COMPARATIVE PATHOLOGY
IN
MONKEYS

National Institute of Neurological Diseases and Blindness
Symposia in Neuroanatomical Sciences
WILLIAM F. WINDLE, *Series Editor*

COMPARATIVE PATHOLOGY IN MONKEYS

By

B. A. LAPIN and L. A. YAKOVLEVA

Institute of Experimental Pathology and Therapy
Academy of Medical Sciences, U.S.S.R.
Sukhumi, Georgia, Russia

With a Foreword by

I. V. Davydovskiy

Member of the Academy of Medical Sciences
U.S.S.R.

ZOOLOGICAL GARDEN
738J
CALCUTTA

1102

BOOK NO.
587

THOMAS BOOKS
SYMBOL OF LEADERSHIP

CHARLES C THOMAS • PUBLISHER
Springfield · Illinois · U.S.A.

Published and Distributed Throughout the World by
CHARLES C THOMAS · PUBLISHER
BANNERSTONE HOUSE
301-327 East Lawrence Avenue, Springfield, Illinois, U.S.A.

Published 1963, by CHARLES C THOMAS · PUBLISHER
Library of Congress Catalog Card Number: 62-20584

Originally published under the title:
OCHERKI SRAVNITEL'NOY PATOLOGII OBEZ'YAN
Moskva, Medgiz, 1960

With THOMAS BOOKS careful attention is given to all details of manufacturing and design. It is the Publisher's desire to present books that are satisfactory as to their physical qualities and artistic possibilities and appropriate for their particular use. THOMAS BOOKS will be true to those laws of quality that assure a good name and good will.

Printed in the United States of America

Translated from Russian
by
U. S. Joint Publications Research Service

Translation was made possible by funds from
National Institute of Neurological Diseases and Blindness
National Institutes of Health
Public Health Service
U. S. Department of Health, Education and Welfare
Bethesda, Maryland

EDITOR'S FOREWORD

The decision to translate and publish this book by B. A. Lapin and L. A. Yakovleva, resulted from a visit to their laboratories in Sukhumi by Dr. Carl B. Koford, of the NINDB Laboratory of Perinatal Physiology, in June of 1960. The translation was made by the U. S. Joint Publications Research Service, from the copy of *Comparative Pathology in Monkeys* presented to Dr. Koford by Professor Lapin. After translation, a copy of the manuscript was sent to Sukhumi for the authors' criticisms and corrections. We are grateful to them for their hospitality on the occasion of Dr. Koford's visit and for their cooperation in facilitating this translation of the book.

The importance of the studies reported in this monograph has been stressed in the preface by Dr. I. V. Davydovskiy. There has been a great increase in scientific interest in America in nonhuman primates during the last few years. The use of monkeys, especially the species *Macaca mulatta*, has become more prevalent. The establishment of new centers for primate research in biomedical sciences, and the growing use of them in existing institutions, has led to demands for more information about diseases to which they are prone. No group of investigators has had so much experience in this matter as the scientists at Sukhumi, under the leadership of Professor Lapin.

The translation follows the original text as closely as possible. Illustrations are placed in approximately the same relationship to the text as in the original. Professor Lapin was able to provide photographic prints of all except four of the original figures. The list of references at the end of the monograph is carried into the translation in the same sequence as they appear in the original. Russian names and titles have been translated, and this accounts for the fact that the references are not in alphabetical sequence. The table of contents has been transferred to the front of the monograph, and an index has been added.

W. F. Windle

AUTHORS' NOTE

This monograph will acquaint the reader with the pathological anatomy of the main diseases of monkeys observed in the Sukhumi animal house over the past thirty years.

The descriptive material is comparative and therefore of interest not only to biologists specializing in the pathology of monkeys but also to the medical profession as a whole, particularly the pathoanatomists.

The reader will find a detailed description of the course and morphology of a number of diseases of monkeys that are also found in man—tuberculosis, dysentery, pneumonia, atherosclerosis, etc. Although the authors emphasize the morphological similarity of the main diseases of monkeys to those in man, they show that the prevalence of the individual nosological forms in monkeys and in man is quite different.

ZOOLOGICAL GARDEN
7385
CALCUTTA

FOREWORD

B. A. Lapin and L. A. Yakovleva's monograph deals with a subject about which medical scientists know comparatively little and veterinarians know only little more. Yet those working on problems in the pathology of man always meet up with the opposite question of how this or that pathological process looks in animals, primarily the higher mammals, monkeys in particular.

This question is tremendously important because a correct answer may provide us with a concrete idea of just what it is that marks man as a conscious being standing above the animal world and at the same time containing within himself certain phylogenetic elements. It is obvious that pathological processes always reflect physiological processes, and since the latter are very similar in the higher mammals of different species, one must expect that the pathology of higher animals will have much in common with the pathology of man. Lapin and Yakovleva's monograph gives a positive answer to this question. However, the authors clearly show how sharply and fundamentally the diseases of monkeys differ from the analogous diseases of man. This fact alone opens up a vast field of research to determine the true causes of these major differences and, above all, to try to understand to what extent the social factors created by man and affecting the animals shape or deform the nosology of animals, monkeys in particular. For, diseases will always be a "regular" phenomenon, a reflection of the continuous interaction of the organism with the environment. The authors are correct in stressing that the diseases of monkeys they describe are not diseases of monkeys in general, but diseases under the specific conditions of the Sukhumi animal house. These conditions, of course, do not duplicate their normal habitat. However, the authors make an interesting attempt to link changes in climate, diet, etc., to the diseases of the animals. Their discussion of radical changes in the way of life of the monkeys (restrictions on movement, rhythm in feeding, digestion, etc.) and the possible relation of these factors to morbidity are also interesting.

It is difficult to ascertain just what diseases are peculiar to monkeys in their normal habitat. Yet the authors are undoubtedly correct in their view that the very fact that diseases normally not observed in monkeys can be reproduced in the animals testifies to the tremendous importance of the environmental factors and way of life of man in the development of disease.

The material for this work comes from the dissection of 1,000 monkeys. This guarantees the soundness of the authors' general findings, which are by no means diminished by the fact that the animals died under the special conditions obtaining in the Sukhumi animal house. One of the cardinal findings on the predominance of infectious diseases among newly arrived monkeys (dysentery, pneumonia) bespeaks the obvious importance of unnatural conditions and way of life in the development of infections (chiefly autoinfections, it would seem) and in complicating their course.

Despite the similarities between monkeys and man, the authors succeeded in demonstrating that the strains of dysentery bacilli obtained from man are almost nonpathogenic in monkeys, even when used in massive doses. Yet it is precisely from dysentery (spontaneous) that a great many animals die, especially among those newly arrived. As for tuberculosis and the sharp reduction in morbidity, the authors justly emphasize the importance of proper care of the animals. State and public measures aimed at regulating work, rest, diet, social security, etc., have led to the inclusion of tuberculosis among those infectious diseases whose eradication is a practical possibility. In the case of both tuberculosis and dysentery, the authors note the apparent paradox that experimental infection and natural disease are theoretically different things. Nevertheless, this is a fact. As is to be expected, monkeys under natural conditions do not suffer from cardiovascular diseases so typical of man with his unique and highly tense mental and emotional activity. Neuroses arising in the animal house and those experimentally induced can cause such conditions as hypertension. This indirectly confirms the view held on the role of mental and emotional acts in the development of these diseases in man and on the mediation of these acts by the vasomotor centers. The authors offer no explanation for the actual absence of tumors in monkeys even under the conditions of the animal house, i.e., after applying to the monkeys several additional irritants.

It is apparent that the authors' paradoxical findings on the comparatively high resistance of monkeys to dysentery and tuberculosis follow naturally from their data on the rather low morbidity of animals in the main group, especially those living in open-air cages, despite the prevalence of bacilli carriers among them. Noteworthy too is the absence of changes typical of tuberculosis in the monkeys that for many years have had positive allergic reactions to tuberculin.

This work also describes in detail the pathological anatomy of the diseases of monkeys encountered in the Sukhumi animal house. It will be read with interest by those concerned with problems of infectious and comparative pathology.

I. V. DAVYDOVSKIY

CONTENTS

COMPARATIVE PATHOLOGY
IN
MONKEYS

INTRODUCTION

In recent years monkeys have come to be increasingly used in medical and biological experiments. The need for experimental models of various human diseases in order to study their etiology and pathogenesis has made the monkey a convenient if not at times irreplaceable experimental animal due to his anatomical and physical resemblance to man. The result is a substantial increase in the number of studies of monkey anatomy, physiology, and biology. This research is both theoretical and practical in value because without fairly accurate ideas about the anatomy and physiology of this animal it is impossible to interpret experimental findings intelligently.

However, before we can significantly expand medical research on monkeys we must also become more familiar with the diseases that arise without experimental intervention. Otherwise diseases originating spontaneously might be taken for those experimentally reproduced. A knowledge of monkey pathology and the conditions under which it develops and a comparison of it with the pathology of man and other animals can help us to gain a deeper understanding of the causes and nature of several human diseases.

The present study is an attempt to describe the diseases of monkeys comparatively in terms of the corresponding or similar nosological forms in man. At the same time we fully realize that we are not describing monkey diseases in general, but only those arising under the specific conditions prevailing in the animal house. We tried our utmost to duplicate the conditions of their natural habitat, but could only approximate them. Changes in the climate and diet, limited movement because of the lack of need to search for and obtain food, etc., promote the development of a number of pathological processes in monkeys.

Contact with human beings undoubtedly has a profound impact on the range of diseases to which the monkeys may be prone.

The complex interrelations between man and animals in the animal house has forced the monkeys to adopt to some extent the rhythm of the physiological functions characteristic of man. Feeding routines, methods of cleaning the rooms and open-air cages, catching the animals for experiments, etc., have their effect along with exposure to a variety of injuries, irritants, and the causative agents of infectious diseases that attack man. Of apparent significance too are the changes in inhaled air due to increased content of the combustion products of various fuels, inclusion in the diet of foods eaten by man as well as monkey foods thermally treated, etc.

It is a fair assumption, therefore, that the diseases of the animals in their natural habitat, the nosological character of their illnesses, will differ substantially from the situation prevailing when they are in close contact with man. Some help in solving the problem will come from comparing the morbidity of monkeys recently brought to the animal house with that of the animals that have been there for some length of time. Inadequate care, prolonged harmful irritation and unfavorable situations resulting in traumatization of the animals' central nervous system have sometimes led to the development of such "human" diseases as hypertension, coronary insufficiency, etc.

Monkey pathology both resembles and differs from human pathology. In comparing the two, it must be remembered that we observed diseases in animals that were in contact with man for a comparatively short period of time over one generation, less frequently over two generations. An animal just taken from its habitat still retains acquired and inherited characteristics not peculiar to man. At the same time it does not have a great many of the new characteristics acquired by man in the course of his social evolution.

Thus, despite their great biological resemblance to man, monkeys should naturally be expected to react differently to various injuries.

In analyzing their diseases we have tried to take into account such significant factors as the way they are kept in the cages, use in and nature of the experiments, length of time in the animal house, circumstances of transportation, etc. That is, through analysis of the conditions to which a given animal was exposed, we endeavored to find in its way of life those harmful factors which may have caused an existent disease or promoted its development. This, unfortunately, did not always prove to be a simple matter.

We believe that the diseases arising in monkeys kept in captivity are indicative not so much of the prevalence and frequency of these diseases among the animals as of the theoretical possibility of reproducing them. We do not intend to present the pathology of monkeys in general because the nosology of diseases in monkeys is largely influenced by the way they are kept in the animal house and may well change if the conditions are modified. Elucidation of the factors conducive to the development and acquisition of various pathological characteristics without experimental intervention may be useful to experimenters in obtaining models of the various diseases of man.

This investigation was carried out in the Sukhumi monkey house of the Institute of Experimental Pathology and Therapy, Academy of Medical Sciences, U.S.S.R. There are now about 1,000 animals, chiefly of two species—macaques and hamadryads. The number and proportion of species vary with shipments of new batches of animals, births, and deaths either in experiments or from diseases. Every year about 100 or 120 rhesus monkeys, hamadryads, and green marmosets are born in the animal house and 500 animals are acquired for use in a variety of acute experiments.

A warm humid climate with a mean annual temperature of about +14.5° C., a great many hot sunny days, luxuriant evergreen vegetation, and an abundance of vegetables and fruits in Sukhumi tend to make the conditions partially resemble those of the monkeys' natural habitat. The animals do not all live in the same way. The breeding group is kept in open-air cages the year round. A few animals are also kept there in between experiments. The monkeys used in experiments remain in regular cages.

The records of the animal house and monkey clinic from 1927 to 1959 along with the data from 1274 autopsies made between 1952 and 1959 served as material for the investigation (Table 1).

This material is distributed as follows: 417 autopsies—the main group of animals dead of diseases or killed in experiments;

TABLE 1

AGE OF THE MAIN GROUP OF MONKEYS AND OF THE IMPORTED MONKEYS THAT DIED FROM 1952 TO 1959

	Main Group									*Imported*		
	Macaques			*Baboons*			*Green Marmosets*			*Macaques*		
Age of dead monkeys, years	*Female*	*Male*	*Total*	*Female*	*Male*	*Total*	*Female*	*Male*	*Total*	*Female*	*Male*	*Total*
Up to 1	23	29	52	17	34	51	9	8	17	9	6	15
1-2	7	21	28	5	22	27	1	2	3	218	350	568
2-3	10	19	29	3	10	13	1	4	5	28	34	63
3-4	3	7	10	—	7	7	—	3	3	9	8	17
4-5	2	6	8	—	3	3	1	1	2	9	9	18
5-6	2	5	7	4	3	7	1	—	1	10	11	21
6-7	4	10	14	2	2	4	—	—	—	16	6	22
7-8	3	7	10	2	7	9	2	1	3	12	2	14
8-9	6	4	10	1	5	6	—	2	2	6	4	10
9-10	5	2	7	2	3	5	—	2	2	3	1	4
10-11	4	4	8	1	1	2	—	2	2	4	—	4
11-12	1	—	1	2	3	5	—	—	—	2	—	2
12-13	3	2	5	1	2	3	1	—	1	1	2	3
13-14	5	2	7	—	1	1	—	—	—	—	—	—
14-15	3	—	3	1	1	2	2	—	2	—	—	—
15-16	5	—	5	4	—	4	2	1	3	—	—	—
16-17	2	1	3	1	—	1	1	—	1	1	—	1
17-18	1	1	2	—	—	—	—	—	—	—	—	—
18-19	1	—	1	1	—	1	—	—	—	—	—	—
19-20	1	—	1	1	—	1	—	—	—	—	—	—
20-21	—	—	—	2	1	3	—	—	—	—	—	—
21-22	—	—	—	—	—	—	—	—	—	—	—	—
22-23	2	—	2	—	—	—	—	—	—	—	—	—
23-24	1	—	1	—	—	—	—	—	—	—	—	—
Total	94	120	214	51	105	156	21	26	47	327	435	762

762 autopsies—animals imported from India and China dying within the first two years of their arrival in the animal house; 95 autopsies—stillborn animals. As regards the 762 imported animals, the usual causes of death were dysentery, salmonellosis, pneumonia, parasitosis, and, less commonly, tuberculosis. Dysentery was the major cause of death. Among the noninfectious diseases, gastric adenomatous polyps were occasionally found among the imported animals. The nosological pattern in monkeys of the main group is somewhat more varied owing to a number of diseases academically noted during autopsy but not the usual causes of death. In addition to the above-mentioned infections, poliomyelitis, measles, jaundice, Morgan's toxinfection, and some other infectious diseases. Such noninfectious diseases as hypertension and coronary insufficiency, atherosclerosis, and possibly cholelithiasis may well be related, in our opinion, to the way the animals are kept in the monkey house.

We should like to begin by emphasizing that in principle these diseases can be found in other animals too. Some of them are described in veterinary textbooks in connection with domestic animals and in laboratory manuals in connection with experimental animals. For example, the infectious diseases cited by us, except dysentery, are found in rodents while cholelithiasis is prevalent in cattle. A process in the aorta closely resembling atherosclerosis has been noted in swine and cattle. However, it seems to us that these pathological conditions in monkeys are closer to the analogical phenomena in man. In calling certain noninfectious diseases "purely human" we meant merely to point out that they are associated with activities characteristic of man alone. In hypertension and coronary insufficiency, emotional tension with frequent overstrain of higher nervous activity and conflicts is a major factor.

G. M. Cherkovich's research on monkeys has shown that artificial disruption of the normal daily rhythm of physiological functions very quickly results in severe neurotic states and a pathological condition of the cardiovascular system. For the monkey—an animal with complex higher nervous activity—the mere fact of confinement in an animal house is traumatic enough to lead to neurosis and eventual disorders of the cardiovascular apparatus.

We believe that it is theoretically possible to reproduce cardiovascular diseases in other animals too (but perhaps less similar to the corresponding diseases in man) provided that these animals are subjected to those irritants which are most significant for the given species.

Our material consists essentially of two parts: infectious diseases and noninfectious diseases. An in-between position is occupied by the commonest helminthic and parasitic diseases in monkeys. We have presented the material by nosological feature, deviating on occasions to describe the data in terms of tissues or organs. The information on clinical symptoms is based partly on our own observations, but mostly on case records of our monkey clinic and on published reports.

INFECTIOUS DISEASES

Among the infectious diseases dystentery, tuberculosis, and salmonellosis are most fully treated in the literature. Most of the reports deal with descriptions of clinical and bacteriological observations of enzootic outbreaks of the diseases among monkeys in animal houses and zoos. In recent years a good deal of attention has been accorded in the literature to the observations of control laboratories of institutes and laboratories manufacturing poliomyelitis vaccine. These observations are valuable because of the extensive material and because in most cases the animals died or were sacrificed fairly soon after they were taken from their natural habitat. We may assume, therefore, that any diseases found in the animals are characteristic of their habitat. There are some exceptions in the form of acute infections that are apparently not associated with the animals' habitat, although they develop soon after they are brought into the animal house, as we shall try to show later.

An analysis of more than 13,000 autopsies of monkeys sacrificed for the preparation of vaccine or that died of various diseases in two poliomyelitis institutes in Moscow shows that the number of nosological forms in imported monkeys is extremely limited (A. P. Savinov and A. V. Tyufanov, 1957; L. A. Porubel; I. A. Prokhorova, A. N. Sergeyev, and Yu. M. Slavin, 1958). We know of almost no diseases of monkeys peculiar to their natural habitat. Lovel (1929) says that wild monkeys have no bacterial infections. It is a safe assumption that there are not many of these and generally it is a question of diseases peculiar to monkeys and not found in man. Savinov and Tyufanov, relying on the pathoanatomical data of autopsies on monkeys sacrificed for the production of poliomyelitis vaccine, report on malaria as a disease of monkeys. The basis for this finding was the presence in many animals of an enlarged spleen and pigment comparable to those in malaria cases. However, the authors failed to find the malarial plasmodium, and so we have to treat their conclusions with some caution. Thompson (1929) told about the discovery of plasmodia in the blood of chimpanzees and gorillas, stating that it was hard to say whether the animals were suffering from malaria or how pathogenic the plasmodia were. Rigdon and Stratman (1942) demonstrated the possibility of experimentally reproducing the disease in monkeys by injecting them with plasmodia. Thompson mentioned finding trypanosomes in the blood of monkeys living in areas of Africa where sleeping sickness is prevalent. He referred to the possibility of reproducing the disease in the animals, adding that they can develop the disease spontaneously.

Rhesus monkeys are frequently carriers of virus B (K. S. Blinnikov, 1958), which is only slightly pathogenic or nonpathogenic for them. However, experimental intracerebral infection of the animals with the virus caused severe meningo-encephalomyelitis with spastic paralysis. Pathoanatomical examination revealed deep involvement of the blood vessels and, apparently, secondary involvement of nervous tissue (N. E. Rozina, 1958). Work and Trapido (1957) and Work and others (1957) described an outbreak in a forest in the state of Mysore. Since similar mass deaths of monkeys have been accompanied from time to time by epidemic outbreaks of "forest yellow fever" among people, the authors made a study of the monkeys and established the viral nature of this disease. The susceptibility of the animals to a particular infection varies from species to species. Monkeys in the New World are highly sensitive to the yellow fever virus, whereas chimpanzees are not (Hindle, 1929).

Thus, data in the literature justify our speaking of the sick rate of wild monkeys from yellow fever, from the disease caused by the virus of human "forest yellow fever," and possibly from malaria and sleeping sickness. We may also speak of monkey carriers of virus B, which is highly pathogenic for man and certain animals (rabbits, cotton rats), but nonpathogenic or only slightly so for monkeys. The bacterial infections, as mentioned above, include dysentery, salmonellosis, and tuberculosis. There have been occasional cases of poliomyelitis in anthropoid apes (Howe and Bodian, 1944, and others), an outbreak of icterohemorrhagic leptospirosis among chimpanzees (Wielbert and Delorme, 1929).

pasteurellosis (E. D. Dzhikidze. and S. M. Pekerman, 1958; Smitl , 1954) and an outbreak of measles among monkeys (N. Ye. Ryazantseva, 1956). As far as such diseases as poliomyelitis and measles are concerned, we are quite sure that they are caused by close contact with man.

Our material deals with dysentery and penumonia, which are very common, tuberculosis, which is less common, and the isolated cases of poliomyelitis, Morgan's toxinfection, and paratyphoid that we personally observed. Meningitis, brain abscess, myocarditis, and pericarditis occasionally occur as a complication of other diseases.

DYSENTERY

Dysentery is now recognized as one of the most common diseases of monkeys in captivity. Monkeys seem to be the only animals that develop the disease spontaneously. Hill's account of a case of dysentery in a camel in the London zoo (1952) lacks a detailed analysis and therefore cannot be taken into consideration. We must emphasize once again that we are concerned with dysentery only in captive monkeys, for at the present time there isn't a single report mentioning the disease in the wild animals.

Many scientists have published articles on dysentery in monkeys (Baumann, 1910; Stadie, 1930; Fairbrother and Hurst, 1932; Preston and Clark, 1938; Jonson, 1939; Hamerton, 1941; Rewell, 1948; Hill, 1951, 1952, 1957; Ye. V. Abramova, 1949; G. I. Rozenbaum, 1953; E. K. Dzhikidze, 1954; and many others). Several of these authors (Stadie, Dzhikidze, and others) note the prevalence of the carrier state without any clinical symptoms of the disease. An outbreak of the disease usually causes the death of many animals.

