiccation, since the sick animals readily developed a problem with inadequate moistening of their sclera.

Discussion

This histopathologic survery of galagos, dying or killed because of severe illness in a captive population utilized for genetic and behavioral studies was prompted by the finding of a high frequency of proliferative inflammatory or other glomerular lesions (26 out of 33 animals). Initially it was thought that the variety of nephritides observed might be hereditary, because most of the animals with severe renal disease were of the *G. c. argentatus* and *G. c. crassicaudatus* subspecies and several of the animals were siblings. A review of clinical and pathological material from all animals necropsied over a four year period revealed that factors other than familial or hereditary ones might be responsible for the nephritis since several species were involved with various forms of glomerulonephritis. Hereditary constitutional factors may determine susceptibility to development of glomerulonephritis in these animals, but also to be considered are environmental factors, such as chronic cutaneous or other infections, and hypersensitivity reactions suggested by the localization of host antibody and a component of complement (C3) in glomerular tufts of several nephritic animals. The electron microscopic demonstration of glomerular subendothelial capillary deposits and subepithelial "hump-like" deposits is similar to features of the proliferative hypersensitivity glomerulonephritides of several other animals and man (Burkholder and Bradford, 1969; Dixon *et al.*, 1961; Henson *et al.*, 1969; Henson *et al.*, 1968; Mellors, 1965; Muehrcke *et al.*, 1957; Nairn *et al.*, 1966; Oldstone and Dixon, 1969). The glomerular lesions in the galagos are, however, somewhat different in that progressive lesions have a surprisingly high content of collagen fibers and the few subepithelial nodules observed possessed a crystalline substructural lattice. The special significance of these latter two rather unique findings is yet obscure.

A curious, but not unexpected finding in this study, was rather severe calcific atherosclerosis of the ascending thoracic aorta in five animals (Strong *et al.*, 1968; Wissler, 1968). When observed in context with other pathologic findings, the atherosclerosis occurred in four of the six *G. c. argentatus* and in one of the three *G. c. crassicaudatus*, all of whom also had glomerulonephritis. It is not known whether these animals had, in association with their nephritis, hyperlipemia or hypertension, conditions that in humans can be associated with enhancement of the atherosclerotic process. The apparent clustering of the occurrence in this admittedly small sample of *G. c. argentatus* and *G. c. crassicaudatus* of nephritis, atherosclerosis, hemosiderosis of the liver and spleen, and fatty liver may

reflect a constellation of lesions interrelated as consequences of a single disease process, most likely the renal disease. On the other hand, some of the lesions occurring commonly in these two subspecies of galagos may be independent disease conditions reflecting an underlying common hereditary predisposition or susceptibility of these animals to develop the variety of diseases.

The hepatitis, either focal or extensive, was observed in some animals of each species and its etiology remains unknown at this point.

The hemosiderosis of spleen (12 animals), liver (6 animals), or spleen and liver (5 animals) occurring in a total of 13 animals is a finding for which no other pathologic or clinical correlate is obvious other than possibly sporadic anemia. The fatty change of the liver, observed in 11 animals, is also of unknown cause. It may be that the artificial diet provided for these animals in captivity is not entirely sufficient or appropriate compared to the diet available in the natural habitat. On the other hand, it may be that animals in the wild may have fatty livers as well as other pathologic conditions described here, and it will be important in future comparative clinical and pathologic studies to determine whether the pathologic conditions described here are unique to captive animals. Cholelithiasis, peptic ulcers, adrenalitis, reticuloendothelial and lymphoid hyperplasia of the spleen as well as several of the other conditions already described (atherosclerosis, glomerulonephritis, hepatitis, and carditis) may be the result at least in part of the artificiality (physical and psychological) of life in captivity.

Spontaneous tumors (hepatoma, questionable thymoma) were not very common among these animals, but the present study includes a small population of animals and may not reflect a real incidence of tumors in galagos.

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