Spontaneous Cardiac Findings in Research Colony Cynomolgus and Rhesus Macaques: A 3-Year Survey

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Introduction

Nonhuman primates (NHPs) are important models in biomedical research and preclinical toxicity studies. Background microscopic cardiac lesions are common in NHPs and may confound findings that are potentially test article-related (Chamanza 2006, Chilton 2023). Awareness of the incidence of these background findings, how the incidence changes over time, and the ability to distinguish them from experimentally induced change are essential for accurate data interpretation and colony health management. This retrospective survey aims to characterize incidence, sex and age distribution, and species differences in incidence of spontaneous cardiac lesions of cynomolgus macaques (*Macaca fascicularis*) and rhesus macaques (*Macaca mulatta*) in a large NHP colony.

Methods

A retrospective review of NHP colony cases submitted for diagnostic necropsy from 2023 to 2025 was conducted to identify and describe background cardiac findings. These animals were housed at an AAALAC-accredited CRO in compliance with all federal regulations and Inotiv policies on the care, welfare, and treatment of laboratory animals. Only animals that were not exposed to test materials were included. Terminology was harmonized for similar microscopic findings based on INHAND recommendations (Colman 2021).

Results

Over the three-year survey period, heart was evaluated microscopically in 405 cases (236 rhesus and 169 cynomolgus macaques) with cardiac microscopic findings described in 151/405 (37.3%) cases comprising 94 rhesus and 57 cynomolgus macaques. Microscopic findings are summarized in **Table 1.** The most common cardiac microscopic findings were mononuclear infiltrates, cardiomyocyte degeneration/necrosis, cardiomyocyte karyomegaly/karyocytomegaly, and fibrosis. Sarcoplasmic pseudocysts containing amastigotes or kinetoplasts, consistent with *Trypanosoma cruzi* infection (Chagas disease), were described in 8 cases (4 rhesus and 4 cynomolgus), and often (6/8) associated with cardiac moribundity/mortality. Neoplasia involving the heart occurred in 2 older adult rhesus, one with a pericardial paraganglioma and the other a metastatic hepatocellular carcinoma.

In 29/405 cases (23 rhesus, 6 cynomolgus), cardiac lesions were considered the primary contributor of moribundity/mortality, as summarized in **Table 2**. Myocarditis and cardiomyopathy were the most common cardiac diagnoses associated with moribundity/mortality.

Discussion

- Rhesus macaques with cardiac findings were predominantly older adults (63/94; 67%), with higher prevalence of chronic cardiac changes that increased sharply with age.
- Rhesus macaques 10 years or older accounted for approximately 73.0% (27/37) of all recorded cardiomyopathy cases.
- In contrast, few Cynomolgus macaques with cardiac findings fall into this age group (3/57; 5%).
- While both myocarditis and cardiomyopathy were frequently described, they often occurred incidental to moribundity/mortality.
- No significant differences in the prevalence of microscopic cardiac findings between sexes were seen in this survey.

Background cardiac microscopic findings are relatively common in NHPs and may be primary causes of moribundity/death or incidental findings. Understanding the background incidence of these findings is critical for accurate evaluation of NHP research studies and is vital to responsible research animal care and use through colony heath monitoring.

Table 1. Frequency of Cardiac Findings in Research Colony Macaques (2023-2025)

Cardiac Microscopic Findings	Rhesus (*Macaca mulatta*) (236)						
	Male			Female			
	< 5 yrs	5-10 yrs	≥ 10 yrs	< 5 yrs	5-10 yrs	≥ 10 yrs	Total (%)
Number of Affected Animals	**10**	**8**	**22**	**6**	**7**	**41**	
Infiltrate, mononuclear cell, myocardium	5	4	11	4	2	16	42 (17.8)
Degeneration/Necrosis, cardiomyocyte	3	1	11	2	2	15	34 (14.4)
Fibrosis, myocardium	-	1	13	-	2	21	37 (15.7)
Karyomegaly/karyocytomegaly, cardiomyocyte	-	1	14	-	3	15	33 (14.0)
Infiltrate, mixed cell, myocardium	1	2	2	1	1	3	10 (4.2)
Increased cellularity, adipocytes, myocardium	-	1	6	-	1	3	11 (4.7)
Vacuolation, cardiomyocyte	-	-	3	-	1	2	6 (2.5)
Parasite, protozoa	-	1	1	1	1	0	5 (2.1)
Hypertrophy, cardiomyocyte	-	-	3	-	-	6	8 (3.4)
Inflammation, pericardial	-	-	4	-	1	2	7 (3.0)
Degeneration, myxomatous: Heart valves	-	-	1	1	-	4	6 (2.5)
Pigment, cardiomyocyte	-	-	1	-	-	2	3 (1.3)
Infiltrate, neutrophilic, myocardium	1	-	-	-	1	0	2 (0.8)
Hemorrhage, subendocardium	1	-	-	-	-	0	1 (0.4)
Serous atrophy of fat	-	-	-	1	1	0	2 (0.8)
Thrombus, atrium	-	-	-	-	-	1	1 (0.4)