In studying the dysentery bacillus carrier state and the disease itself in the Sukhumi monkey house, E. K. Dzhikidze (1954) found no distinct seasonal variations in the spread of the disease. She discovered that the commonest causative agent was Flexner's bacillus transmitted from animal to animal by contact. The rods were found in the feces of animals as young as two or three months, and they were generally suffering from dysenteric colitis. According to Dzhikidze, monkeys up to three years old are the most susceptible to dysentery. Ye. V. Abramova (1949), E. K. Dzhikidze (1954), A. S. Aksenova and O. P. Viktorova (1949) described several outbreaks of the disease in the Sukhumi animal house, noting that an increase in the number of cases usually coincided with the arrival of a new batch of animals. They believe that newly arrived animals suffering from dysentery facilitated the spread of the disease in the original herd.

It is clear from the materials on dysentery in monkeys that the colitis rate of the animals that have been in the monkey house a long time differs considerably from that of newly arrived animals. This has become particularly apparent of late when deliveries of large batches have been stepped up.

One gets the impression from studying the data of the above-mentioned authors that it is the newly arrived rather than the older animals that make up most of the cases of dysentery occurring during outbreaks. To determine the frequency of dysentery in the main group, we analyzed the years when no new animals were brought to the monkey house so as to avoid mingling the morbidity rate of the new animals with that of the main group. These years include the period from 1940 to 1948 when, according to A. S. Aksenova (cited in E. K. Dzhikidze, 1954), there were only isolated cases of dysentery.

The difference in rates is apparently not directly related to the greater incidence of the disease among the new animals. For example, 14% of a fresh batch arriving in 1937 were found to be carrying bacilli; 6 out of 53 or 11.3% died of colitis (the number of sick animals could not be ascertained). In 1940, on the other hand, according to Aksenova, the main group included 21% carriers. Moreover, out of 133 monkeys only 4, or 3%, had clinically pronounced dysentery. Dzhikidze's systematic examination of the main group from 1950 to 1952 made to determine the prevalence of the dysentery carrier state revealed that a great many animals had the disease. In 1952, the total number of carriers in the group amounted to 38.3%. The author further notes that despite the prevalence of the carrier state, the dysentery rate was relatively low, averaging 10 to 14% of the carriers. She offered no explanation for this, but did say that in some cases the disease remained undetected possibly because it was asymptomatic. The same thing was observed the following years. In 1954, for example, 45% of the main group were carriers, but the dysentery rate was only 7.1%.

Quite interesting in this connection are the 1957 data when 400 Indian rhesus monkeys were delivered to the animal house between May and December. It turned out that 76.5% of the animals (306 out of 400) were clinically sick, as revealed by the presence of diarrhea of different kinds and severity that showed up at the initial examination. Dysentery bacilli, chiefly of the Flexner type, were found in the feces of 256 animals (64%) during the second and third examinations. Within the first two months of their arrival 124 (31%) died. During the same period of time the main group of 600 monkeys in the animal house included 195 carriers or 32.5%. Of these 26 animals or 4.3% were sick and 13 eventually died of the disease.

Our figures relate for the most part to macaques, chiefly those imported from India. However, despite the comparatively low dysentery rate in the main group, the mortality rate among the sick animals was substantial. This was also observed in 1958 when 9 out of 13 sick monkeys in the main group died of dysentery.

According to Dzhikidze, dysentery is rare among marmosets and baboons. In 1952, despite the considerable number of bacillus carriers in the band of baboons, none of them seemed to have dysentery. The author thinks this is due to the low species susceptibility of baboons to the disease.

An analysis of the bacteriological examinations and data on the morbidity and mortality of baboons leads to the same conclusion.

It is unfortunate that we have no information on the carrier state and dysentery rate of the baboons from 1927 to 1950. The slight incidence of the disease among these animals is indirectly attested by the low ratio of dysentery mortality to total morbidity. During this time only 7 baboons died of the disease. Annual bacteriological examination of the animals from 1950 to 1956 (the number of animals examined in the different years ranged from 72 to 227) showed that the percentage of carriers varied from 37% to 16.5%. Throughout this period a total of 10 monkeys had dysentery, 3 of which died. In 1957, 24.6% of the animals were carriers. This figure, however, does not include cases of the disease. An-o her bit of indirect evidence of low susceptibility is the fact that there wasn't a single outbreak of dysentery in the batch shipped from Africa in 1948 (largely baboons).

Among the macaques Indian monkeys seem to be more susceptible than Chinese monkeys. For example, despite the substantial number of carriers among the animals imported from China in 1955-1956 (13 carriers out of 28 examined), there was virtually no clinically pronounced case of the disease.

According to Abramova (1952), Dzhikidze (1952), Preston and Clark (1938), and others, clinically acute dysentery in monkeys occurs in the form of a mucopurulent colitis. In addition, the feces are more or less admixed with blood. I. S. Gvazava (1958) mentions the polymorphism of dysentery symptoms in monkeys. In severe cases of an acutely developing disease where the animal may die on the second or third day, the author observed sharp deterioration in the animal's general condition—sluggishness, immobility, rejection of food. Body temperature drops along with blood pressure and the skin becomes pallid. Pronounced signs of dehydration accompanied by sunken eyes and decreased skin turgor are common. The latter may develop very quickly, in less than a day, as we have ourselves observed. A typical symptom, according to the author, is diarrhea with an admixture of mucus and blood and frequent tenesmus. Vomiting is common. Dysentery may also develop in a mild form when the diarrhea stops within three or four days and the animal recovers spontaneously without medication. The diarrhea is characterized by varying amounts of mucus in the feces. There are also apparently transitional forms when the symptoms are more or less distinctly pronounced. Gvazava has noted even milder forms of the disease with a blurred clinical picture. The diagnosis here requires confirmation by bacteriological examination and sigmoidoscopy.

Dzhikidze, Gvazava, and other investigators of dysentery in monkeys state that colitis often recurs in the same animal. They regard this as a form of chronic dysentery. It may show up clinically during periods of exacerbation of the process as a typical purulent hemorrhagic colitis or develop atypically when the animal has so-called loose stools with frequent mild bouts of diarrhea. None of the investigators, unfortunately, mentions whether there is any difference in clinical symptoms between monkeys that have been in the animal house for some time and those recently brought there.

What has been said above applies chiefly to macaques and green marmosets. Observing baboons, Gvazava found that at times dysentery develops in typical fashion, while at other times the disease shows up as ordinary diarrhea resembling dyspepsia.

There are just a few references in the literature to the nature of the pathomorphological signs of dysentery in monkeys and they deal mostly with macroscopical lesions of the intestine (Preston and Clark, 1938; N. P. Tsvetayeva, 1941; Revell and Bridge, 1948; Ye. V. Abramova, 1949; B. A. Lapin and L. A. Yakovleva, 1957). After noting the great similarity between the morphological manifestations of the disease in monkeys and those in man, the authors generally characterize dysentery in monkeys as an ulcerative diphtheritic process. Tsvetayeva notes that in prolonged illnesses the process developed sluggishly in the mucosa of the large intestine together with hemorrhage and edema in numerous retention cysts. Yakovleva (1958) describes the morphology of dysentery in monkeys, emphasizing its polymorphism as well as its resemblance to the pathoanatomical manifestations in man.

Over a period of six years we observed a total of 582 cases of dysentery of which 58 were in the main group of animals and 524 were imported animals.

The pathomorphological manifestations of dysentery in monkeys differ both macroscopically and microscopically in nature and degree of injury to the walls of the intestine. An autopsy generally shows a distended intestine, especially near the cecum. This distention is almost always uneven. Distended areas of the intestine alternate with contracted areas. Less commonly the intestine is contracted almost throughout while the intestinal lumen is sharply constricted.

Desquamative muccous catarrh is the mildest form of intestinal wall injury. The lumen of the large intestine is ordinarily filled with masses of liquified feces admixed with varying amounts of mucus. The mucosa of the large intestine is unevenly swollen, pink, with occasional hemorrhages. The folds of the mucous membrane are thickened (Fig. 1). A microscopical examination reveals a thickening of the mucosa due to edema and distinct signs of

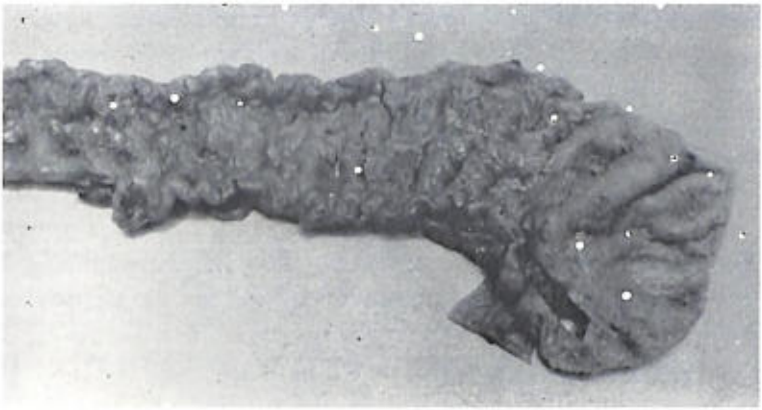


Fig. 1. Catarrhal colitis. The Javanese macaque Yagdar.

Fig. 2. Photomicrograph. Mucodesquamative colitis. The green marmoset Isa. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

desquamation and necrosis of the epithelium (Fig. 2). The epithelium abounds in goblet cells. The crypts are generally enlarged and overflowing with mucus. Together with the mucus the desquamative cells form a layer of varying thickness on the inner surface of the intestine where occasional lymphoid and leukocytic cells are visible in the midst of the necrosing epithelial cells. Retention cysts of varying sizes filled with mucus are frequently found in the mucous membrane. The connective-tissue stroma of the mucous membrane is infiltrated by cellular elements somewhat larger than usual. Accumulations of macrophages and, less commonly, of leukocytes can be found. Small craterlike defects can be observed in areas of thickened edematous mucosa where the mucosa has been destroyed to the base. The resultant defects are filled with an exudate containing varying amounts of leukocytes.

The blood vessels of the mucous and submucous layers are dilated. Here and there one encounters hemorrhages. The submucous layer is slightly edematous generally in the area of the folds of the mucosa. There is no perceptible infiltration of the submucous layer; only small, mostly perivascular infiltrates can be seen. The connective-tissue cells of the submucous membrane, in particular the endothelial cells of thin-walled blood vessels, usually have large, rounded, light-colored nuclei.

In some cases of catarrhal desquamative colitis the edema and thickening of the intestinal wall are much more pronounced and the surface of the mucosa is jellylike in character, mottled, with a great many hemorrhages. The folds are generally coarse and thickened. Every now and then small superficial defects appear on the inner surface. Microscopical examination in these cases reveals the necrosis of intestinal epithelium both facing the intestinal lumen and in the crypts. Remnants of the crypts can be found only in the basal portions of the mucosa. In places the epithelium of the crypts is almost completely necrotic so that the only thing remaining of the intestinal mucosa is loose, edematous connective-tissue stroma. There is no evidence of abnormal production of mucus in these portions of the mucosa. On the contrary, the crypts seem to be collapsed and, as a rule, lacking in goblet cells (Fig. 3). The lumens of the vessels are often filled with fibrinous thrombi. Infiltration of the submucosa is very slight.

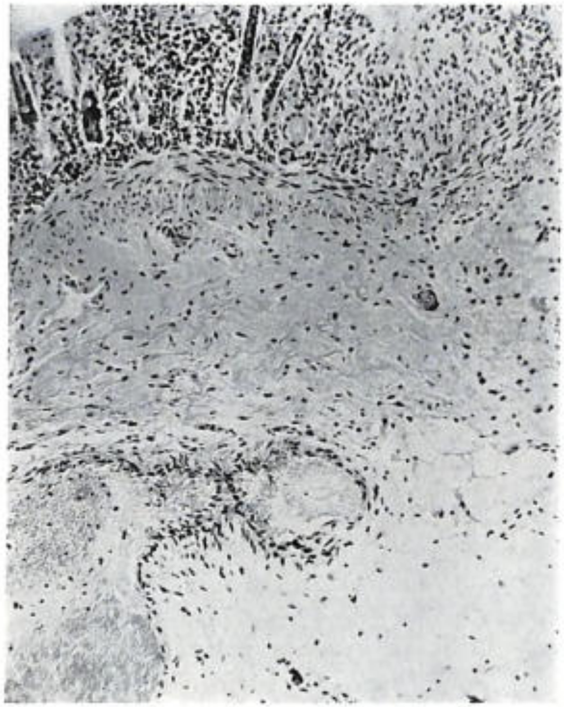


Fig. 3. Photomicrograph. Severe desquamative catarrh. Marked edema and hyperemia of the intestinal mucosa and submucosa. The rhesus monkey Shchurka. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

The microscopical picture described above ordinarily is not uniform. Less damaged areas showing a marked increase in the production of mucus can be seen throughout the large intestine along with destroyed areas.

However, the process in the large intestine is more frequently not limited to edema, hyperproduction of mucus, and necrosis of crypt epithelium. Here and there it acquires the character of a mucopurulent inflammation, sometimes slightly admixed with fibrin and necrotic areas in the mucosa. Macroscopically, one can see here on the inner surface of the intestine islets of yellowish-gray deposits tightly adhering to the injured portion of the mucosa. Infiltration of the mucous and submucous layers chiefly by leukocytes is more sharply pronounced.

Fig. 4. Diphtheritic colitis. The rhesus monkey No. 2230.

In cases where the process resembles diphtheritic colitis, the mucosa of the large intestine is found to have scattered islets of rough, dirty gray films tightly adhering to it. Much more rarely fibrinous deposits can be seen almost everywhere on the mucosa of the large intestine (Fig. 4).

Microscopical examination of the affected areas of the intestine shows deep necrotic patches not only embracing in places the entire thickness of the mucosa, but also reaching at times the submucous layer, which may result in the formation of pockets of pus. The necrosed tissues and adjacent areas of surviving intestinal wall contain an extremely large quantity of cellular elements chiefly made up of segmentocellular leukocytes.

Infiltration and edema cause the mucosa to thicken to four or five times its normal size. Intestinal crypts partially undergoing necrosis are generally preserved only in the basal portions of the mucosa. In some of them the lumens are enlarged and filled with a leukocytic exudate. In places the necrosed tissue saturated with the exudate is torn away while the bare surface of the intestinal wall is lined with young epithelium starting from the surviving portions of the crypts (Fig. 5). The young epithelial cells of the newly formed crypts covering the base of the defect are frequently flattened and have a large light-colored nucleus. No mucus can be seen in the protoplasm of these cells. Regeneration of intestinal epithelium is more readily observed in places where there are no fibrinous purulent deposits on the surface of the mucosa. Detach-

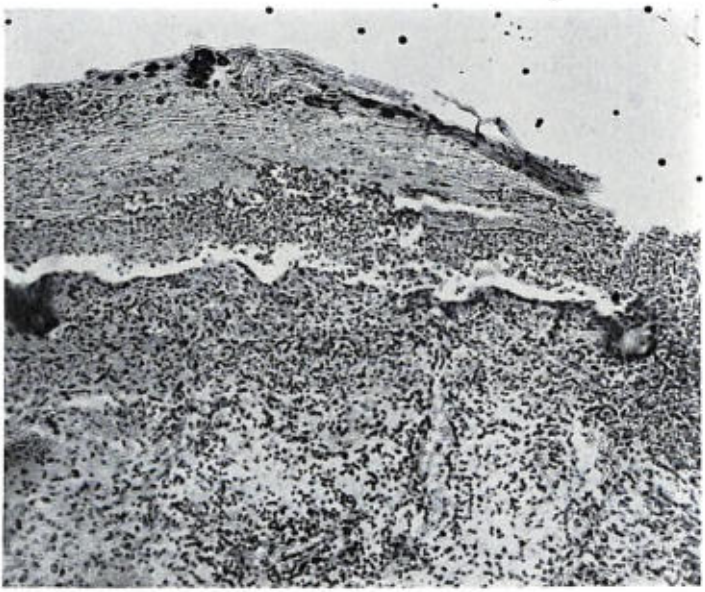


Fig. 5. Photomicrograph. Epithelial regeneration in diphtheritic colitis. The rhesus monkey Zukkur. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

ment of the exudate may lead to the development of numerous ulcerative defects (Fig. 6).

This process is accompanied by the development of edema in the submucous layer and by intensive leukocyte and histiocyte infiltration of the latter, especially near the tunica muscularis mucosae.

A great many leukocytes are found in the lumens of the blood vessels, filling them almost completely.

Many hemorrhages can be seen throughout the intestinal wall, especially where it borders the affected portions and in the general area of these portions. The vessels in diphtheritic colitis are dilated, but there is no indication of the pronounced dilatation of the thin-walled vessels that can sometimes be observed in a severe case of acute desquamative catarrh.

Much rarer by comparison with the above forms of colitis are cases with a predominance of the necrotic process in the mucosa

Fig. 6. Ulcerative colitis. A rhesus monkey.

of the large intestine, in which the cellular character of the infiltration in involved areas is not marked.

Macroscopically the process does not differ from the usual diphtheric colitis. However, microscopical study of such cases shows that the widespread necrosis, frequently affecting the entire mucousa, and extending in places to the submucous layer, contains almost no cells. The lumen surface of the intestinal wall shows definite features of microbism. The necrotic portions are frequently filled with an albuminous exudate. In some areas there is little exudate, in others the abundant accumulation of exudate on the mucosal surface leads to its marked thickening. Occasionally it is possible to distinguish contours of former crypts and vessels in the anuclear necrotic tissue. Such blood vessels are filled with homogeneous thrombi. On the periphery of the necrotic zone, at the boundary of intact tissues, are seen large quantities of cell fragments and greater or lesser accumulations of cells, predominantly leukocytes; there is marked proliferation of histiocytic elements. Accumulations of leukocytes and homogeneous thrombi are seen in the dilated blood vessels. The vascular endothelium is markedly swollen. Cellular infiltration continues along the course of the blood vessels. Perivascular small hemorrhages are frequent. In places necrotic sections of tissue are separated from the intestinal wall forming various size ulcers.

The submucous layer is thickened four, five to six times because of edema. Various degrees of hyperemia and edema of the serous layer is frequently observed. Rarely one can see areas where necrotization is extensive enough to include not only the mucous but virtually the entire submucous layer, down to the muscle tissue. In such cases one can easily see that the repeating necrotic process has spread along the former cellular torus as well as along the periphery of the previously involved area. Accumulations of cellular elements are not found along the edges of the secondary deep necrosis. Only dilatation and engorgement of many blood vessels is noted.

Together with the above-described cases of dysentery, in which macro- and microscopical studies of the large intestine revealed well developed inflammatory lesions, a considerable percentage of monkeys perishing from far-gone diarrhea showed a different picture at autopsy. The intestinal wall, in the large as well as in the small intestine and the stomach, was thinned out. The lumen of the large intestine was dilated and filled with foul smelling, dirty-grey liquid. The mucosa was pink, with poorly defined folds, and showed varying numbers of small hemorrhages.

Microscopical study showed a thin mucous membrane, its height frequently varying in different parts of the large intestine. There was a distinct decrease in the number of crypts (Figs. 7, 8) which frequently were seen only in the basal portions of the mucousa. The epethelium lining of the intestinal lumen was frequently missing. Interspread with this were mucous membrane portions with engorged blood vessels. In these cases the tissue of the mucosa is often diffusely saturated with blood for a considerable distance. Some parts of the surface of the mucosa contain small deposits of fibrin with a few leukocytes included. The submucosa may be quite edematous, especially in the areas of hemorrhagic saturation of the mucosa. The blood vessels are dilated, with a great many leukocytes frequently present in the lumens. Thus, in acute cases the morphological manifestations of dysentery may be different. Sometimes desquamation of the epithelium and edema of the mucosa accompanied by intensified production of mucus predominate. At other times when necrosis of epithelium reaches substantial proportions, intensified production of mucus

Fig. 7. Photomicrograph. Liquefaction of crypts in the mucosa of the large intestine in dysentery. The rhesus monkey Ruta. Stained with hematoxylin-eosin. Obj. 20, oc. 10.

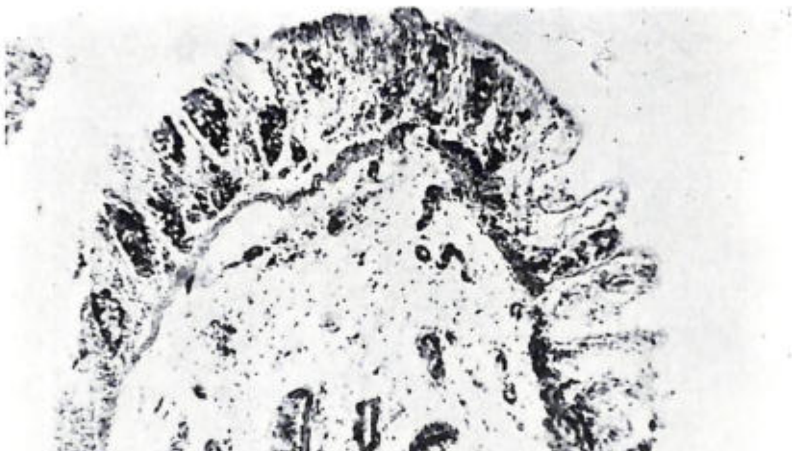


Fig. 8. Photomicrograph. Atrophy of the mucosa of the large intestine, edema of the submucosa. The rhesus monkey No. 2420. Stained with hematoxylin-eosin. Obj. 10, oc. 7.

is not in evidence. Manifestations of dysentery in the form of diphtheritic colitis may also vary in accordance with the nature of the cell reaction in the areas affected. In some cases this is characterized morphologically by copious leukocyte infiltration of necrotic portions, in others there is extensive necrosis with vague cell reaction. Finally, the colitis may be morphologically characterized by distinct signs of atrophy in the mucosa of the large intestine, which clearly predominate over the inflammatory process. In distinguishing the individual forms of dysentery, it should be pointed out that the process is never uniform throughout the large intestine so that one can speak of the morphological forms of the disease only in the sense of this or that process being predominant in the intestine. For example, along with severely affected necrotic portions of the mucosa there are portions exhibiting lesser injury in the form of a mucodesquamative catarrh, etc.

Morphologically, the mildest form of acute dysentery appears to be desquamative colitis, which is accompanied by a sharp increase in the production of mucus. However, the catarrhal form of the disease often follows a very severe course. It is important,

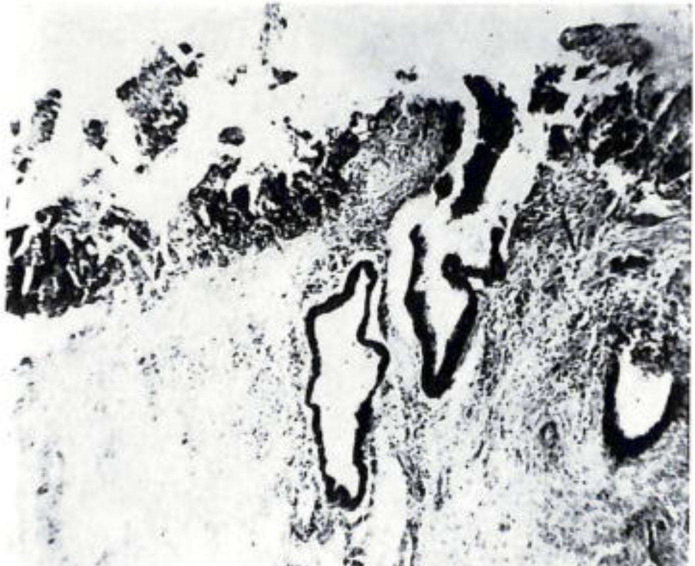


Fig. 9 Photomicrograph. Ingrowth of deformed crypts in the submucosa. The rhesus monkey Shalik. Stained with hematoxylin-eosin. Obj. 10, oc. 7.

Fig. 10. Photomicrograph. Repair of an old ulcer. The rhesus monkey Shustraya. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

in our opinion, to divide catarrhal dysentery into mild and severe forms because the impression exists that the clinical course of the latter is apparently just as severe as in diphtheritic colitis. This is also stressed by M. A. Skvortsov, who has frequently observed in infants' dysentery in the form of a severe catarrhal colitis.

In those cases where not only the epithelium of the intestine but also the connective-tissue stroma of the mucosa undergoes necrosis, the process also appears to develop in various ways depending on the reactivity of the organism. Sometimes there is a strong cell reaction in the form of a ridge on the border of necrotic tissue or marked infiltration of necrotic portions, which may result in their becoming liquefied or detached. Moreover, physiological regeneration of the epithelium is not suppressed so that very often at different periods of death of the animals one can trace the regeneration of epithelium both in the form of new crypts developing on the site of the necrosis and in the form of pronounced epithelization of the defects produced in the mucosa (Figs. 9 and 10).

In other cases the cell reaction is poorly expressed. The necrotic process progresses and spreads to the intestinal wall, tending to embrace here and there the cell ridge previously formed. This severe necrotic, essentially a reactive type of colitis does not seem to be too common and we observed it only among animals newly arrived in the monkey house.

Finally, in cases of death from diarrhea characterized chiefly by atrophy and destruction of the mucous membrane, one can scarcely speak of colitis. Atrophic changes in the large intestine were caused, in our opinion, primarily by nutritional disorders, intestinal dysbacteriosis, and avitaminosis (chiefly B-complex). Dysenteric changes were added to intestinal atrophy caused by the aforementioned factors, although some of the diarrheas were undoubtedly not of dysenteric origin, but were due to atrophic changes in the intestine.

A comparison of the data derived from morphological examination of the intestines of monkeys in the main group and of the imported animals that died one or two months after arrival in the monkey house showed that, despite the general resemblance in morphology, dysenteric colitis in both groups developed as a catarrhal ulcerative inflammation of the intestine.

We noted five cases of diphtheritic colitis and five cases of atrophic colitis among monkeys in the main group (58 animals). At the same time there were 40 cases of diphtheritic colitis and 127 cases of atrophic colitis among 524 imported animals. In terms of percentages (if one can speak of percentages at all with such a comparatively small amount of material), the frequency of diphtheritic colitis was almost identical in both groups – 8.6% of the main group, 7.6% of the imported animals. Atrophic colitis was much more common among the imported animals (24.3% as against 8.6% among the main group in the monkey house).

In comparing the course of colitis in both groups of animals, we were unable to evaluate the effect that may have been exerted by the various antibiotics used. In general, the drugs were administered in about the same combinations and amounts.

Some of the animals we examined (15 macaques of the main group) had frequent recurrences of diarrhea while they were alive, sometimes with a pronounced colitic syndrome. In most cases, however, the picture was blurred. Dysentery bacilli, chiefly the Flexner type, were noted with varying frequency in the feces. The animals were treated with antibiotics when the diarrhea became exacerbated.

Varying degrees of injury to the large intestine were noted macroscopically during the autopsy. The contents of the intestine were generally liquid or pulpy, more or less admixed with mucus. In two instances the contents were formed and resembled "sheep dung" in the sigmoid colon and rectum.

The intestinal wall in most cases was thickened, faintly pink, frequently with coarse folds. In some portions, and sometimes throughout the entire large intestine, the mucous membrane was smooth, almost devoid of folds. The intestinal wall was attenuated in some animals. It was often possible to see a deposit of pigment, which imparted a slate-gray color to these portions of the mucosa. Sometimes it was pale and fine-grained.

Different sections of the large intestine frequently contained ulcerative defects of varying sizes and extent, mostly irregular and geographical in form. The margins of the ulcers were generally well defined due to the ridgelike thickening of the mucosa in these sections. The base of the ulcers was mostly smooth, sometimes fine-grained, and lacking in normal folds. In some cases it was clear, but more often was covered with a grayish deposit. It was often possible to see in the margins and throughout the ulcer different sized, irregularly rounded islets of the mucous membrane protruding into the intestinal lumen in the form of polypous growths.

In two cases there was marked constriction of the intestinal lumen at the sites of extensive ulcerative defects. As a result, the large intestine in one animal was obstructed at the place where the sigmoid colon passed into the rectum. This took place slowly over about a month when the baby monkey's stomach gradually enlarged, becoming two and one half times the normal size when it died. The autopsy revealed extreme distention of the large intestine and lower portion of the small intestine with malodorous, liquid, yellowish-gray feces filling these areas.

Histologically, the structure of the intestinal wall was wholly abnormal in the region of the ulcer. The wall was generally thick-

Fig. 11. Photomicrograph. Chronic cecal ulcer. The rhesus monkey Tara. Stained with hematoxylin-eosin. Obj. 10, oc. 7.

ened at the site of the ulcer. The base of the ulcer contained granulation tissue with varying degrees of maturity, representing part of the submucosa of the intestinal wall (Figs. 11 and 12). These portions had many blood vessels in some of which the lumens were constricted and the walls hyalinized. We could often see scattered bits of muscle fibers in the midst of the sclerosing granulation tissue near the intestinal lumen. Of the mucous membrane in the region of the ulcer there generally survived only individual islets of irregular, disfigured, short, sparsely distributed crypts, often found not only in the mucosa, but also partly in the submucosa (Fig. 9).

Here and there we could see layers of thickened epithelial cells growing on granulation tissue on the side of the surviving crypts. The margins of the ulcer devoid of epithelium on the surface extended considerably over the base; they were made of long, sometimes slightly twisted crypts rich in goblet cells. In some places we saw round cysts filled with mucus or leukocytes. Sometimes we found uneven crypts, the epithelium of which formed papillate protuberances. This type of islets of hypertrophic mucous membrane appeared all over the ulcer. They formed polypous growths in the intestinal lumen.

In some instances the base of the ulcer was almost clear, but

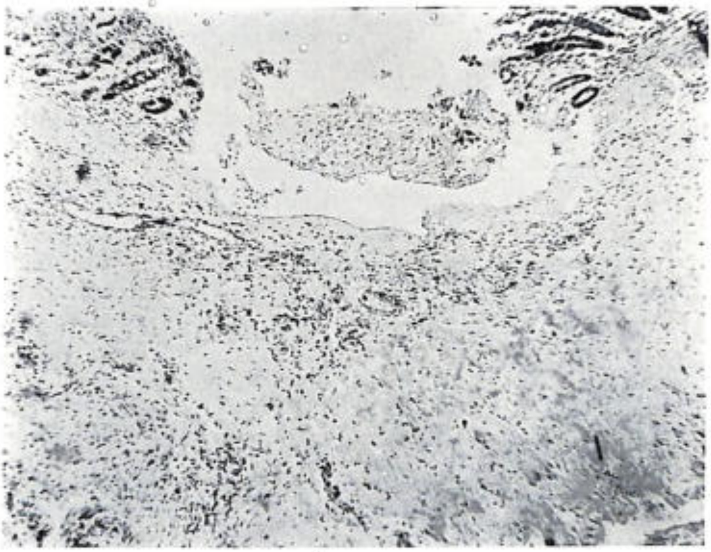


Fig. 12. Photomicrograph. Chronic ulcer of the large intestine with sclerosed base. The rhesus monkey Vil'ya. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

generally the resultant defect was filled with a dense exudate abounding in leukocytes. Irregularly formed portions of the mucous membrane near the base of the ulcer were frequently liquefied into pus and destroyed. Here and there we observed partial detachment of the exudate with a young epithelial layer growing underneath. Wherever there was an accumulation of a purulent exudate in the lumen of the ulcer, we noted intensive infiltration of granulation tissue, chiefly by leukocytic, but also by histiocytic and lymphocytic cellular elements.

In cases where the base of the ulcer was virtually clear, infiltration of the surviving portions of the mucous and submucous membranes tended to be indistinct (Fig. 12). Lymphocytes and histiocytes often predominated among the infiltrating cells. Macrophages and plasma cells could also be seen.

The submucous membrane near the base of the ulcer were sclerosed as well as edematous. In places the serous membrane was moderately edematous. The intestinal wall outside the ulcers likewise frequently appeared to be changed. The mucosa was of uneven height. Atrophic portions were encountered with sparsely distributed crypts. The crypts of the mucous membrane often contained cysts of varying sizes filled either with mucus or with a leukocytic exudate. The submucous membrane here was normal or moderately edematous.

Without going into a detailed discussion of whether or not chronic colitis is "chronic dysentery," we should like to point out that frequent recurrences of diarrhea in monkeys (during which the causative agents of dysentery are often disseminated) lead to extensive reorganization of the intestinal wall. Despite constant regeneration, chronic ulcers are not completely epithelized. The newly formed mucous membrane is very mostly atypical in structure. Disrupted regeneration is characterized not only by the abnormal formation of new crypts in the mucosa, but also by the growth of epithelium into the submucosa with the development there of cysts and deformed crypts. The process of ulcer regeneration is accompanied by sclerosis of the underlying tissues with marked changes in the blood vessels through hyalinization of their walls. In addition, signs of acute intestinal catarrh in all its manifestations can be seen.

The lymph nodules of the large intestine are always edematous in acute cases of dysentery and contain necrosed lymphoid elements, the stroma in the central portions of the nodules being exposed. These portions are sometimes covered with albuminous masses. In some cases of fibropurulent dysentery one can see an accumulation of macrophages in the nodules along with almost complete displacement of lymphoid tissue, which survives only along the periphery of the nodules (Fig. 13).

Involvement of the nodules in some animals, chiefly young monkeys, is more extensive than the process described above. The animals frequently exhibited at necropsy distinct enlargement of the nodular process of the intestine and, at times, small ulcerative defects in the central portions. Only once were we able to see what appeared to be the start of this process. There was a very large accumulation of segmentonuclear leukocytes just under the epithelium near the natural recess normally found in the mucous membrane and corresponding to the nodule located there. The recess

Fig. 13. Photomicrograph. Atrophy of a follicle of the large intestine in dysentery. The rhesus monkey Shut. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

was enlarged and filled with mucus. A small ulcer was developing on the site (Fig. 14). The base of the ulcerative defect was being gradually epithelized. The process of regeneration of the mucosa is often accompanied by the growth of crypts in the tissue of the nodule. The crypts are mostly deformed, becoming closed cysts filled with a leukocytic exudate or with mucus. As the process develops, the tissue of the nodule becomes partially destroyed and sclerosed so that the lymphoid tissue is frequently indiscernible only along the periphery of the nodules.

Involvement of the nodules never occurs as an isolated process. Inflammation of the mucosa is often accompanied by the development of ulcerative defects of various sizes in all cases of nodular dysentery.

Whenever an animal recovers from dysentery, the inflammatory process in the intestine very frequently, if not invariably,

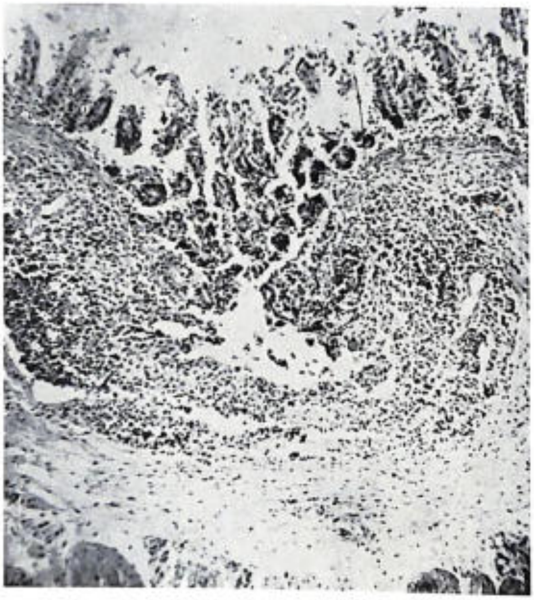


Fig. 14. Photomicrograph. Follicular ulcer. The rhesus monkey No. 1502. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

leaves definite morphological traces. For example, in examining the intestines of animals that had dysentery but died of different causes, we always saw indications of reorganization in the mucous membrane, i.e., individual small round cysts filled with mucus. There were often atrophic portions in the mucosa in the form of contracted and evacuated crypts, sometimes portions with deformed crypts near which the submucosa was thickened, showing traces of sclerosis. Isolated crypts in the submucosa were also visible, usually near the nodules. Fairbrother and Hurst (1932) dissected more than 600 monkeys and found in a microscopic examination that the large intestine of most of the animals exhibited cystoid enlargement and infiltration of the mucous glands with leukocytes. There are indications in the literature (Bach, 1931, and others) that even in monkey bacillus carriers the intestine may be unchanged. This is conceivable on the assumption that the carrier state is transitory and that no pathological process has developed.

After studying a great many cases of dysentery in monkeys, we have come to the conclusion that localization of the pathological process in the large intestine is highly variable. Sometimes the intestine is rather extensively affected and shows changes from the cecum to the rectum. At other times the upper section of the large intestine (or only the cecum or the area of Bauhin's valve) is affected. In approximately one-third of the cases the process is localized in the lower section of the intestine, i.e., in the sigmoid colon and rectum.

Thus far we have discussed involvement of the large intestine, the main site of the pathological process. However, not infrequently the small intestine (chiefly the lower division) and stomach are involved in the process. This is expressed in acute cases chiefly by the development of a desquamative mucous inflammation. Desquamation of the epithelium is so intense in the small intestine that the villi generally have no epithelial lining. Masses of mucus and cast-off epithelial cells coat the inner surface of the intestine. The mucosa, particularly the villi, is frequently edematous. Edema of the submucosa varies in degree. The blood vessels are always dilated. Superficial necrosed areas are much less common in the small intestine. Diphtheritic inflammation of the wall of the lower sections of the small intestine was very rare in our material. Involvement of the stomach was usually marked by intensified desquamation of the epithelium and production of mucus. Occasional shallow erosions were confined to the mucous membrane. In some cases of chronic colitis the gastric mucosa was found to contain small ulcers with moderately sclerosed base extending to the submucous membrane.

In cases with a chronic inflammatory process in the large intestine, especially when the mucosa was atrophied, it was possible to trace the atrophic process both in the small intestine and near the gastric mucosa. The latter was very low, with clearly defined but scanty crypts.

In some cases of acute desquamative purulent catarrh of the large intestine it was noteworthy that the process had spread to the gastrointestinal tract, embracing the entire small intestine and stomach. On the other hand, in severe diphtheritic colitis the process was confined to the large intestine, frequently with no perceptible inflammation of the small intestine or stomach.

Besides the gastrointestinal tract, the mesenteric lymph nodes may also be involved in the process. In acute cases these nodes are enlarged, pale, and succulent when cut. The enlargement of the lymph nodes, as is evident from an histological examination, is not due to hyperplasia of lymphoid tissue. On the contrary, the cortical layer of the node is generally narrow while the nodules are small. The light-colored centers in the nodules are small and sometimes invisible. Their cells are rather sparsely distributed. One can often see here an albuminous exudate and macrophages loaded with fat. Cell disintegration is frequent with the formation of chromatin lumps. The sinuses of the nodes are always dilated and their lumens filled with a serous fluid. This fluid contains varying amounts of macrophages in the protoplasm of which ingested erythrocytes can often be seen in addition to cellular fragments. There are also leukocytes. In some cases of purulent necrotic colitis large numbers of leukocytes are found in the marginal sinuses of the lymph nodes. The pulp of the nodes frequently contains not only mature leukocytes but also younger myeloid elements. In occasional cases of acute colitis oxydase-positive cells in the mesenteric nodes become very numerous, filling almost the entire tissue of the nodes and not extending only to the area of the nodules. The blood vessels of the nodes are generally dilated. Small hemorrhages are common; the endothelium of the sinuses and vessels is succulent and swollen.

Histologically, therefore, changes in the mesenteric lymph nodes in acute colitis include chiefly hyperemia, hemorrhage and edema, transudation of an albuminous fluid, and the presence of varying amounts of myeloid elements.

In chronic colitis the lymph nodes, especially in the mesentery of the large intestine, are comparatively small, round, compact formations, pale yellow-pink in cross section. Besides the phenomena noted in acute colitis, one can see the growth of connective tissue in the nodes and the resultant marked thickening of the septa between the sinuses.

The spleen, as a rule, is not too enlarged. It is somewhat enlarged in acute colitis, especially when the process is accompanied by enlargement of the lymphatic apparatus of the intestine. In such cases the splenic pulp may have numerous nodules, some-

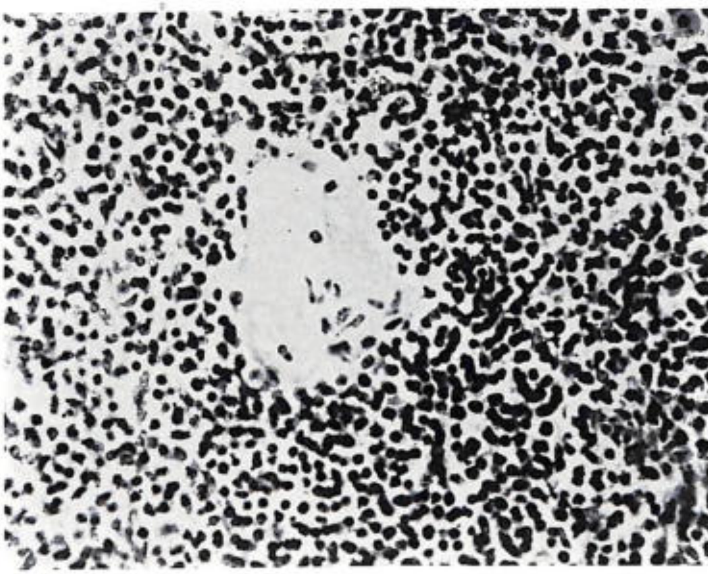


Fig. 15. Photomicrograph. Albuminous saturation of the central arterial wall of a splenic nodule in acute desquamative colitis. The rhesus monkey Shurka. Stained with hematoxylin-eosin. Obj. 20, oc. 10.

times with round, light-colored centers. Most of the time the spleen is normal in size or somewhat shrunken with mucronate edges. The splenic pulp in acute cases is hyperemic while the sinuses and blood vessels, including the central arteries of the nodules, are engorged. The walls of the latter are often frayed, friable, saturated with a pale albuminous fluid (Fig. 15). Albuminous masses can often be seen in the central part of the nodules as well. The walls of the central artery are very often changed in cases where edema of the intestine and hyperemia of the intestinal wall are very pronounced. The nodules of the spleen are generally small. Their central portions, consisting of occasional pale cells, contain varying amounts of lumps of nuclear detritus. Small hemorrhages can frequently be observed in the splenic pulp.

The spleen shrinks together with atrophy of the mucosa of the large intestine. The nodules of the spleen are usually very small. Sometimes one can observe a large accumulation of erythro-

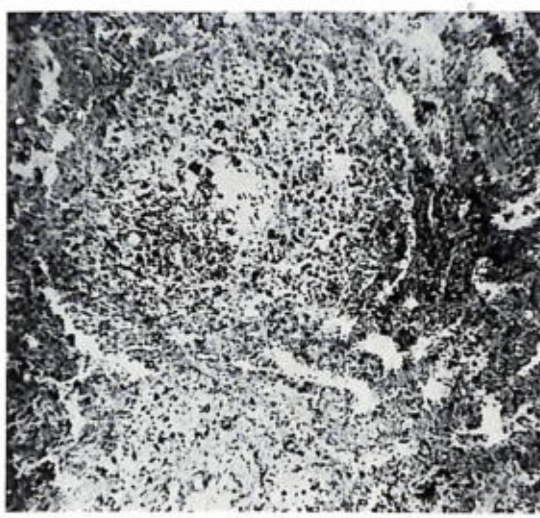


Fig. 16. Photomicrograph. Tissue destruction and hemorrhage of a splenic nodule in atrophic colitis. The rhesus monkey No. 1126. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

cytes around the central artery at the place where the nodule is atrophying (Fig. 16).

In chronic colitis too the spleen tends to be small. Histologically, besides hyperemia it is sometimes possible to observe hyalinosis of the walls of the central arteries as well as deposits of a brown pigment in the septa between the sinuses. Macrophages and plasma cells are often visible among the cells of the pulp.