Cardiac Microscopic Findings	Cynomolgus (*Macaca fascicularis*) (169)						
	Male			Female			
	< 5 yrs	5-10 yrs	≥ 10 yrs	< 5 yrs	5-10 yrs	≥ 10 yrs	Total (%)
Number of Affected Animals	**7**	**16**	**2**	**20**	**11**	**1**	
Infiltrate, mononuclear cell, myocardium	6	10	2	12	6	1	37 (21.9)
Degeneration/Necrosis, cardiomyocyte	2	8	0	7	3	-	20 (11.8)
Fibrosis, myocardium	-	3	1	-	1	1	6 (3.6)
Karyomegaly/karyocytomegaly, cardiomyocyte	1	4	1	1	2	1	10 (5.9)
Infiltrate, mixed cell, myocardium	-	2	-	6	3	-	11 (6.5)
Vacuolation, cardiomyocyte	1	1	-	1	-	-	3 (1.8)
Parasite, protozoa	-	2	-	1	1	-	4 (2.4)
Pigment, cardiomyocyte	-	-	1	-	-	-	1 (0.6)
Infiltrate, neutrophilic, myocardium	-	-	-	-	1	-	1 (0.6)
Hemorrhage, subendocardium	1	1	-	-	-	-	2 (1.2)
Parasite, cestode	-	-	-	1	-	-	1 (0.6)
Infarct, myocardium	-	-	-	-	1	-	1 (0.6)

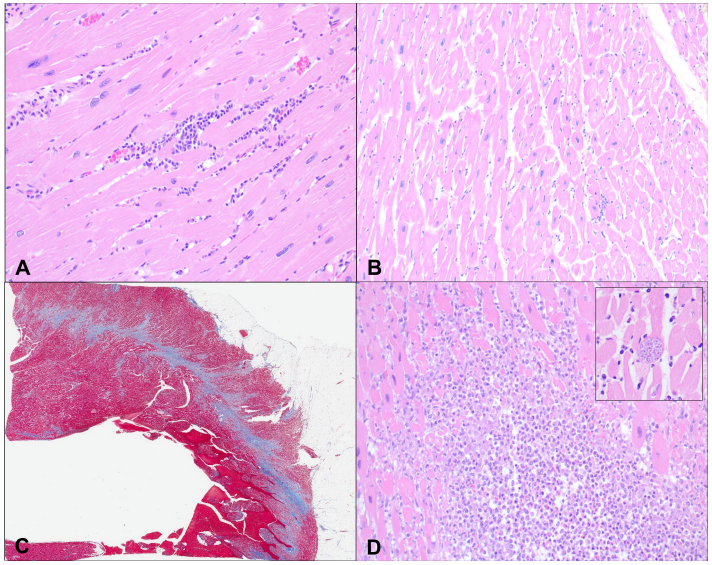

Figure 1. Microscopic Cardiac Lesions in Cynomolgus and Rhesus Macaques. **A**: Myocardial infiltrates of lymphocytes and plasma cells, rhesus macaque, H&E. **B**: Cardiomyocyte karyomegaly and anisokaryosis, rhesus macaque, H&E **C**: Myocardial fibrosis, rhesus macaque, Trichrome **D**: Neutrophilic and lymphocytic inflammation with myofiber necrosis **(inset:** Sarcoplasmic pseudocyst (consistent with *Trypanosoma cruzi*), cynomolgus macaque, H&E.

Table 2. Incidence of Cardiac-associated Conditions

Condition[1]	Rhesus		Cynomolgus		Total
	Mortality-Associated	Incidental	Mortality-Associated	Incidental	
Number of Affected Animals	**23**	**43**	**6**	**25**	
Myocarditis[2]	12	20	3	16	51
Cardiomyopathy	10	20	2	6	38
Myxomatous valvular degeneration	-	3	-	-	3
Hemorrhage, subendocardium	-	-	1	1	2
Pericarditis	-	-	-	1	1
Parasite, cestode	-	-	-	1	1
Neoplasia	1	1	-	-	2

[1] Animals with more than one condition were counted for each

[2] In cases of myocarditis, 4 rhesus and 4 cynomolgus macaques had histologic evidence of Chagas disease.

References:

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