In acute colitis the adrenal glands become enlarged due to thickening of the cortex. Macroscopically, the latter seems to be swollen, yellowish-pink, and comparatively deficient in lipoids. The virtually complete lack of lipoids in the cortex is also easily traced histologically. Fairly small amounts of fatty inclusions are found only in the cells of the glomerular zone and in the central portions of the fascicular zone. The organ is invariably hyperemic and sometimes there are small hemorrhages in the cortical substance. Hyperemia is present in varying degrees in the other internal organs. It is particularly prominent in the liver where histologically one can see marked dilatation of all the blood vessels up to the intertrabecular capillaries. The lumens of the capillaries often

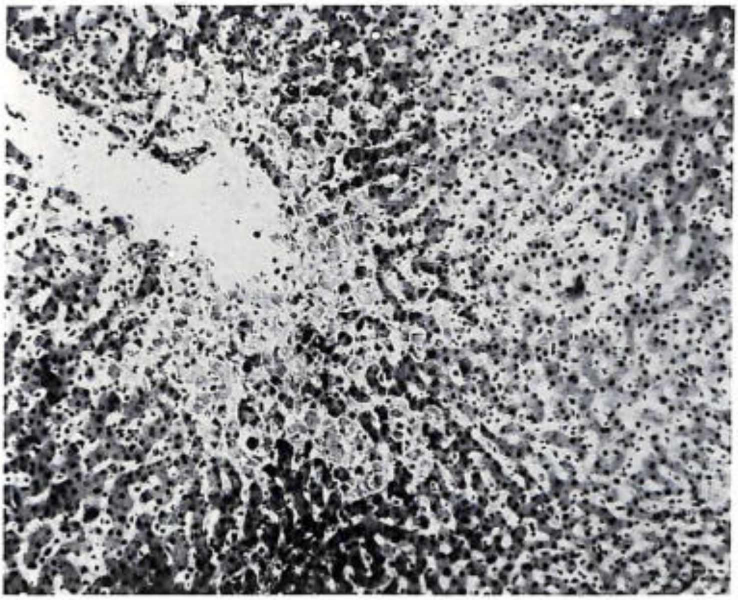


Fig. 17. Photomicrograph. Necrosis of the liver in acute dysentery. The rhesus monkey Shurka. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

contain varying amounts of leuocytes. In these cases there is occasional necrosis of individual groups of liver cells, quite often near the central vein (Fig. 17).

Adiposis of liver tissue is not present in all cases and it is often indistinct. Small perivascular, chiefly round-cell, infiltrates are frequently found. Similar infiltrates are sometimes found in the myocardium. In only one instance was infiltration of the myocardium more pronounced, i.e., when the process assumed the character of interstitial myocarditis with moderate proliferation of histiocytic elements of the stroma and marked round-cell infiltration. According to O. L. Vishnevetskaya (1938), the development of myocarditis in human dysentery is also a rare phenomenon.

Hyperemia of the tissues and varying extent of epithelial degeneration of the convoluted tubules are frequently observed in the kidneys. Swelling of the epithelium is sometimes associated with faint fine-droplet fatty infiltration of the latter. The lumens of the capsules sometimes contain finely-granulated masses that stain weakly with eosin. Similar accumulations are encountered from time to time in the lumens of the straight tubules. Hemorrhages in kidney tissue are rare. Masses of erythrocytes are occasionally visible in the lumens of Bowman's capsules.

Thus, the morphological manifestations of dysentery in monkeys are quite similar to those of dysentery in man. In the large intestine, the organ most affected, the morphological characteristics of the process depend on the extent of tissue injury and nature of the exudate elaborated. Although the process throughout the large intestine is generally variegated, one form or other of the inflammatory process tends to dominate.

Observations of dysentery in man (L. S. Bibinova, 1954) indicate that regeneration of intestinal epithelium takes place throughout the illness simultaneously with the processes involved in destruction of the intestinal wall. We were frequently able to confirm this during our investigation of dysentery in monkeys.

Extensive deformation of the intestinal wall creates the conditions for transformation of an acute process into chronic colitis.

Not having gone into this problem directly, we shall not discuss here the question of deep involvement of the nervous system in the disease and particularly, of the nervous apparatus of the intestine. The latter is well known in human dysentery and undoubtedly plays an important part in transforming an acute inflammatory process in the intestine into a chronic one by first disrupting normal regeneration of the intestinal wall.

Of no little significance in the development of dysenteric colitis and its transformation into a chronic condition is deep involvement of the blood vessels with stasis, albuminous saturation of the vascular wall, and thrombosis. These changes occur in the spleen and lymph nodes as well as in the intestinal wall. These may possibly be the cause in part of the small necrotic patches found in the liver in severe cases of dysentery.

The process is characterized, as a rule, by the absence of an active reaction by the lymphatic system and spleen, which is well known, particularly in dysentery in children (M. A. Skvortsov, 1946). On the other hand, these symptoms, especially the spleen, contain evidence of atrophy. It is a fair assumption that this peculiarity of the process in suppressing rather than in mobilizing these organs is responsible for the lack of sufficient immunity to this disease.

Morphological manifestations of dysentery in monkeys closely resemble those in man. The main differences between the disease in man and in monkeys is that the course is more severe in the latter with a high percentage of deaths (about 50%) and that the process in man takes place in the lower divisions of the large intestine (the sigmoid colon and rectum), whereas in monkeys the changes are generally localized in the area of the cecum and ascending colon.

As against the view set forth in the literature that monkeys are extremely susceptible to dysentery, we should like to point out that the main group of monkeys in the animal house, particularly those living in open-air cages, are highly resistant to the bacilli. Cases of clinically pronounced dysentery are rare and there never has been an outbreak of the disease that affected many animals at one time. Yet dysentery frequently strikes large batches of imported animals. We believe that this is due to the sudden change in diet after capture and the resultant intestinal dysbacteriosis and avitaminosis, the most significant factors being B avitaminosis and, above all, folic acid insufficiency (I. V. Davydovskiy, 1956; S. Ryss, 1958; Ruch, 1959). The experiments of Saslaw and co-workers (1942-1943) have shown that folic acid insufficiency greatly increases the susceptibility of monkeys to infections, primarily dysentery.

The prolonged administration of antibiotics, particularly those of broad-spectrum action, aggravates dysbacteriosis and avitaminosis by suppressing the intestinal microflora which provides for the organism's vitamin requirements, primarily the B-complex vitamins.

This explains the favorable results obtained by putting monkeys suffering from dysentery into open-air cages. This procedure is sometimes more effective than intensive treatment with antibiotics (B. A. Lapin, 1958). We attribute the prevalence of dysentery among monkeys recently taken from their natural habitat—both—to heavy microbial insemination and to nutritional disorders that invariably arise after the animals are captured. Therefore, dysentery in monkeys is primarily a problem of improper diet, intestinal dysbacteriosis, and avitaminosis.

MORGAN'S TOXINFECTION

The part played by Morgan's bacillus in the pathology of man and the type of microbes with which it should be classified are still matters of discussion. Investigations of diarrhea in children (Morgan, 1907; E. L. Garnitskaya, F. V. Shul'ts, and S. A. Gavrilov, 1934; P. N. Stepanov, 1946; others) and of toxinfections in adults (Gildmeister and Barthlein, 1913; Yu. A. Tyumyakova, 1939; M. R. Nechayevskaya, K. V. Goncharova, and M. Ye. Kishenevskaya, 1946; others) have revealed the presence of the microbe in feces or the presence of antibodies to it in the blood serum of persons who have recovered from the disease. Studying the bacteriological nature of summer diarrhea, V. A. Friauf (1949) found Morgan's bacillus in the feces of 35.7% of all the cases examined. He concluded that Morgan's bacillus was the causative agent in some cases of summer diarrhea, but regarded it as an independent type of microbe. According to the latest official guide on the microbiological classification of causative agents, Morgan's bacillus is to be regarded as relatively pathogenic and classified with *Proteus*.

There are isolated references in the literature to the possibility of finding these microbes during epizooties of rodents, which caused a great many of the animals to die (Gildmeister and Baerthlein, 1913; others). In 1929 Lovell found them in the feces of captive birds, reptiles, and mammals (including monkeys) during outbreaks of diarrhea. In 1930 he again isolated Morgan's bacillus from animals (including rhesus monkeys) in the London zoo suffering from enteritis. Enteritis caused by this bacillus sometimes resulted in death of the monkeys (Hamerton, 1929, 1934).

The feces of monkeys in the Sukhumi animal house have not been investigated specifically for the presence of Morgan's bacillus. However, it has been detected from time to time during the annual mass bacteriological examination.

Between August 8 and September 1, 1953 three monkeys ranging in age from two months to one year and three months developed a disease of the gastrointestinal tract and died shortly thereafter. They were among the monkeys in the Sukhumi animal house fed artificially since birth and kept together in one room. On August 8, 1953 the rhesus monkey Lisichka displayed a poor appetite and great thirst, vomited repeatedly, and was flatulent. The stool remained formed. The animal died one and a half days after the onset of the illness.

The disease was observed for five days in the hamadryad Kuram. It was characterized clinically by general sluggishness of the animal, flatulence, occasional regurgitation, and diarrhea.

The symptoms were the same in the third animal, the hamadryad Adler. The disease lasted two days.

Thus, the clinical course of the disease was marked by sharp deterioration in overall condition (sluggishness, rejection of food, etc.), flatulence, vomiting, and diarrhea. Diarrhea had apparently been unable to develop in the animal that died within 36 hours of the onset of the disease. A bacteriological examination of the contents of the large intestine in all three monkeys resulted in the isolation of Morgan's bacillus. In two animals the bacillus was isolated posthumously from the blood and parenchymatous organs. It proved to be pathogenic for white mice.

Autopsy of all three animals revealed involvement of the gastrointestinal tract, chiefly the stomach and small intestine. The mucosa of the stomach and small intestine was edematous and pinkish with many punctulate and larger hemorrhages. An unusually large number of hemorrhages were found in the mucosa of the stomach and duodenum of the animal that died within 36 hours. The stomach and, to a lesser degree, the small and large intestines contained a good deal of mucus. The contents of the large intestine were liquid or semiliquid.

Microscopical examination revealed hemorrhages in the mucosa and submucosa, moderate edema and hyperemia of these membranes, and necrosis and desquamation of the epithelial lining in various parts of the gastrointestinal tract (Fig. 18).

We found extensive portions of gastric and intestinal mucosa in which the epithelium lining the crypts was involved in the dystrophic process. We also noted superficial necrosis of the mucosa of the stomach and small intestine (Fig. 19). The gastric and intestinal walls were not perceptibly infiltrated. The abovementioned manifestations were scarcely visible in the large intestine.

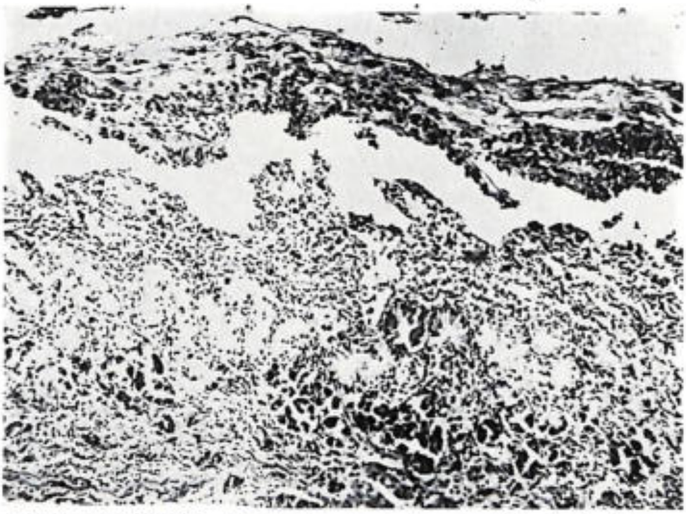


Fig. 18. Photomicrograph. Acute desquamative gastritis. The rhesus monkey Lisichka. Stained with hematoxylin-eosin. Obj. 8, oc. 10.

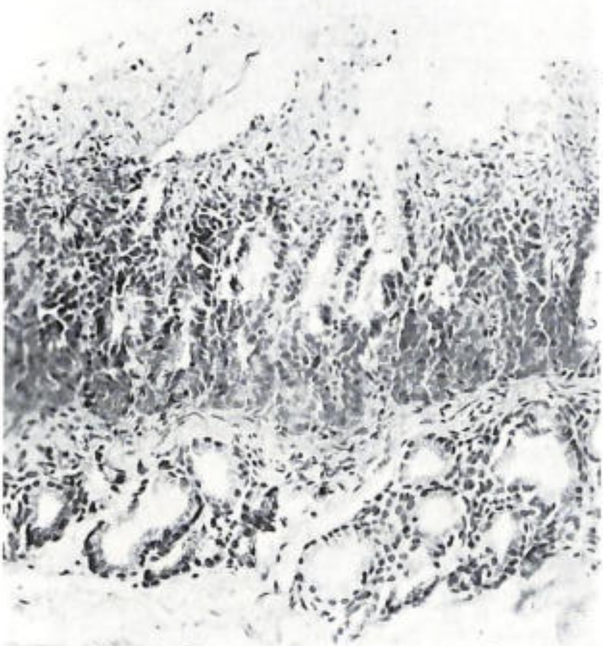
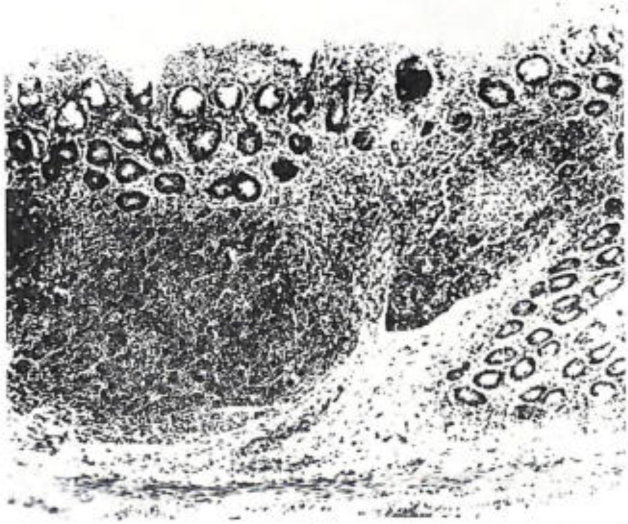


Fig. 19. Photomicrograph. Dystrophic changes and edema in the duodenal mucosa. The rhesus monkey Lisichka. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

We were struck in all cases by hyperplasia of Peyer's patches and solitary intestinal nodules. Microscopical examination of the patches revealed hyperplasia of lymphoid tissue and hyperemia (Fig. 20). The lymph nodes of the mesentery proper were invariably much enlarged. The nodes of the mesentery of the large intestine, peripheral lymph nodes, and tonsils were less enlarged. Enlargement of the lymphoid formations was due to thickening of the cortex. The nodules were enlarged with big, light-colored centers consisting chiefly of large, light-colored cells. The boundaries between the individual nodules were indistinct. The pulp of the node rather frequently contained eosinophils as well as immature myeloid elements. The sinuses of the node were somewhat distended. Comparatively few macrophages and occasionally leukocytes were present in the lumens. The nodal tissue was hyperemic. Endothelial cells of the sinuses and blood vessels were large and succulent. Besides hyperplasia of the lymph nodes, we noted considerable enlargement of the spleen in all cases. In cross section the pulp was dark cherry in color and finely granulated. A small blood scraping was taken from the surface of the section.



ZOOLOGICAL GARDEN CALCUTTA

Fig. 20. Photomicrograph. Lymphoid hyperplasia of Peyer's patches. The hamadryad baboon Adler. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

The splenic nodules were large under the microscope. They frequently had large, light-colored centers. The sinuses were engorged.

While examining the internal organs we noted some enlargement of the liver, plethora of its tissue, and varying amounts of fat in the liver cells in the central portions of the hepatic lobules. Small lymphocytic and histiocytic infiltrates and some edema of the stroma were found in the myocardium. Hyperplasia of Peyer's patches in the lymph nodes of the mesentery and moderate enlargement of the spleen were observed in all three cases of Morgan's toxinfection. In one animal marked hyperplasia of Peyer's patches along with a cluster of hyperplastic lymph nodes in the ileocecal junction led us at first to make an anatomical diagnosis of typhoid fever at the stage of medullary swelling. However, an histological examination brought out the theoretical differences between these pathoanatomical changes and those found in typhoid fever. The main difference is that in the above-described cases enlargement of Peyer's patches and lymph nodes of the ileac mesentery was due to genuine hyperplasia of lymphadenoid tissue.

We should like to conclude this section with a comment on the epidemiological aspect of the problem. The illnesses developed at one time among animals kept together and fed artificially. This fact does not contradict the relatively pathogenic nature of Morgan's bacillus and the observations of microbiologists who have periodically isolated the microbe from clinically healthy monkeys in the animal houses. It can apparently be explained the same way as the outbreaks of intestinal diarrhea among children in orphan asylums caused by relatively pathogenic bacteria. The simultaneous onset of the disease in our animals may well have been due to the fact that they were all kept the same way, were fed artificially over a long period of time, etc., i.e., they were exposed to conditions conducive to "transforming" normal intestinal flora into pathogenic bacilli.

In the absence of sufficient data on the incidence of the carrier state in monkeys or on the connection between Morgan's bacillus with those cases of diarrhea where dysentery microbes are not isolated, we simply assume that Morgan's bacillus might have been the causative agent of the disease in some cases. Two of the three cases described above were severe and quickly ($1\frac{1}{2}$ to 2 days) killed the animals. The third was mild and proceeded favorably. The animal died on the fifth day of an intercurrent disease (necrosis of the intima of the aorta with detachment and pericardial tamponade).

Thus, Morgan's toxinfection occurring clinically as enteritis was characterized morphologically by catarrhal desquamative involvement of the small intestine and, to a lesser extent, of the stomach. The lymphatic apparatus, chiefly of the small intestine, was also involved in the process.

The process may also show a polymorphic clinical and morphological picture, developing in some cases as colitis, as Hamerton (1934) observed. His work was based on another species of monkey (capuchins).

PARATYPHOID DISEASES

Almost all kinds of animals—mammals, birds, reptiles—suffer from diseases caused by paratyphoid bacteria. Salmonellas pathogenic for animals belong principally to bacteria of the B, Breslau, and Gaertner types. The diseases show a polymorphic clinical and pathoanatomical picture (N. P. Tsvetayeva, 1941). Tsvetayeva points out that over 50% of the typhoid cases among mammals are made up of rodents, especially white rats and mice. In artiodactyls paratyphoid has occurred in the form of catarrhal or catarrhal hemorrhagic enteritis. Enteritis in some species of artiodactyls (roe deer) is essentially acute septicemia. In birds the disease has occurred in the form of catarrhal, hemorrhagic, or fibrinosus enteritis. In reptiles paratyphoid assumes the character of a sepsis.

The outbreak of paratyphoid in the Moscow Zoo featured severe fibrinous hemorrhagic or ulcerative colitis. Describing the paratyphoid carrier state and outbreak of the disease in the Sukhumi monkey house, A. S. Aksenova and L. M. Khutsishvili (1949) also stated that the disease was in the form of catarrhal or hemorrhagic ulcerative colitis.

Studies of paratyphoid diseases of monkeys have been made by Dobberstein (1936), Hamerton (1934, 1935, 1937), Rewel (1948), and others. Only a few, however, refer to the pathoanatomical manifestations. Hamerton (1937) described a disease in green marmosets resembling typhoid fever in man and involving ulceration of Peyer's patches in one of the animals. There was no bacteriological confirmation of paratyphoid in any of the animals, but paratyphoid bacilli were isolated from healthy animals that had come in contact with sick ones.

During the paratyphoid outbreak in the Sukhumi monkey house described by Aksenova and Khutsishvili, 14 animals (hamadryads, apunders, and rhesus monkeys came down with the disease, 10 dying. There was another outbreak in 1946 when two animals died. Bacteriological analysis revealed that most of the sicknesses were caused by *S. breslau*, occasionally by *S. paratyphosa* and *S. schotmülleri*.

Following the report of Aksenova and Khutsishvili (1949), the laboratory of infectious pathology identified a small number of paratyphoid carriers in the main group of the Sukhumi monkey house, but did not detect any cases of the disease. From 1957 on, when there were large-scale shipments of animals from India and China paratyphoid bacteria were again isolated. However, no cases of the disease developed, despite the fairly large number of bacillus carriers. In 1957 six monkeys were found to be carrying *S. paratyphosa*, 16 in 1958. At the end of 1958 out of a large group of animals shipped from India (300 rhesus monkeys) 11 were carrying *S. breslau*, *Gaertner*, and *paratyphosa*. It is difficult to speak categorically about the origin of this bacillus carrier state, but the most probable cause was contact with man at the place where the captured monkeys were assembled or en route to Sukhumi.

We do not have much material of our own. Our description of the pathological anatomy of paratyphoid is based on an investigation of four cases of the disease confirmed bacteriologically. All four exhibited primary involvement of the small intestine in the form of catarrhal enteritis. The mucosa of the intestine was very swollen, hyperemic, and covered with varying amounts of mucus. Hypertrophy of Peyer's patches was manifested differently in each case. There was marked hyperplasia of the mesenteric lymph nodes located in the ileocecal junction. The spleen in all cases was enlarged, sometimes substantially so. The large intestine and stomach were moderately inflamed, but they were less involved than the small intestine.

Microscopical examination of Peyer's patches and solitary nodules showed a proliferation of large, light-colored reticular cells shaped here and there like nodules. Sometimes the reticular cells were isolated in the midst of lymphoid tissue. Marked parenchymatous dystrophy was visible in the internal organs. The stomach exhibited moderate hypersecretion of mucus while the small intestine (besides hyperplasia of Peyer's patches) had signs of desquamative catarrh.

Thus, the morphological picture of this disease closely resembled that found in experimental Breslau's paratyphoid in monkeys and in human paratyphoid (B. A. Lapin, L. A. Yakovleva, and S. M. Pekerman, 1956). The rarity of paratyphoid in monkeys, despite the crowded conditions under which they are kept and the comparatively high percentage of bacillus carriers, shows that the animals are highly resistant to paratyphoid bacteria. However, if resistance is lowered and the disease does develop, it follows a course like that of paratyphoid in man and its morphological manifestations testify to a similar point of application of the stimulus and to a uniform type of reaction.

GASTRITIS AND BEZOARS

Gastritis in man is a clinically distinct and normally chronic disease. We have not discovered in monkeys any disease that approximates this nosological form in man. Acute gastritis as an independent disease was noted in three monkeys (two hamadryads and one capuchin). It was evidently of alimentary origin and developed like an acute poisoning accompanied by vomiting. It generally lasted about 24 hours.

In the hamadryad baboons the process was essentially a catarrhal inflammation of the stomach with copious elaboration of mucus and desquamation of cells from the surface of the mucous membrane. At the same time there was edema and hyperemia of the gastric wall. In both cases the liver and stomach were severely affected, as manifested in a diffuse, very pronounced adiposis of liver cells.

Fig. 21. Bezoar (of plant fibers) in the stomach of the rhesus monkey Vil'ya.

The process in the stomach of the capuchin was markedly hemorrhagic in character. The mucosa and submucosa abounded in hemorrhages coalescing in places. At one spot a large, dark red clot adhered to the gastric wall. The mucosa was hemorrhagic and here and there looked necrosed.

Gastritis was generally found as a complication of the dysenteric process. It was usually catarrhal, occasionally ulcerative in character. In one case inflammation of the stomach was specifically tuberculous (p. 000).

In four monkeys that generally had dysentery for some time and suffered recurrences (the macaques Kair, Vil'ya, Ilek, Shurka), autopsy of the stomach revealed sol:d formations filling almost the entire lumen. Following the contours of the stomach cavity, the bezoars were irregularly oval, sometimes fusiform (Fig. 21). In two

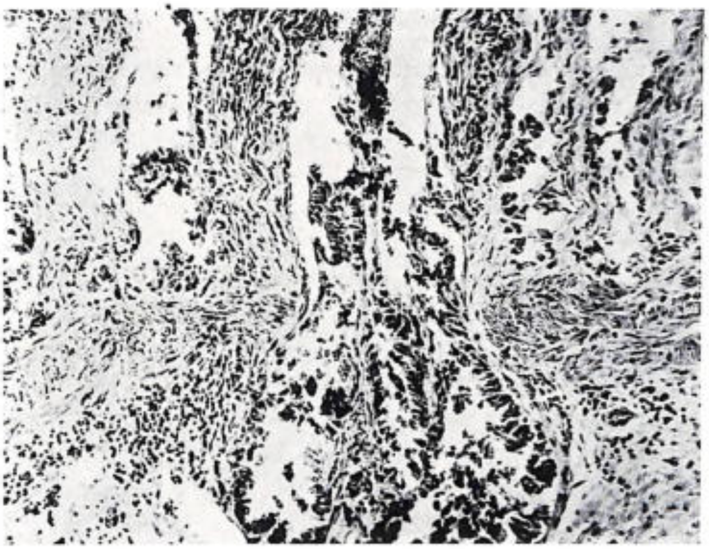


Fig. 22. Photomicrograph. Chronic gastritis with ingrowth of crypts in the submucosa. The rhesus monkey Vil'ya. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

instances these formations consisted of remnants of food and fibers held together by mucus. The composition of the bezoar was uncertain in another animal. It was a dirty gray, solid, finely porous formation. In another animal the bezoar was a solid, sticky (with mucus) ball of plant stems. The inflammatory process in the stomach was chronic in character, accompanied by coarse reorganization of the mucous membrane with the growth of crypts into the submucosa (Fig. 22).

The reason for the presence of these foreign bodies in the stomach is the disruption of its secretory and motor functions following prolonged inflammation of the gastrointestinal tract. The accumulation of hairs in the stomach is possibly due to the fact that monkeys frequently swallow them, pull them out and put them in the mouth while "searching" one another. The formation of bezoars of hair (Wollbälle) has also been noted in other animals, including farm animals (Nieberle and Kohrs, 1954).

PNEUMONIA

Diseases of the respiratory tract are as frequent a cause of death of wild animals in captivity as are diseases of the digestive tract. A study of the reports of the London Zoo over a period of years reveals that the main cause of death is lesion of the respiratory and digestive organs, the former being the more frequent. Pneumonia is one of the commonest diseases of the respiratory apparatus and a major cause of death of monkeys. Lovell (1929), Stadie (1930), Fairbrother and Hurst (1932), Hamerton (1932, 1933, 1935, 1937, 1944), Kennard (1941), Hill (1953), and others report on cases of death from pulmonary infections. Sometimes the cause is bronchopneumonia, which may arise like influenza in man (Hamerton, 1933, 1935, 1944). At other times it is lobar pneumonia with indications of "hepatization" of the affected lung (Hamerton, 1937, 1944; Kennard, 1941; Hill, 1953; A. P. Savinov and A. V. Tyufanov, 1957; I. A. Prokhorova, L. A. Porubel', and others, 1958).

Many cases of bronchopneumonia, especially if treated with sulfanilamides and antibiotics, end in recovery. The prognosis is not too favorable in lobar fibrinous pneumonia, which may develop under particularly adverse conditions for monkeys and result in a high percentage of deaths despite treatment (Kennard, 1941; A. P. Savinov and A. V. Tyufanov, 1957; L. A. Porubel' and coworkers, 1958; and others).

We shall consider in this section the results of investigating 117 cases of pneumonia which were autopsied in the institute between 1952 and 1958. The findings are divided into two groups, chiefly according to morphological features: bronchopneumonia and lobar fibrinous pneumonia. We have used the latter term by analogy with croupous pneumonia in man.

Bronchopneumonia

Most of the cases of bronchopneumonia involved the macaques. Out of a total of 101 cases, 63 were macaques, 24 baboons, and 14 green marmosets.

Dysentery was the commonest major disease associated with bronchopneumonia (in 45 out of 101 cases). Bronchopneumonia may also be complicated by dyspepsia, nutritional dystrophy, cerebral hemorrhage, or Morgan's toxinfection.

Pneumonia was the main disease in the overwhelming majority of cases involving all species of monkeys over one month old (Table 2). Out of 15 monkeys of this age (macaques, baboons, green marmosets) 13 had pneumonia as the main disease and only two had it as a complication of some other disease. In one animal there was hemorrhage under the brain membrane (birth injury); in another pneumonia developed in infancy with marked nutritional dystrophy.

TABLE 2

Distribution of Cases of Bronchopneumonia by Age

	Number of Monkeys by Age Groups					
	Up to 1 month	*From 1 month to 1 year*	*1-3 years*	*3-15 years*	*Over 15 years*	*Total*
Total number of monkeys in the age group	15	31	28	24	3	101
Main disease	13	12	3	3	1	32
Complication	2	19	25	21	2	69

The disease was still the main disease in animals up to one year old. Thus, out of 31 cases of pneumonia it was the main disease 12 times, a complication of other diseases 19 times. Dysentery was the main disease in seven cases, dyspepsia in three cases, sepsis in three cases, severe exhaustion in three cases, different causes in three cases. But in animals one year and older bronchopneumonia was almost invariably a complication of other diseases. Thus, in 55 animals over a year old pneumonia was a complication of another disease 48 times, the main disease only seven times. In 38 out of these 48 cases the main disease was dysentery. Bronchopneumonia developed in five animals after surgery involving the abdominal cavity. It developed in three monkeys after protracted labor with incomplete placental separation. Finally, two cases of pneumonia developed as a complication of other diseases.

In all the age groups both lungs were generally affected. Pneumonia was double in 46 animals and single in 17 animals out of a total of 63. The proportion was somewhat different among the baboons, being double in 23 animals and single in one animal out of a total of 24. The principal site of the pneumonic foci was the lower lobes of the lungs (Tables 3 and 4).

TABLE 3

SITE OF THE PNEUMONIC PROCESS IN THE LUNGS OF MONKEYS IN RELATION TO AGE

	Number of Monkeys by Age Groups					
	Up to 1 month	*From 1 month to 1 year*	*1-3 years*	*3-15 years*	*Over 15 years*	*Total*
Total number of monkeys in the age group	6	15	23	16	3	63
With involvement of one lung	0	5	7	4	1	17
With involvement of both lungs	6	10	16	12	2	46

TABLE 4

SITE OF THE PNEUMONIC PROCESS IN THE LUNGS OF BABOONS IN RELATION TO AGE

	Number of Baboons by Age Groups					
	Up to 1 month	*From 1 month to 1 year*	*1-3 years*	*3-15 years*	*Over 15 years*	*Total*
Total number of baboons	6	11	3	4	—	24
With involvement of one lung	0	0	1	0	—	1
With involvement of both lungs	6	11	2	4	—	23

The affected areas upon dissection generally appeared somewhat variegated due to the differing character of the pneumonic exudate and the almost invariable presence of atelectatic and emphysematous areas along with areas containing the exudate.

Bronchopneumonia in almost half the cases involving the various species of animals was interstitial in character. There was no correlation between the nature of the pneumonia, species, and age of the monkeys. Nor was it possible to link the morphological characteristics of the pneumonia with the type of bacillus found.

In interstitial pneumonia cases the alveoli were for the most part almost free from the exudate. However, some exudate was observed in the alveoli in nearly all the cases. Sometimes when the exudate was in the lumens of the alveoli, varying degrees of leukocytic infiltration of the alveolar septa were noted both within the areas containing the exudate in the alveoli and outside of those areas. In a few cases (about 7%) exudation into the alveoli and leukocytic infiltration of the alveolar septa were pronounced.

Microscopical examination reveals the variable nature of the alveolar exudate in bronchopneumonia. The exudate is frequently purulent, i.e., it consists of segmentonuclear neutrophilic leukocytes. It was leukocytic in 70% of the cases we investigated. It was generally admixed with erythrocytes, desquamative cells of alveolar epithelium, and occasionally a little fibrin.

The nature of the exudate varies in different parts of the lung—leukocytic, hemorrhagic or serous. A purely serous exudate in bronchopneumonia is quite rare. Alveolar macrophages are fairly abundant in the serous fluid found in the alveoli. In four out of the five cases of bronchopneumonia that we investigated the serous fluid contained some cellular elements (chiefly macrophages); it was almost wholly serous just once. This particular case presented exceptional difficulties in differentiating pneumonia from pulmonary edema. Predominance of a hemorrhagic exudate was noted in only two cases.

In all cases the connection between the pneumonic foci and the bronchial tree was distinctly visible. Small bronchi located in the pneumonic foci were generally inflamed. In one case this was manifested by moderate infiltration of the bronchial mucosa

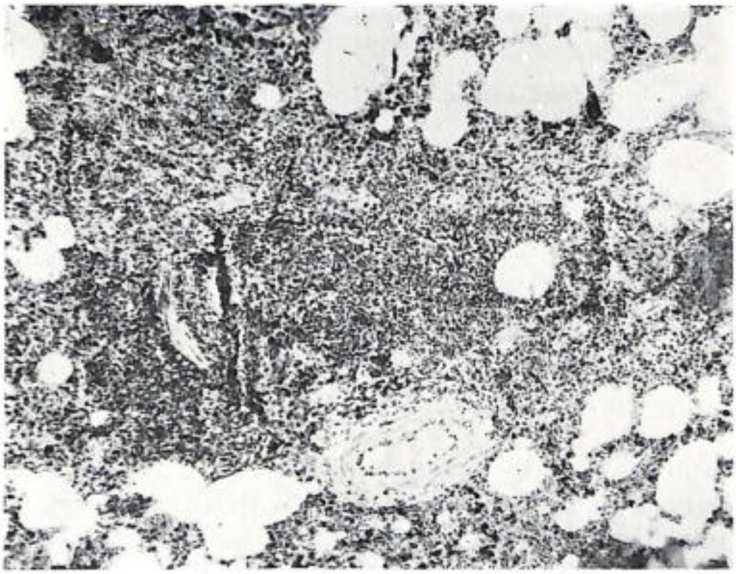


Fig. 23. Photomicrograph. Destructive panbronchitis. The hamadryad baboon Malka, two years old. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

and accumulation in its lumen of an exudate composed of leukocytes and mucus; moderate epithelial desquamation was sporadic. The process occasionally extended to the middle membrane of the bronchus. Panbronchitis was noted in a number of cases. Ulcerative bronchitis was found in the most severe cases. Sometimes substantial leukocytic infiltration of the bronchial wall and indications of mucosal destruction combined with copious exudation into the lumens of the bronchi made it possible to trace the bronchus in the exudate only by the muscular bands of the middle membrane (Fig. 23). The bronchioles in pronounced cases were markedly dilated and their lumens filled with the exudate (Fig. 24).

The lumens of large bronchi usually contain a small amount of exudate. The indications of infiltration of the walls are faint or lacking altogether. There is hypertrophy of the mucosa accompanied sometimes by the formation of polypous papilliform protuberances. The submucous membrane is moderately edematous. Once in a while a broad edematous zone in the form of a cuff can be seen around the bronchi.

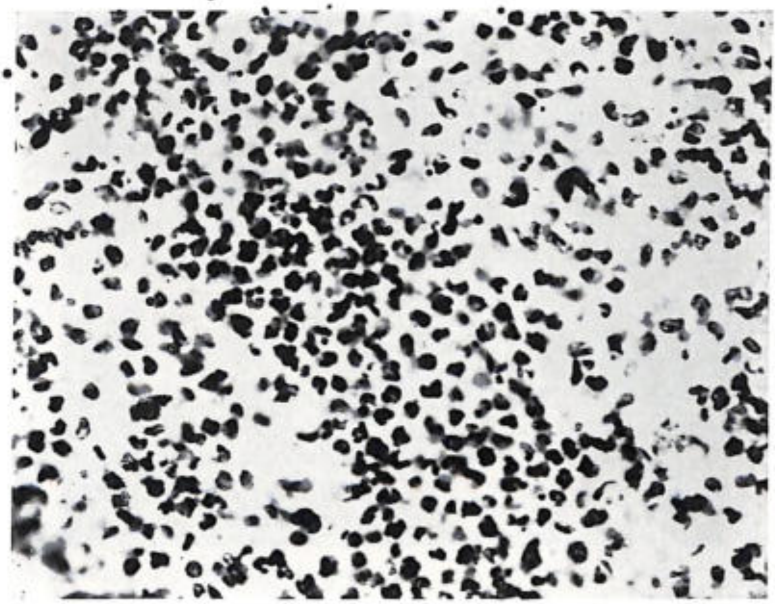


Fig. 24. Photomicrograph. Suppurative bronchiolitis. Pus in the lumen of a highly dilated bronchiole. The hamadryad baboon Malka. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

Bronchopneumonia in baby monkeys is usually associated with very pronounced bronchitis. The bronchi may be so severely affected that inflammatory changes in the alveoli seem to be pushed to the background. For example, the small bronchi and bronchioles of two animals about one month old and another animal two and one half months old were found in a microscopical examination to be heavily involved. The walls of the bronchioles were so extensively infiltrated by leukocytes that they could be distinguished only by the remnants of concentrically arranged muscle fibers in the middle membrane and from the contours of their cavities filled with a leukocytic exudate. The exudate in individual bronchioles contained a great deal of mucus. The large bronchi were also involved in the process in these cases, but their mucosa showed for the most part indications of hypertrophic catarrh. There was marked hypertrophy of the epithelium, which had become stratified and succulent, together with an accumulation of an mucous

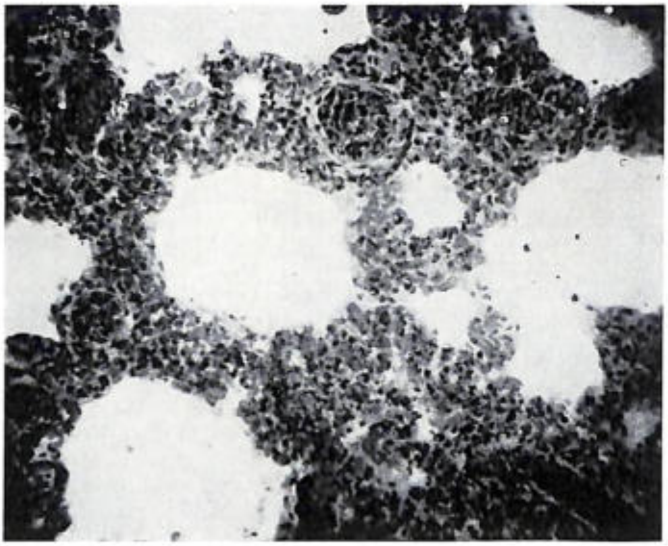


Fig. 25. Photomicrograph. Interstitial pneumonia. The rhesus monkey Shurka. Stained with hematoxylin-eosin. Obj. 40, oc. 7.

exudate in their lumens. The epithelial lining remained intact. As for inflammatory changes in the alveoli, they were by far less pronounced than those in the bronchi.

In cases of interstitial pneumonia the alveolar septa look very thickened with the lumens of the alveoli constricted (Fig. 25). This thickening is caused by proliferation of the connective-tissue elements of the stroma. However, it is mainly due to edema and some infiltration of the septa by cellular elements (mostly segmentonuclear leukocytes). There is also a mass of leukocytes in the small blood vessels, sometimes with leukostasis.

The bronchial tree is affected in most cases of interstitial pneumonia. Sometimes it consists of varying degrees of infiltration of the bronchial walls by segmentonuclear leukocytes and histiocytes and an exudate in the lumens of the bronchi containing mucus and leukocytes admixed with desquamative epithelial cells of the bronchi. At other times there is only moderate edema of the submucosa of the bronchial walls, slight epithelial desquamation, and the formation of leukocytic cuffs around the bronchi.

Bronchopneumonia generally ends in recovery with resorption of the exudate. However, complications are not uncommon. One sequela may be carnification. We observed it in three out of 101 cases along with hypertrophy of the bronchial mucosa and the formation here and there of papilliform protuberances of epithelium in the lumens of the bronchi. However, similar hypertrophic changes in the mucosa are fairly common even without carnification at various stages in the development of pneumonia. Thickening of the alveolar septa is evidently a possibility in bronchopneumonia. This is also true of prolonged interstitial pneumonia.

We saw (in two cases) areas where the septa were coarsened and sclerosed while pneumonia was still present.

Sometimes the pulmonary exudate may undergo necrosis rather than resorption or carnification. The necrosed exudate may eventually become abscessed (we observed this in one case). The second case of a purulent pneumonia was somewhat different in that the formation of abscesses was apparently due to aspiration. The monkey in question—an animal that died seven days after it was born—had bronchopneumonia with numerous small abscesses in the lower lobes of both lungs.

Some cases of bronchopneumonia that we observed were complicated by pleuritis marked by fibrinous deposits on the pleura. The exudate was admixed with leukocytes. In three cases the complication was purulent pneumococcal meningitis and meningoencephalitis. One of the monkeys had focal leukocytic myocarditis in addition to meningitis.

Cultures of pulmonary tissue, impressions of the lung made during autopsy, and the staining of bacteria in histological sections reveal the rather considerable polymorphism of the microbes. However, the coccal and pneumococcal bacteria were most frequently involved.

We accidentally discovered during autopsy an atypical case of bronchopneumonia deserving of special mention. Microscopy of a lung at low magnification disclosed a mottled preparation. The alveoli were filled with an exudate consisting almost entirely of eosinophilic leukocytes. Fairly wide cuffs of basophilic cells—plasma cells, leukocytes, and a few lymphocytes and neutrophils—were observed against a reddish background of alveoli filled with eosinophils. The walls of the bronchi were densely infiltrated by neutrophilic and eosinophilic leukocytes; the epithelial lining of the bronchi was missing.

Despite the clear manifestation of the process, clinical symptoms of the disease were not in evidence. Changes in the lungs were accidentally discovered during an histological examination of the lungs of the monkey which was sacrificed in an acute experiment. Thus the changes we observed are comparable to the eosinophilic infiltrate of man, which also has virtually no clinical manifestations.

Lobar-fibrinous Pneumonia

In 16 out of 117 observations of pneumonia the disease was of the lobar variety, affecting one or two lobes of either lung, both together, or one lung as a whole. There was double involvement in the majority of cases (12 out of 16). In only four cases was there isolated involvement of the right lung and none at all of the left lung. Out of 12 cases of double pneumonia three were total, with all the lobes of both lungs completely involved. Three out of four cases of one-sided involvement were localized in the right lung, all the lobes being completely affected.

Involvement of the different lobes was consolidated in a variety of ways. However, in most cases the disease was localized in the middle and lower lobes of one lung in combination with some other site in the other lung. The upper lobe was involved in only two cases.

Lobar pneumonia in most monkeys is essentially pleuropneumonia with very thick films of fibrin enveloping the surface of the lung. The affected lung is greatly enlarged, very firm, airless; the anterior margins of the corresponding lobes are acuminate (Fig. 26). The lung tissue is quite brittle. Sectioned lung tissue looks hepatized. The surface is slightly granular and red or reddish-gray in color (Fig. 27). It mostly looks mottled, indistinct fields of gray alternating with areas of different shades of red. The lobar nature of the process is not completely sustained in all cases. Sometimes small portions of pulmonary parenchyma retaining air cells are observed in contrast to involvement of most of a lobe (or of an entire lung) along the anterior margin of the lungs (more rarely elsewhere).

Fig. 26. Lobar pneumonia. The right lung is markedly enlarged. A rhesus monkey.

V. N. Fadeyeva (1958) also mentions the comparatively high frequency of cases in which a narrow border of lung tissue free from an exudate remains in the anterior portions of the lungs. The exudate evidently moves from the posterior to the anterior portions. Microscopical examination of the lungs showed that the nature of the exudate differed in the various pneumonic areas. There were areas where the exudate was a serous fluid with a small admixture of leukocytes. Erythrocytes predominated in distinctly red areas containing a mixed exudate of leukocytes, fibrin, and erythrocytes. Leukocytes predominated in the exudate found in the gray areas. The amount of fibrin varied in each case, even in different areas in the same animal. Here and there individual groups of alveoli, sometimes substantial portions of alveolar parenchyma, were completely filled with fibrin. Sometimes this fibrin was delicately fibrous in structure. Elsewhere it was in the form of solid, homogeneous casts duplicating the outline of the alveoli. In these cases the fibrinous exudate frequently contained numerous round or

Fig. 27. Lobar pneumonia, chiefly lobar spread of the process. A rhesus monkey.

oval vacuoles with leukocytes or alveolar macrophages in their centers. The formation of numerous cavities around the leukocytes and macrophages imparted to the pneumonic focus a structure resembling cartilage (Fig. 28).

As mentioned above, the nature of the exudate may differ from area to area in the same animal. In some areas one may find that it consists almost entirely of leukocytes; in other areas it is mixed with fibrin or is composed almost entirely of fibrin; in still other areas it contains varying amounts of erythrocytes. Nevertheless, we can distinguish in each case within a single lobe the characteristic quality of the exudate—leukocytic, leukocytic-fibrinous, fibrinous, or hemorrhagic.

At first the fibrin in the alveoli is marked by a delicate reticular structure and the appearance of effusions of an albuminous fluid

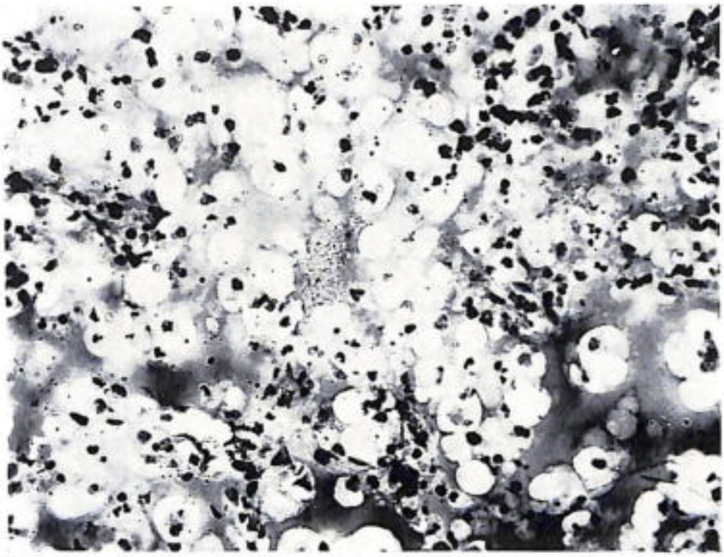


Fig. 28. Photomicrograph. Liquefaction of a fibrinous exudate around leukocytes and macrophages. A rhesus monkey. Stained with hematoxylin-eosin. Obj. 20, oc. 10.

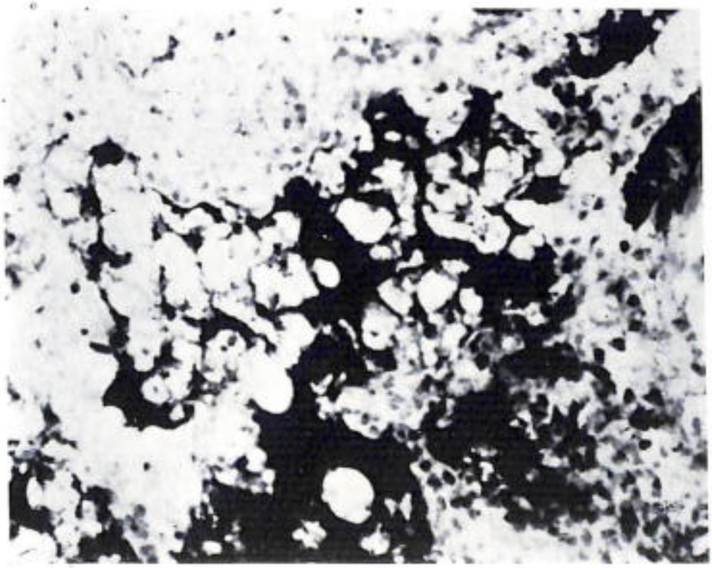


Fig. 29. Photomicrograph. Almost total liquefaction of fibrin by macrophages. Stained with gentian violet. Obj. 20, oc. 7.

and fibrin forming wide cuffs around the bronchi and blood vessels. The fibrin later loses its reticular structure, becoming solid and compact. Like Fadeyeva, we were able to observe changes in the nature of the fibrinous exudate between the posterior and anterior portions. Whereas in the posterior portions the fibrin was solid and compact (frequently with indications of resorption), toward the front it became looser with a delicate reticular structure. In our opinion, this confirms the view of V. D. Tsinzerling and V. G. Fadeyeva that the pneumonic focus spreads from the posterior toward the anterior portions.

The fibrin is later resorbed with the help of leukocytes and macrophages. Oral cavities form in the solid, compact fibrin around the leukocytes and macrophages as a result of fermentative liquefaction. These cavities grow in number, coalescing here and there to form queer shapes. The fibrin between the cavities also becomes less compact and thins out as though melting away (Fig. 29). Tsinzerling (1958) notes that in human lobar pneumonia fibrin is resorbed with the help of macrophages, never with the help of leukocytes. He also points out that fibrin is never resorbed by liquefaction. However, this occurred in our observations.

The alveoli filled with the exudate looked enlarged. Here and there the walls are ruptured and fairly big cavities become filled with the exudate. The bronchi in the pneumonic foci also fill up with the exudate. The nature of the exudate in the lumens of the bronchi is substantially the same as that in the alveoli. In some cases the bronchial exudate consists of leukocytes, in others it is mixed. Sometimes it consists almost entirely of fibrin with a few leukocytes surrounded by numerous round or oval cavities—zones of resorption. The quantity of exudate in the lumens of large bronchi ranges from very little to enough to fill them completely. Sometimes the exudate is represented by a small amount of mucus admixed with leukocytes.

The walls of the bronchi are infiltrated by leukocytes. In individual bronchi there are few signs of infiltration, but the submucosa is markedly edematous. Sometimes the walls of the bronchi are so infiltrated in places that their structure can only be surmised. In some places the epithelial lining is torn away, in others it is missing

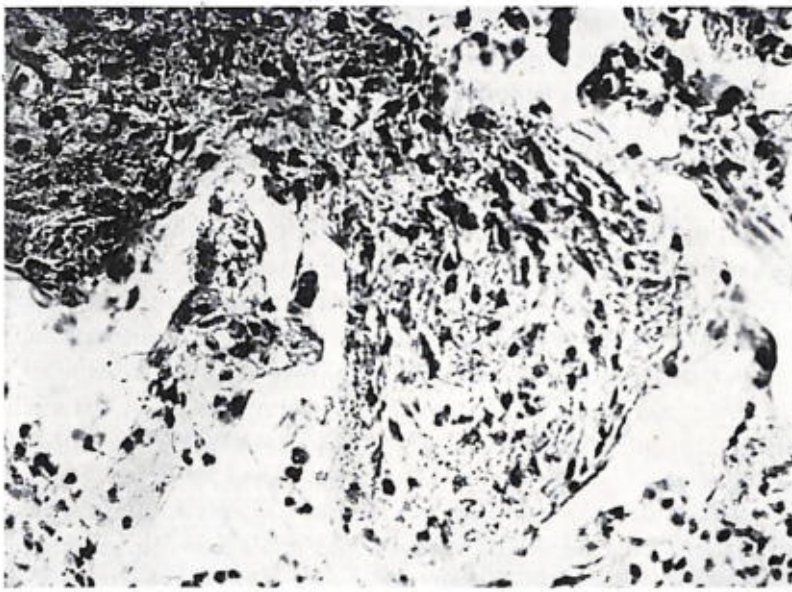


Fig. 30. Photomicrograph. Carnification. A rhesus monkey. Stained with hematoxylin-eosin. Obj. 60, oc. 7.

entirely. There are ulcerative defects in the walls of individual bronchi. The bronchioles are generally quite dilated and filled with the exudate. The exudate disappears from the lumens of the bronchi at about the same time that the alveolar exudate disappears. However, the walls of the bronchi remain infiltrated for some time after the exudate from the alveoli has been resorbed. Resorption of the alveolar exudate may be held up for a considerable length of time.

In two cases we were able to observe signs of carnification when we found connective-tissue fibers in a nonresorbed exudate. Besides the initial indications of carnification there were foci where the alveoli were completely filled with connective tissue interpenetrating the exudate (Fig. 30). In the same cases we found very thick growths of connective tissue in the pleura due to the organization of the pleural exudate. This view is confirmed by the fact that islets of a fibrinous exudate with initial indications of ingrowing connective-tissue fibers can be distinguished here and there in the midst of the connective tissue in the pleura. The epithelial lining of the bronchi is regenerated before the exudate is resorbed. The epithelium is low at first, but then assumes its usual form. When alveolar resorption is held up and carnification sets in, the epithelium of the bronchi becomes succulent and hypertrophic, forming polypous protuberances.

Hamerton (1946) mentions gangrene and the formation of abscesses as possible complications of pneumonia. Lobar pneumonia in monkeys is much more similar to croupous pneumonia in man as regards the pathogenesis and nature of the etiological factors than is croupous pneumonia in swine and cattle, which bears only some formal resemblance to pneumonia in man. The outbreak of pneumonia resulting in the death of a great many animals described by Blake and Cecil (1920) and Wisner (1928), the outbreak in the animal house of Yale University in 1938 when in a group of 100 animals 10 out of 27 animals ill with lobar pneumonia died (Kennard, 1941), the many deaths caused by lobar fibrinous pneumonia in the Institute for the Preparation of Poliomyelitis Vaccine, the outbreak of lobar fibrinous pneumonia in our animal house—all these do not necessarily mean that the disease is contagious or that it is like the so-called croupous pneumonia of domestic farm animals. As in man, lobar fibrinous pneumonia in monkeys (we shall henceforth call it croupous pneumonia) is a typical autointoxication. In most cases we found pneumococci in the lungs. Kennard reports type I pneumococci were isolated in all cases of croupous pneumonia. Its simultaneous outbreak in a closed group was caused by some common factors that decreased natural immunity and resistance of the organism to the normal flora of the respiratory tract. In our observations 14 out of 16 animals were shipped together in the winter and exposed to extreme cold while the plane was on the ground for a long time. Apparently other unfavorable factors in transportation and abnormal feeding routines, not to mention the transition from freedom to captivity, were also of considerable significance.

Analyzing the literature as well as our own observations, we believe it posible to distinguish in the croupous pneumonia of man several points of resemblance to the croupous pneumonia of monkeys. There is, to begin with, the lobar character of the lesion and the fibrinous character of the exudate. Both in man and in monkeys the upper lobes of the lungs are rarely affected and the process spreads from back to front. As a rule, the disease in monkeys is associated with fibrinous pleuritis; an occasional case, as in man, may be complicated by carnification, the formation of abscesses, or gangrene of the lungs.

Lacking adequate material from bacteriological examination of cases of croupous pneumonia, we are unable to discuss the types of pneumococci involved. However, we can say with confidence that it is definitely the pneumococcus that is the causative agent.

We may now note a number of differences between croupous pneumonia in monkeys and in man. Extensive perivascular and peribronchial effusions of serous fluid and fibrin are not characteristic of man. The processes of fibrin resorption develop in different ways. In man, according to V. D. Tsinzerling, the resorption of fibrin never involves leukocytes nor is there any "liquefaction" of the fibrin. In monkeys, on the contrary, leukocytes play a major part in the resorption of fibrin and at a certain stage there is also "melting" or "liquefaction" of the substance. Despite these differences, however, croupous pneumonia in monkeys adheres to its distinctive pattern with the typical stages of the process.

TUBERCULOSIS

All the available data on tuberculosis in monkeys indicate that the animals are highly susceptible to this disease. According to Calmette (1923, 1929), Krischman (1936), V. G. Shtefko and A. A. Khar'kov (1940), Kennard (1941), M. B. Ariyel' (1949), Benson and co-authors (1955), and many others, tuberculosis in monkeys is marked by a progressive course, rapidly ending in death. It was Hamerton's view (1935) that the disease is never overcome spontaneously and that there are no remissions.

We were unable to find any references in the literature to chronic tuberculosis in monkeys nor any mention of the forms of the disease affecting the organs except S. G. Kaktin's description of spina ventosa in macaques. Records of the animal house indicate that tuberculosis is a major cause of death. For example, from 1927 (when the monkey house was built) to 1958 out of 1,709 deaths from various diseases and experiments 112 or 6.5% were due to tuberculosis.

Tuberculosis throughout these years has clearly been linked to the delivery of new animals. However, not all the deliveries have resulted in a rise in the tuberculosis rate. In 1927, none of the 31 imported animals died during the years immediately following delivery. The same thing was noted in 1928 when 19 hamadryads were delivered.

The first deaths occurred among hamadryads of the 1930 shipment. Eight of 16 imported animals died during the year. None of the 11 macaques in the same shipment died of tuberculosis. For several years thereafter, despite annual deliveries there were no deaths at all or only one a year. The next major outbreak occurred in 1938 and was linked to the ill-fated deliveries of November 1937 and mid-1938. Out of 18 animals in the 1937 shipment 10 died during 1938 and seven in 1939. Out of 118 animals in the June 1938 shipment eight died the same year and four in 1939. Thus, these two shipments included 18 monkeys that died in 1938 and 11 in 1939. However, in addition to the 18 imported animals nine more died from among those born in the monkey house or brought there more than four years before. The lack of details on the condition of the imported animals from the time of importation until their death is a possible basis for assuming that some of the animals imported more than four years before were already infected when they arrived, having suffered from a chronic form of the disease for several years.

In 1939, 15 monkeys died of tuberculosis, 11 from the November 1937 and June 1938 shipments. Four more died in 1939, two born in the animal house and two brought there more than five years before.

During the following three years (1940, 1941, and 1942) the mortality rate dropped sharply. One or two monkeys from shipments made many years previously died each year. In 1943, the rate rose somewhat when five of the animals (macaques) died. However, in 1944 only one (born in the animal house) died. No new batches were delivered between 1939 and 1948. In 1943, five more animals died. These animals were part of the September 7, 1933, June 4, 1938, and May 30, 1939 shipments. We are not sure as to what brought on the disease. It is possible that they suffered from some chronic, clinically undetected tuberculous process, which was aggravated during the war by the deterioration of feeding and maintenance procedures in the monkey house.

In 1944, there was only one death from tuberculosis and none in 1945. In 1946, and 1947 there were two major outbreaks, eight animals dying in 1946 and seven in 1947, chiefly macaques, and only one baboon each year. All were young, having been born in the monkey house. Thus, the 1946-1947 outbreak cannot be directly attributed to the importation of animals. Lacking precise information on where the animals were during those two years, we can only assume that they were kept close together while alive, thus creating the conditions for mass infection. In favor of this view is the fact that all the diseased monkeys were young macaques, hence the likelihood of their having been kept together.

The years 1948 and 1949 were good, in that there was no death from tuberculosis. In 1949, one monkey—a gelada named Krit from the 1948 shipment—died. In 1950, 8 imported monkeys died. This happened within one-half to one year from the date of their arrival in Sukhumi. The next few years there were only one or two deaths a year. The mortality rate rose once more following a new shipment in 1957-1958.

Thus, most of the 112 deaths from tuberculosis were among the imported animals (86). They amounted to 5.7% of all the imported animals (1485) as against 1.8% of those born in the monkey house (1442). Disregarding the data on the shipments of monkeys that were satisfactory as far as tuberculosis was concerned (e.g., the absence of tuberculous animals), we tried to summarize the data on unsatisfactory shipments (in the sense of tuberculous infections). In view of the close contact of the animals with one another en route and thereafter and the fact that they were cared for by the same attendants, it was to be expected that the number of sick animals present in the group would easily infect the others. However, the data reveal that there were comparatively few deaths from tuberculosis—13.7% (Table 5). Newly imported monkeys suffering from tuberculosis generally die during the first or second year after arriving in the animal house.

TABLE 5

DEATHS OF IMPORTED MONKEYS FROM TUBERCULOSIS IN DIFFERENT YEARS

Year of "unsatisfactory" shipments	*Number of imported monkeys*	*Total number of imported animals that died of tuberculosis*	*Time of death after arrival*							
			Up to 1 year	*Within 1-2 years*	*Within 2-3 years*	*Within 3-4 years*	*Within 4-5 years*	*Within 5-6 years*	*Within 6-7 years*	*Within 7-8 years*
1930	16	8	8	....	....	....	....	....	....	....
1937	53	18	10	7	....	1	....	....	....	....
1938	118	16	8	4	1	2	....	....	....	1
1948	100	2	....	1	....	....	....	....	1	....
1950	35	9	8	1	....	....	....	....	....	....
1957	100	5	5	....	....	....	....	....	....	....
Total	422	58	39	13	1	3	....	....	1	1
Per cent	100	13.7								

We believe that owing to congested transportation facilities many more animals are exposed to infection by tubercle bacilli than is evident right after the delivery is made. Some indirect support for this view comes from the fact that after some of the animals die there still remains a small "train" of diseases that can be observed for several years. Individual deaths from tuberculosis occur many years after delivery. We assume here development or exacerbation of the disease in a previously infected animal. We shall discuss the possible development of chronic forms of tuberculosis in imported monkeys when we describe the pathoanatomical manifestations of the disease in the animals.

A careful analysis of the literature reveals that the tuberculosis rate in animal houses and zoos is largely due to sick imported monkeys. Hamerton (1941) described a major outbreak in the London Zoo when in a short time out of 79 imported rhesus monkeys and seven baboons 43 of the macaques and all seven baboons died of generalized tuberculosis. The surviving animals were subsequently killed and tuberculosis was found in all of them. Hill

(1953, 1954, 1955) described several outbreaks of the disease in the London Zoo when a great many imported animals died. The 1953 outbreak was particularly instructive; 145 animals died on "monkey hill." They were part of a batch of 249 animals recently arrived from Calcutta. Hill did not analyze the data. We have compared the pattern with that in the Sukhumi monkey house. It is evident from Table 5 that monkeys imported during "unsatisfactory" years died of tuberculosis mostly during the first and second years after delivery; a somewhat smaller number died during the third year. A similar picture can be seen in the situation at the London Zoo. For example, out of 249 macaques imported in 1953, 145 died the first year, 58 in 1954, and just a few in 1955.

Fairbrother and Hurst (1932) published data obtained from autopsy of 605 rhesus monkeys, 50 of which died of tuberculosis. The authors point out that these 50 cases date back to the early stage of their work. Later on due to strict rejection of unhealthy animals on arrival tuberculosis cases rarely appeared in their material. Thus, here too, tuberculosis was noted almost exclusively in newly imported animals. Records of the Yale University Medical School monkey house (Kennard, 1941) indicate that 73 cases of tuberculosis were found in 246 autopsies. In 16 animals it was the cause of death; in the other observations, however, it was found only during the autopsy. It is likely that here too the imported animals were the ones most affected.

Along with the widespread belief that monkeys are highly susceptible to tuberculosis, there is the less commonly held contrary view that monkeys are less sensitive to the disease than is generally assumed and that tuberculosis is not a "typical disease of monkeys" (Weidholz, 1928; others). The former view is undoubtedly much exaggerated. Besides the aforementioned data on the comparatively low mortality of monkeys crowded together with sick animals during shipment and after arrival (favorable conditions for mass infection), there is the fact that a substantial number of clinically healthy animals exhibit a positive reaction to tuberculin injections. This indicates that the animals were clearly in contact with the tubercle bacillus. It is interesting to note that the animals can remain tuberculin-positive for a long time without developing clinical symptoms of tuberculosis. In some animals the disease doesn't develop at all and in those dying of other causes or sacrificed in an experiment the autopsy reveals no traces of tuberculous infection whatever.

V. G. Shtefko (1940), P. F. Zdrodovskiy (1950), Burnet (1912), and Urban (1938) believe that the reaction of tuberculous monkeys to tuberculin is often negative. However, a number of investigators (O. P. Viktorova, S. G. Kaktin, I. I. Kas'yanenko, and N. A. Naletov, 1949; A. A. Bochkarev, 1939; Schraeder, 1938; Häbel, 1947; Kennard, 1939; and others) introduced tuberculin in a variety of ways and noted the specificity of the reaction. The negative character of the reaction in some cases is evidently due to the anergic condition of the animal during a severe tuberculous process. We had occasion to observe this phenomenon in two animals delivered to the monkey house in 1956. They failed to have a positive ophthalmoreaction and soon died of acute disseminated tuberculosis. Hill too has reported (1935) on cases of negative reaction in advanced tuberculosis.

The physician in charge of the monkey clinic of the Sukhumi animal house, S. G. Kaktin, examined the animals systematically from 1947 on using the tuberculin ophthalmoreaction. During the first year she found that 45 monkeys had a positive reaction. Most of them (41) had been born in the animal house, the others (4) having been brought there in 1937. Twelve of these 45 animals died of tuberculosis anywhere from two to five years after they were found to react positively to the tuberculin—11 born in the animal house and only one brought there. A few animals died two or three years after the tuberculin test, but a pathoanatomical examination generally failed to show any traces of tuberculosis. Some of the animals were kept under observation until 1952 when a large batch was sent out from Sukhumi. No signs of the disease were noted in these animals before they were sent out. Finally, two of these animals (Sena, El'ba) exhibited clear clinical signs of compensated tuberculosis, which produced a disseminated process after severe experimental intervention, which we shall discuss below.

Kaktin's investigations of allergic reactions in 1948 revealed five tuberculin-positive monkeys among those recently born in the animal house and 13 monkeys among those imported in 1948. Three of the five native-born animals lived eight or nine years from the time the tuberculin-positive reactions were noted. Only two of the group, killed within a year, were found to have the early symptoms of tuberculosis (S. G. Kaktin, 1958). As for the 13 imported animals, clinical symptoms of tuberculosis were seen in only one monkey, which died a year after arrival and after discovery of the positive reaction. The other 12 animals, despite evident contact with tuberculosis and positive reactions to tuberculin, showed no clinical symptoms of the disease for five to eight years: one of them (the hamadryad Cheleken) after a few years developed tuberculous spondylitis. It is quite apparent, therefore, that in imported as well as in native-born animals there may be considerable resistance to tuberculosis (despite obvious infection).

Among the monkeys with no signs of tuberculosis other than a positive tuberculin reaction, 43 died (almost all adults) and were examined by us during the past six years. Positive tuberculin reactions were noted at various times between 1947 and 1957. The length of time between a positive tuberculin reaction and death varied from animal to animal. Among 28 monkeys born in the animal house, a positive tuberculin reaction was noted one year before death in one monkey; two years before, five monkeys: three years before, three monkeys; four years before, four monkeys: five years before, two monkeys; six years before, five monkeys: seven years before, four monkeys; eight years before, three monkeys; and 10 years before, one monkey. Among 15 imported monkeys that lived varying periods of time in the animal house, a positive ophthalmoreaction was noted one year before death in two monkeys; two years before, one monkey; three years before, three monkeys; five years before, four monkeys; six years before, two monkeys; seven years before, one monkey; and eight years before, two monkeys. All these animals remained tuberculin-positive until they died. Among the animals examined 26 were macaques, chiefly rhesus monkeys, 13 hamadryads, three green marmosets, and one gelada. The animals died of various causes unrelated to tuberculosis.

It is evident from the foregoing that the tuberculin-positive monkeys were given a morphological examination quite some time after they had come in contact with tuberculosis.

An investigation of the main collection of monkeys failed to disclose any signs of tuberculosis anywhere in the body despite the fact, as mentioned above, that most of these animals had been tuberculin-positive for many years. Upon dissecting one of these animals (the rhesus monkey Tanga) we found in the lungs, chiefly in the area of the apexes, drawn-in scars with small, solid, calcified foci in the region. Histologically, we observed in these places markedly sclerotic foci with embedded calcareous masses. The lymph nodes of the bifurcation of the trachea in some animals contained an abnormal amount of connective tissue.

Kaktin (1958) says that she discovered isolated tuberculous foci in the bronchopulmonary nodes of a few monkeys that had reacted positively to tuberculin over a long period of time. This was an accidental finding and had nothing to do with the death of the animals. She injected guinea pigs with an emulsion from the bronchopulmonary nodes of tuberculin-positive monkeys that died of various causes and succeeded in producing tuberculosis in these animals. It is evident from what has been said above that monkeys may carry tubercle bacilli and yet not have tuberculosis. This balance between animal and microbe is apparently quite stable.

On several occasions we discovered that such severe experimental action as mass irradiation with ionizing radiation (Forum, Tanga, Zlatka, Ruchey), reproduction (successful) of malignant tumors (Bekas, Shunik, Undina), chronic colitis, etc., did not bring about clinical symptoms of tuberculosis in tuberculin positive monkeys. Moreover, there were no signs of the disease in a morphological investigation. At the same time there are indications (Kaktin, 1958) that some monkeys which react positively to tuberculin for many years but remain clinically healthy as long as they are kept in the open or in cages may unexpectedly show manifestations of severe active tuberculosis ending in their deaths, whether or not they have been previously subjected to strong experimental trauma.

Clinical manifestations of tuberculosis, not to mention deaths in the monkey house from the disease, have become very rare in recent years. This is due not only to acclimatization, but also to isolation of sick and tuberculin-positive animals and systematic immunization since 1938 of native-born and imported monkeys with BCG vaccine (M. A. Linnikova, 1948).

In discussing the positive effect of immunization, Linnikova says that between 1927 and 1938 (before immunization was started) tuberculosis mortality rate in the Sukhumi animal house was 17%, but that it dropped to 10% between 1939 and 1946. However, the high mortality in 1937-1938, as mentioned above, was caused by the delivery of large numbers of sick monkeys during that period of time when there chanced to be only a few animals in the monkey house. Half as many of the latter died of tuberculosis as did the former.

Without denying the usefulness of BCG vaccination, we still cannot agree with Linnikova who attributes the low mortality from 1939 to 1946 to the vaccine. It should not be forgotten that it was precisely from 1939 to 1948 that no new animals were imported. This reduced tuberculosis mortality substantially.

We also recall that there was an outbreak of tuberculosis in 1946-1947 during which 15 native-born, BCG-vaccinated animals died. Thus, tuberculosis mortality in the monkey house was greatest prior to 1939 and was largely caused by sick imported animals. It dropped between 1939 and 1946, but remained fairly high despite the fact that no new animals were brought in during those years.

On the pathomorphological manifestations of tuberculosis, we have comparatively little material. During the last six years five animals of the main group in the monkey house died of the disease; three of them had been sick for a long time, two with tuberculous spondylitis, one with chronic pulmonary tuberculosis. One animal, a two and one-half year old baboon, developed tuberculosis of the mesenteric lymph nodes. In a green marmoset (Kazbek) that died at the age of 22 months, the process was quite unusual and included the development of a single tubercle in the kidney. In addition to these five animals, we investigated 12 Indian macaques two to three years old that died two to four months after arrival. Macroscopical and microscopic examinations revealed the presence of primary acute tuberculosis in all the animals. In 10 animals the main site was the lungs. The lesion was unilateral in

Fig. 31. A primary tuberculous complex. A rhesus monkey.

only two cases in the form of a primary complex (Fig. 31) without noticeable dissemination of the process either in lung tissue or elsewhere. Most animals in this group exhibited a bilateral process that was widespread and, as a rule, accompanied by dissemination of the germs in the internal organs. The spleen was affected in all cases. The tubercles were generally numerous and very large. In those animals whose liver and kidneys were affected, the tuberculous foci tended to be very small, frequently in the form of a miliary eruption.

Besides the bifurcation lymph nodes, which had become caseous in all the cases, lesions were found in the axillary, inguinal, para-aortal, mesenteric, and paratracheal nodes of three animals. In one case marked enlargement of the caseous lymph nodes of the bifurcation of the trachea, paratracheal and para-aortal nodes, and nodes of the mediastinum and neck due to compression of the blood vessels caused marked edema of the cellular tissue of the neck and face as well as edema of the brain with extensive hemorrhage in the membranes of both cerebral hemispheres.

The other organs were less commonly involved. Two animals exhibited a tuberculous eruption on the peritoneum and parietal pleura. One animal with sharply pronounced dissemination had isolated tuberculous foci in the pancreas. In another animal the disseminated pulmonary process was complicated by tuberculous coxitis.

The pathological anatomy of acute tuberculosis in monkeys is now fairly well known due to the research of V. G. Shtefko and A. A. Khar'kov (1940), M. B. Ariyel' (1949), N. A. Naletov and I. I. Kas'yanenko (1955), and others.

In 8 out of our 10 investigations we experienced no difficulty in finding a primary lesion under the pleura, usually in the lower lobes of the right or left lung; in only one instance was the primary lesion in the central lobe of the right lung. Fibrinous pleuritis was discovered in the region of the lesion and often throughout the lung on the side of the lesion. Regional bronchoadenitis, as noted by the above-mentioned authors, was often much larger than the primary lesion and assumed a tumorous character.

We know that a primary lesion in monkeys as in man is the focus of caseous pneumonia (M. B. Ariyel', 1949). We had no difficulty in tracing necrosis of the exudate and alveolar septa, which frequently retained the outlines of their original structure.

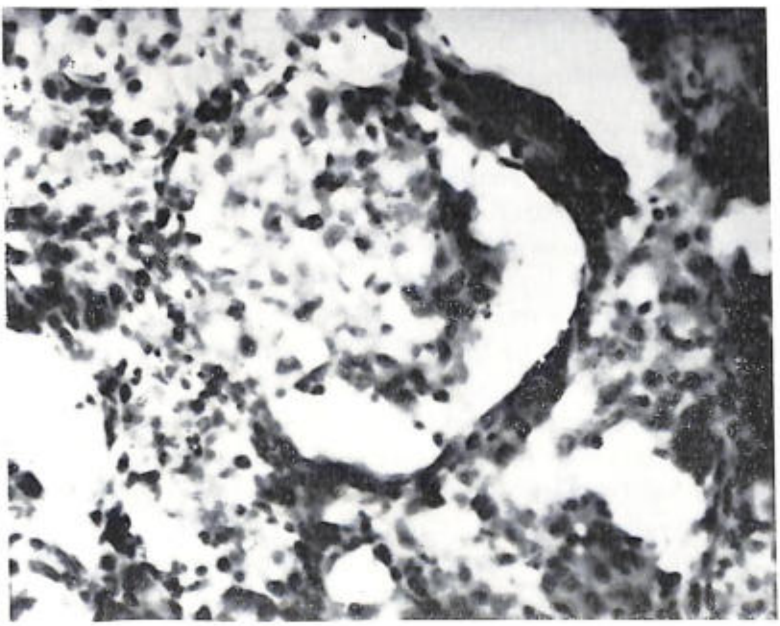


Fig. 32. Photomicrograph. Ingrowth of epithelioid cellular syncytium in the lumen of an alveolus. A rhesus monkey. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

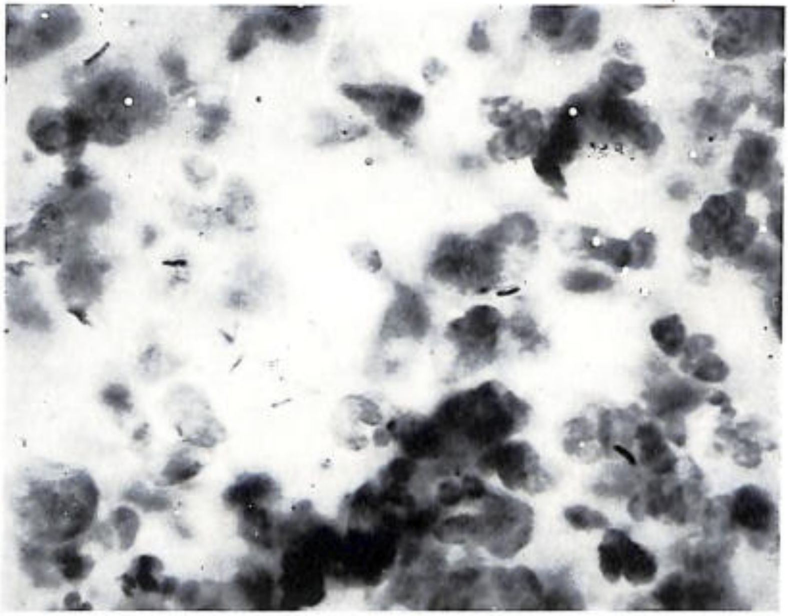


Fig. 33. Photomicrograph. Tubercle bacilli on the periphery of a tuberculous focus. A rhesus monkey. Stained with hematoxylin-eosin. Obj. 90, oc. 10.

Epithelioid histiocytic elements infiltrated the alveolar septa along the periphery of the necrotic focus. Macrophages and occasionally large cells with two or three nuclei were found in the alveoli. In places epithelioid cells appeared to be growing into the lumens of the alveoli, creating small fields of syncytium (Fig. 32). Epithelioid tubercles with totally necrosed centers were encountered along with caseous pneumonic areas. Individual foci frequently merged, giving irregular contours to portions of granulation tissue. Langhans' giant cells tended to be small, but they were very rare. Tubercle bacilli were not found regularly. We sometimes saw large numbers of them not in the necrotic zone but, as mentioned by Ariyel', among the masses of epithelioid cells in the zone of specific granulation tissue (Fig. 33). Together with the above-described areas, we could often see broad fields of lung tissue where the alveoli were filled with a mottled exudate. In places the exudate was purely leukocytic, elsewhere fibrin predominated. Large

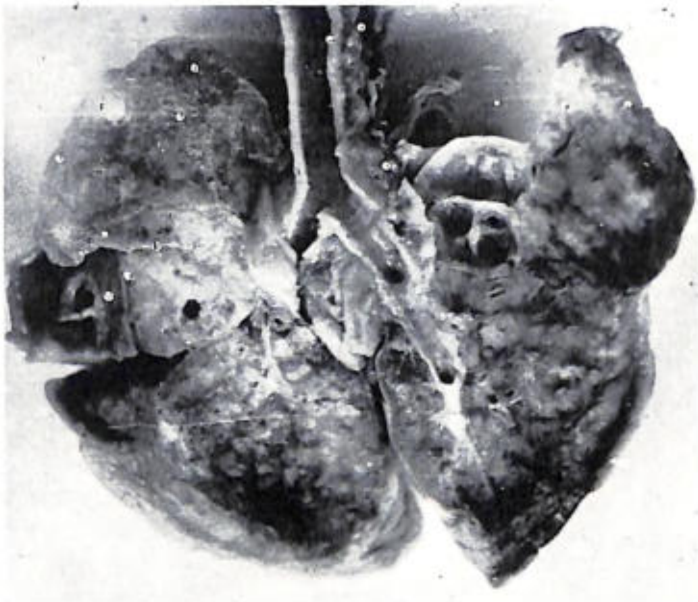


Fig. 34. Primary acute cavities in the lung of a rhesus monkey.

numbers of erythrocytes were very frequently mixed in with the exudate. The cellular tissue around the blood vessels was edematous. Clusters of lymphocytes were noted around the vessels. The walls of the bronchi both within the foci and near them were frequently destroyed. The epithelial lining was often missing, the wall infiltrated, and the lumens of these bronchi filled with an exudate consisting chiefly of leukocytes.

In places where the foci were near the pleura, the latter was considerably thickened, edematous, and infiltrated with an exudate containing many leukocytes. In one case an irregularly rounded multichambered cavity had formed under the pleura, probably at the site of a primary lesion (Fig. 34). The walls of the cavity exhibited broad areas of disintegrating, caseous tissue and numerous tubercles merging. A substantial number of tubercles were also undergoing caseation and liquefaction.

As mentioned above, the process in the lungs very frequently went beyond the primary lesion. Ordinarily the process was wide-

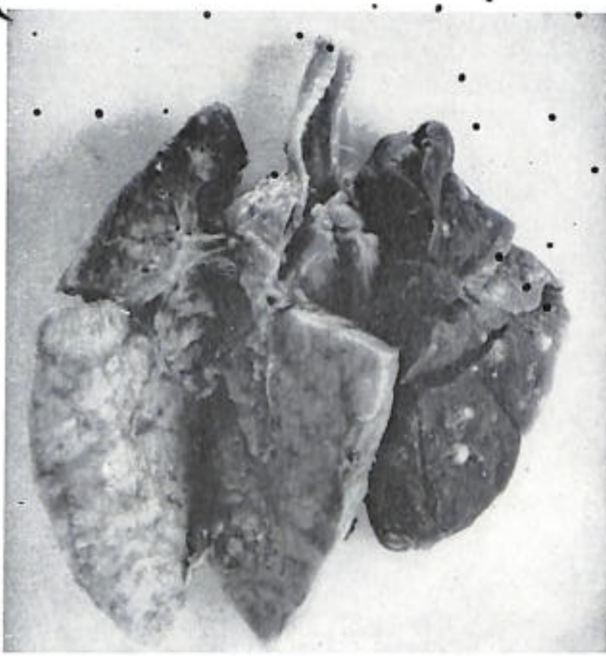


Fig. 35. Lobar caseous pneumonia. A rhesus monkey.

spread with extensive fields undergoing caseous disintegration throughout. Epithelioid cells were found in the peripheral portions of disintegrating foci. Here and there we could see around the foci capsulelike objects in the form of a few precollagenous fibers.

The foci were very frequently scalloped. As Ariyel' observed, this is due to a new wave in the development of the process. Leukocytes accumulate in the peripheral portions of the focus, infiltrating the granulation tissue and, in part, the caseous masses. The granulation tissue disintegrates in the infiltration zone and forms a new caseous focus that fuses with the initial focus.

We observed in two monkeys the development of caseous lobar pneumonia (Fig. 35) similar to primary pulmonary tuberculosis (frequently found in children). Both animals had a break in the main bronchus of the caseous masses from the bifurcation lymph node due to destruction of the bronchial wall. We were unable to locate the primary lesion in the lungs, which was probably hidden, by the extensive caseous disintegration of lung tissue. Microscopical examination revealed the presence in the alveoli of a mottled, frequently macrophagic exudate undergoing caseation in many places and for a considerable distance together with the alveolar septa.

Histolysis in the bifurcation lymph nodes involved in the process was generally so advanced that at times the tissue of the nodes could not be seen at all. Macroscopically, the tissue was a yellowish-gray, friable mass. Sometimes the tissue liquefied forming puriform masses. Histologically, one could see accumulations of epithelioid cells here and there along the periphery of the disintegrated area. Giant cells in the affected lymph nodes were not present in all cases and they were just as infrequent as in the lungs.

Tuberculous foci in the liver were generally small. Sometimes they consisted of tubercles of epithelioid cells on the periphery of which could occasionally be seen aggregations of lymphocytes that ordinarily did not form a solid mass. In other cases there were numerous round, clearly demarcated small nodules whose tissue was everywhere undergoing necrosis with the formation of a great many lumps of nuclear detritus. Epithelioid cells in these foci were either completely lacking or there were only solitary, frequently disintegrating cells in the outermost portions of the nodules.

Tuberculous foci in the spleen were almost invariably numerous and of large size. They were irregularly round, frequently coalesced nodules well demarcated from the surrounding tissue. Histological examination disclosed extensive necrosis of the tissue on the margin of which could usually be seen a narrow band of epithelioid cells. In places outside this zone there was a very thin capsule of elongated connective-tissue cells arranged in one or two rows. Isolated fuchsinophil bacilli were occasionally visible in the zone of epithelioid cells. Tuberculous foci encountered in the other internal organs of some animals were similar to those described above. We emphasize that in the monkeys that died of acute tuberculosis we generally found very few giant cells or none at all.

Tuberculosis developed in a green marmoset in a somewhat peculiar fashion. There is evidence that this species is less susceptible to the disease than other monkeys (S. G. Kaktin, 1958). It was learned from anamnesis that the mother of this animal was tuberculin-positive and that the latter was taken away when four months old. The disease appeared when it was one year and ten months old. The monkey had pronounced pneumonic symptoms and died four days after the diagnosis was confirmed. The autopsy revealed in the lower and upper lobes of both lungs rather large foci (averaging 0.6 to 0.7 cm in diameter) the tissue of which was entirely caseous. The lower lobe of the right lung had a cavity filled with puriform masses. Outside the foci the pulmonary tissue was moderately hyperemic without perceptible lesions. The right kidney was also affected. The entire kidney was greatly enlarged (3 x 5 cm), especially the upper pole, which had a tuberous surface. In cross section the upper pole exhibited numerous fine cavities filled with caseous masses. There was a compact, round, whitish-yellow node about 1 cm in diameter in the center of the lower pole of the kidney between the cortex and the medulla. This formation was surrounded by fine yellowish-gray foci. The other internal organs appeared to be normal.

Microscopical examination of the pulmonary foci revealed extensive necrosis. The alveoli and blood vessels in the nonnuclear masses were well delineated. On the periphery of necrotic tissue was a zone of detritus with a great many nuclear fragments. Around the necrosed area the lumens of the alveoli and bronchi were filled with a leukocytic exudate containing here and there a good deal of fibrin. Farther away the lumens of the alveoli were filled with a serous exudate. Extensive necrosed portions were also observed microscopically in kidney tissue. Along the periphery of the dead tissue lacking in nuclei could be seen a zone of nonspecific inflammation with marked infiltration of the kidney tissue by leukocytes and lymphoid elements.

We also observed a case of acute tuberculosis in which the lungs were not involved. The autopsy revealed extensive caseation in very enlarged mesenteric lymph nodes. The animal was a baboon born two years and ten months before in the monkey house. It died a year after it was removed from its mother and brought for experimentation to an isolation room located alongside the isolation area for tuberculin-positive monkeys. Besides a great conglomerate of highly enlarged (1 x 2, 2 x 3 cm) caseous mesenteric lymph nodes, the autopsy showed infiltration of Bauhin's valve, hyperemia, and slight edema of the wall of the adjacent portion of the small and large intestine. A great many rather enlarged lymph nodules were scattered throughout the large intestine. Histological examination of part of the large intestine next to Bauhin's valve revealed a small section of the mucous membrane to be necrosed. Corresponding to the latter in the submucous membrane was an irregularly oval formation whose central area lacked nuclei and was distintegrating into tiny lumps. There was a small number of epithelioid cells with light-colored nuclei along the boundary of the necrosed portions. This formation was in a place where the lymph nodules were almost totally destroyed. The mucosa and submucosa of the intestine near the caseous focus were somewhat edematous. The epithelium of the mucosa contained many goblet cells and was heavily desquamating in the lumen of the intestine. Histological examination of the mesenteric nodes revealed extensive necrosed areas; frequently no lymphoid tissue survived at all. On the periphery, mostly next to the capsules of the nodes, was specific granulation tissue with isolated Langhans' giant cells appearing in the midst of the epithelioid cells. We could not detect any growth of fibrous tissue in the nodes. There was an occasional small deposit of calcium in the caseous masses.

One rhesus monkey imported from India showed marked deformation of the head of the left thigh six months after arrival in the animal house. A month later it died of widespread tuberculosis in both lungs along with extensive dissemination of the process in the internal organs. Besides these changes, the autopsy revealed edema and enlargement of the area of the left coxofemoral joint. The caput femoris was very depressed, its joint surface irregularly tubercular and covered with pale pinkish-gray granulation and caseous masses. The joint surface of the acetabulum presented the same appearance. The adjoining soft tissues had large isolated caseous foci. The edges of the caput femoris were scalloped as though eaten away. The surface facing the joint was covered with specific granulation tissue consisting mainly of epithelioid cells, Tuberculosis developed in a green marmoset in a somewhat peculiar fashion. There is evidence that this species is less susceptible to the disease than other monkeys (S. G. Kaktin, 1958). It was learned from anamnesis that the mother of this animal was tuberculin-positive and that the latter was taken away when four months old. The disease appeared when it was one year and ten months old. The monkey had pronounced pneumonic symptoms and died four days after the diagnosis was confirmed. The autopsy revealed in the lower and upper lobes of both lungs rather large foci (averaging 0.6 to 0.7 cm in diameter) the tissue of which was entirely caseous. The lower lobe of the right lung had a cavity filled with puriform masses. Outside the foci the pulmonary tissue was moderately hyperemic without perceptible lesions. The right kidney was also affected. The entire kidney was greatly enlarged (3 x 5 cm), especially the upper pole, which had a tuberous surface. In cross section the upper pole exhibited numerous fine cavities filled with caseous masses. There was a compact, round, whitish-yellow node about 1 cm in diameter in the center of the lower pole of the kidney between the cortex and the medulla. This formation was surrounded by fine yellowish-gray foci. The other internal organs appeared to be normal.

Microscopical examination of the pulmonary foci revealed extensive necrosis. The alveoli and blood vessels in the nonnuclear masses were well delineated. On the periphery of necrotic tissue was a zone of detritus with a great many nuclear fragments. Around the necrosed area the lumens of the alveoli and bronchi were filled with a leukocytic exudate containing here and there a good deal of fibrin. Farther away the lumens of the alveoli were filled with a serous exudate. Extensive necrosed portions were also observed microscopically in kidney tissue. Along the periphery of the dead tissue lacking in nuclei could be seen a zone of nonspecific inflammation with marked infiltration of the kidney tissue by leukocytes and lymphoid elements.

We also observed a case of acute tuberculosis in which the lungs were not involved. The autopsy revealed extensive caseation in very enlarged mesenteric lymph nodes. The animal was a baboon born two years and ten months before in the monkey house. It died a year after it was removed from its mother and brought for experimentation to an isolation room located alongside the isolation area for tuberculin-positive monkeys. Besides a great conglomerate of highly enlarged (1 x 2, 2 x 3 cm) caseous mesenteric lymph nodes, the autopsy showed infiltration of Bauhin's valve, hyperemia, and slight edema of the wall of the adjacent portion of the small and large intestine. A great many rather enlarged lymph nodules were scattered throughout the large intestine. Histological examination of part of the large intestine next to Bauhin's valve revealed a small section of the mucous membrane to be necrosed. Corresponding to the latter in the submucous membrane was an irregularly oval formation whose central area lacked nuclei and was distintegrating into tiny lumps. There was a small number of epithelioid cells with light-colored nuclei along the boundary of the necrosed portions. This formation was in a place where the lymph nodules were almost totally destroyed. The mucosa and submucosa of the intestine near the caseous focus were somewhat edematous. The epithelium of the mucosa contained many goblet cells and was heavily desquamating in the lumen of the intestine. Histological examination of the mesenteric nodes revealed extensive necrosed areas; frequently no lymphoid tissue survived at all. On the periphery, mostly next to the capsules of the nodes, was specific granulation tissue with isolated Langhans' giant cells appearing in the midst of the epithelioid cells. We could not detect any growth of fibrous tissue in the nodes. There was an occasional small deposit of calcium in the caseous masses.

One rhesus monkey imported from India showed marked deformation of the head of the left thigh six months after arrival in the animal house. A month later it died of widespread tuberculosis in both lungs along with extensive dissemination of the process in the internal organs. Besides these changes, the autopsy revealed edema and enlargement of the area of the left coxofemoral joint. The caput femoris was very depressed, its joint surface irregularly tubercular and covered with pale pinkish-gray granulation and caseous masses. The joint surface of the acetabulum presented the same appearance. The adjoining soft tissues had large isolated caseous foci. The edges of the caput femoris were scalloped as though eaten away. The surface facing the joint was covered with specific granulation tissue consisting mainly of epithelioid cells,

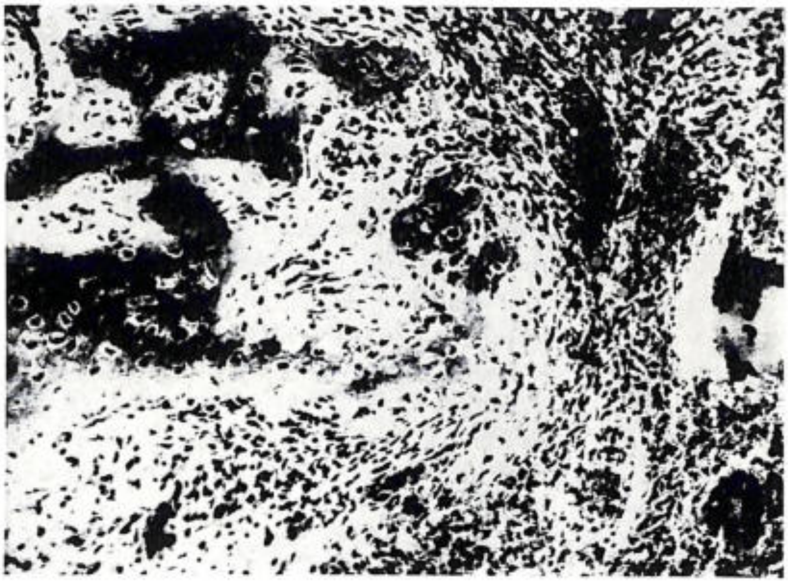


Fig. 36. Photomicrograph. Destruction of the head of the femur by granulation tissue. The rhesus monkey Bazilik. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

which contained many Langhans' giant cells (Fig. 36). Very fine collagenous fibers were found almost everywhere between portions of granulation tissue. Here and there the granulation tissue had penetrated into the Haversian canals of the bone. Islets of specific granulation tissue and extensive caseous masses were noted in a thick fibrous capsule around the joint. Here too giant cells were found among the epithelioid cells.

We must mention another case of acute tuberculosis in our material which is in the nature of an accidental finding. Histological examination of the internal organs of an Indian monkey that died of dysentery revealed in the gastric mucosa tubercles whose epithelioid cells contained many Langhans' giant cells. The central portions of the tubercles were disintegrating.

As is evident from the above and the well known research of Schmidt (1870), V. G. Shtefko and A. A. Khar'kov (1940), and M. B. Ariyel' (1949), acute tuberculosis in captive monkeys is clearly progressive with extensive dissemination both in the lungs and in the other internal organs. General caseous pneumonia frequently develops, particularly from the primary lesion, and after obturation of the bronchi by caseous masses coming from disintegrating bifurcation nodes. In all cases the specific granulation tissue is ready to disintegrate so that the foci sometimes consist entirely of caseous masses. The giant-cell reaction is faint and sometimes is lacking altogether. Also very faint or completely lacking are the signs of limitations on the spread of tuberculous foci in the form of connective-tissue capsules. Sometimes liquefaction of the caseous masses at the site of the primary lesion may produce a cavern. M. B. Ariyel' was able to trace the communication of some of the primary cavities with the lumens of the bronchi. In a few cases he observed partial epithelization of the walls in cleaned caverns.

A somewhat exceptional case was that of an animal with tuberculous coxitis in which, despite the generally progressive character of the process, the foci were found to contain a substantial number of giant cells and collagenous tissue was in evidence. These phenomena may well have resulted from the fact that the animal had received streptomycin for a month.

The primary site of tuberculosis in monkeys need not be the lungs, as indicated by the development in one native-born baboon of tuberculous foci in the wall of the large intestine and extensive involvement of the mesenteric lymph nodes. Due to the appearance of individual tubercles in the stomach—a very rare occurrence —the tuberculous process was apparently still recent and localized.

Besides the acute cases described above, we observed three other cases in which the disease was clinically traced for several years. In one case pulmonary tuberculosis developed in a macaque born in the animal house in 1940. It was administered BCG vaccine orally when it was between one and two years old. In 1942, x-rays revealed enlargement of the bronchopulmonary lymph nodes. Marked clinical manifestations of the disease in the form of considerable emaciation, sluggishness, and diminished appetite were observed only in March 1947. X-rays taken that month showed fusiform shadows in the hili of both lungs and indications of adhesive pleuritis to the left. During the course of a general check of tuberculin reactions (ophthalmoreaction) made at this time the results were positive in this animal.

The monkey remained somewhat sluggish the next few years. From time to time it lost weight, after which it received additional food, more vitamins, and occasional intravenous injections of glucose. It was given PASA for a short time in April 1952. Throughout its life the animal had a positive ophthalmoreaction. In 1953 it was used in an acute experiment involving opening of the thorax and production of a unilateral pneumothorax. The operation sharply worsened the animal's condition and it died two days later.

Besides traces of the operation, the autopsy revealed individual adhesions between the lungs and parietal pleura. Numerous small grayish foci were visible under the pleura in both lungs. They varied in size from a millet seed to a match-head. Isolated grayish-white foci with indications of caseation were also found deep in the lung parenchyma. We were unable to locate the primary lesion or traces of it. The lymph nodes in the bifurcation of the trachea formed a huge, almost totally caseous mass. The mucous membranes of the large bronchi were hyperemic, somewhat edematous. In one place the wall of the main right bronchus was ulcerated at the point where it adhered to a caseated lymph node. Caseous masses had penetrated the bronchial wall and showed up as individual granules in the lumens of the right bronchus.

Histological examination of the lungs revealed numerous tubercles of epithelioid cells in addition to broad foci almost completely undergoing caseation. The tubercles were either not disintegrating at all or their central portions contained small groups of disintegrating cells with leukocytes interspersed. Giant cells were frequently visible in the central portions and on the periphery of the tubercles, which were usually surrounded by round-cell elements and connective-tissue capsules (Fig. 37). Massive coarse sclerotic fields were encountered in isolated portions of lung tissue. The flattened alveoli here looked like narrow slits or ducts lined with cuboidal epithelium. This tended to make the lung tissue resemble adenomatous structures. The pleura was often somewhat thickened due to the growth of collagenous tissue there and moderate infiltration by cells, chiefly histiocytes and lymphocytes.

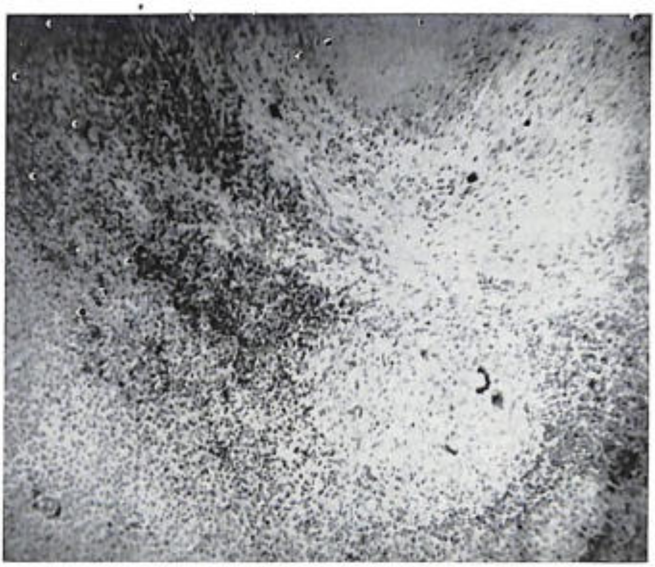


Fig. 37. Photomicrograph. Encapsulated tuberculous focus with signs of exacerbation in the capsule. The rhesus monkey Sena. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

A similar picture was observed in the bifurcation nodes of the trachea—massive caseation along with distinct signs of tissue sclerosis along the periphery of the nodes. Large caseous nodes surrounded by compact fibrous capsules were found in the liver and pancreas. The caseous masses of the latter often contained calcium deposits. Small tubercles of epithelioid giant cells appeared in the liver alongside old encapsulated foci. They were sometimes located in the fibrous capsules of old foci, destroying the latter all along the diameter.

The spine was involved in two other cases of a prolonged tuberculous process that we investigated. One of the animals (the hamadryad Cheleken) brought to the monkey house in 1948 when it was about three years old reacted positively to tuberculin (ophthalmoreaction) soon after arrival. The animal was not immunized with BCG vaccine. After treatment with an antibiotic (the preparation Yermol'yeva 15) the animal was placed in an open-air cage. The ophthalmoreaction remained negative until August

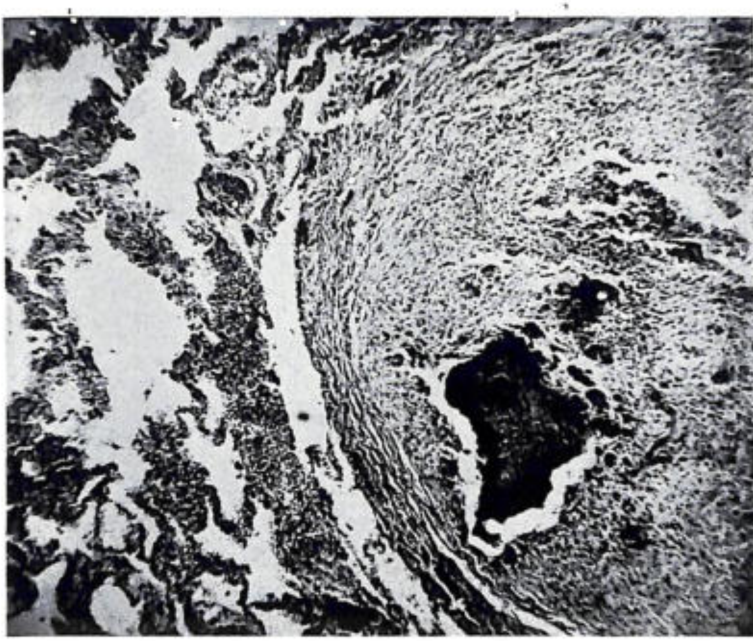


Fig. 38. Photomicrograph. Calcification in a tuberculous focus. The hamadryad baboon Cheleken. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

1955. In 1955 at the same time that the animal reacted positively to tuberculin, we observed that it was experiencing some difficulty in moving its right hind leg. An x-ray showed darkened foci in the lungs for the first time. The animal was somewhat sluggish, pale, and anorectic. The ESR rose to 40 to 50 mm an hour. During a short period of time (about one month) in mid-1955 the monkey was given streptomycin, isonicotinic acid hydrazide, and PASA. An x-ray made in September 1955 revealed partial destruction of the lumbar vertebral bodies. Weakness in the rear extremities gradually increased and the spine became very tender to the touch. During the last eight days of the illness severe paresis of both the hind and front paws set in so that the animal remained recumbent, rejecting food and not reacting to any stimuli. Occasionally it had spells of vomiting and convulsions.

The autopsy revealed lymphadenitis of the bifurcation nodes of the trachea with many caseous and calcareous foci. The primary

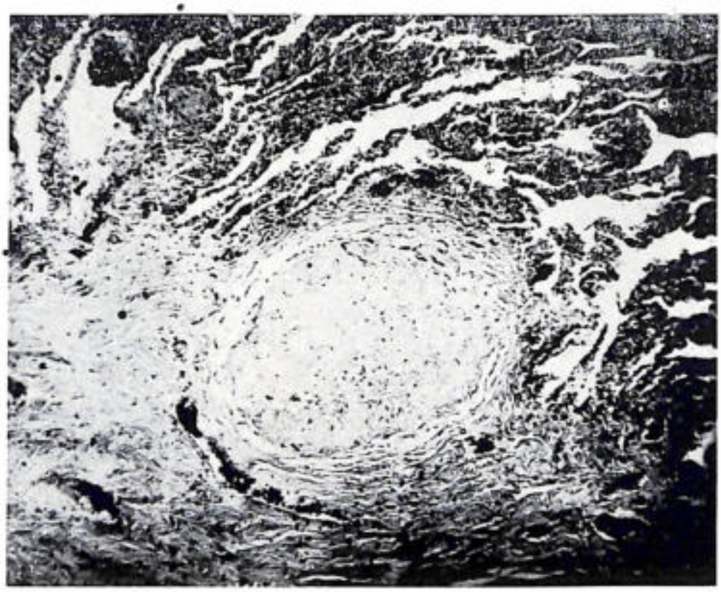


Fig. 39. Photomicrograph. Fibrosis of a tubercle. The hamadryad baboon Cheleken. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

lesion was probably located in the lower lobe of the right lung, joined in its lower sections to the parietal pleura by thick adhesions. Portions of gray granulation tissue and numerous small tubercles were distributed between the adhesions.

It was determined from an histological examination that the thick layers of fibrous tissue that considerably thickened the pleura extended only to the superficial layers of lung tissue. Masses of specific granulation tissue were visible among the coarse collagenous strands that were comparatively deficient in cells. In the center of these masses of granulation tissue we frequently saw deposits of calcium (Fig. 38). Many giant cells were found among the epithelioid cells in the peripheral sections. In some places the granulation tissue could not be seen. The collagenous tissue contained deposits of calcium. Isolated tubercles in which granulation tissue was wholly (Fig. 39) or almost wholly replaced by connective tissue were present in the pleura and in lung tissue. In addition, the lung tissue also had small, isolated epithelioid giant

Fig. 40. Tuberculous spondylitis with pronounced signs of sclerosis in the vertebrae. The hamadryad baboon Cheleken.

foci whose peripheral sections contained only a few delicate collagenous fibers. A thickening of the pleura was traced from the lymph nodes of the root of the right lung to the area of the most pronounced adhesions along the outer surface of the lower lobe of the right lung. Here and there it looked like a very dense strand, sometimes with deposits of calcium. Elsewhere in different parts of both lungs we found occasional small tubercles that in places were completely calcified. The basic mass of lung tissue, however, was normal. A few foci the size of a pinhead were present in the cortical substance of the kidneys.

An examination of the vertebrae showed that the bodies starting from about the fifth thoracic and ending with the last lumbar vertebrae had lost their usual uniformly cancellous structure. The bodies of most of the vertebrae were mottled (Fig. 40). Areas of very compact, homogeneous, yellowish-gray bone tissue almost completely displaced the ordinary cancellous bone tissue. Totally destroyed tissue together with an accumulation of thick gray-green pus in the carious areas could be seen in individual vertebrae of the infrathoracic and lumbar sections. Due to deformity of the vertebrae the spinal cord in the lumbar region was quite compressed. Histological examination of the areas of destroyed bone tissue revealed the presence of granulation tissue with many fine blood vessels and delicate collagenous fibers. Here and there the

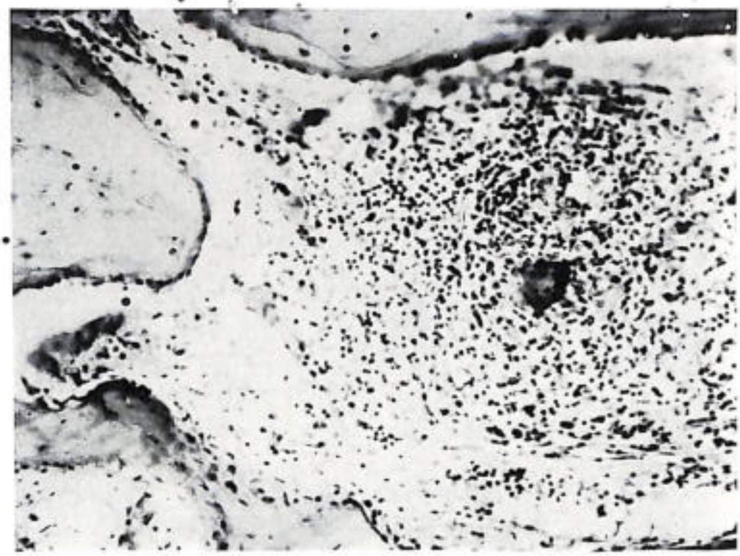


Fig. 41. Photomicrograph. Tuberculous granulation in vertebral tissue. The hamadryad baboon Cheleken. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

tissue was undergoing suppurative liquefaction. Masses of epithelioid cells frequently admixed with very large Langhans' cells were noted along with areas of nonspecific granulation tissue and accumulations of macrophages, lymphocytes, and plasma cells. From the focus of destruction the granulation tissue was partly growing into the adjoining medullary canals (Fig. 41). The trabeculae were quite thickened almost everywhere, especially on the border between the destroyed areas. The intervening medullary canals had become very small, sometimes disappearing altogether with the formation of compact, malformed bone (Fig. 42). Near the place where the vertebra was destroyed the marrow was gone from the canals, only its reticular stroma surviving. Portions of destroyed tissue along with the proliferation of specific and nonspecific granulation tissue were numerous in some of the vertebrae.

In addition to the above-mentioned site of the tuberculous process, we found a tuberculous proliferation of specific granulation tissue together with the formation in one place of a large (the size of a cherry stone) solitary tubercle at the base of the brain,

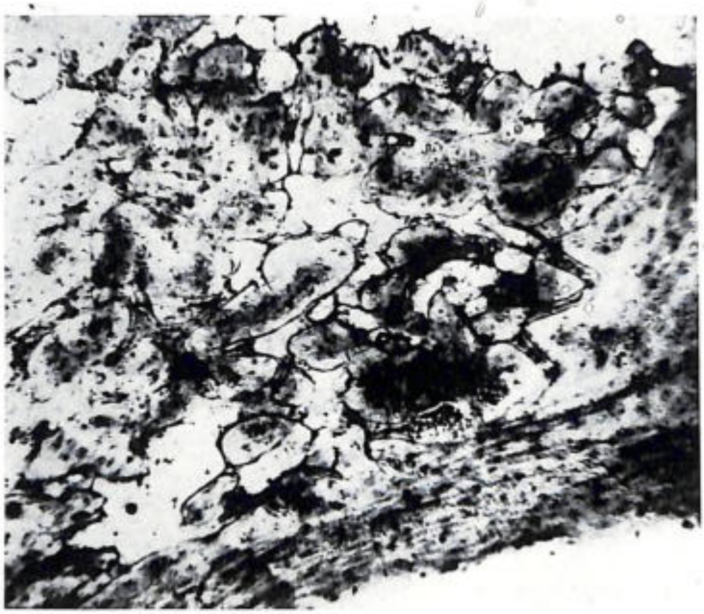


Fig. 42. Photomicrograph. New malformed bone along the periphery of a tuberculous focus in a vertebra. The hamadryad baboon Cheleken. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

around the medulla oblongata, and partly on the left hemisphere of the cerebellum. The center of the tubercle was completely caseous. Numerous tuberculous foci (1 to 2 mm in diameter) were visible in the same sections on the membranes, especially where the spinal cord meets the medulla oblongata.

This site of the tuberculous process is evidently very rare. Even by way of generalization of the process, such cases are either not encountered (Fairbrother and Hurst, 1932) or described as isolated (Hill, 1955, 1957).

Another rhesus monkey, which had been in the animal house for five years, died after exhibiting symptoms of tuberculous spondylitis. The animal had not been immunized with BCG vaccine. It reacted positively to tuberculin six months after coming to the animal house. This pronounced tuberculin reaction coincided with the onset of a lung disease diagnosed as pneumonia. The monkey had been placed in an isolation area following a positive ophthalmoreaction where it was briefly in contact (about two months) with very ill animals that subsequently died of tuberculosis. From the moment it reacted positively to tuberculin and almost to the end of its life (except the last year) the animal was periodically treated with streptomycin, PASA, and isonicotinic acid hydrazide. The first symptoms of vertebral involvement showed up one year and seven months before death in the form of progressive adynamia of the hind paws. The vertebral involvement was confirmed by x-rays, which showed destruction of the bodies of the eleventh and twelfth vertebrae. The animal died of uremia after chronic impairment of urination (development of phimosis).

The autopsy revealed marked distention of the bladder, ureters, and renal pelvis as well as a disseminated tuberculous process, which was most pronounced in the region of the bifurcation nodes of the trachea and in the spine. The bodies of the eleventh and twelfth thoracic vertebrae were partially destroyed. Some displacement toward one another produced a small hump and partial compression of the spinal cord. Unlike the tuberculous spondylitis of the baboon described above, the process here was confined to two vertebrae and was not accompanied by widespread sclerosis of the cancellous bone of the vertebrae.

Marked osteosclerosis with considerable thickening of the trabeculae was noted only in the partially destroyed vertebrae. Granulation tissue (chiefly epithelioid cell tissue) at the site of the destroyed bone tissue and adjacent lacunae contained a number of giant cells. Here and there the granulation tissue was undergoing necrosis and liquefaction. The surfaces of the two affected vertebrae facing each other were lacking in cartilage. The intervertebral space was filled with specific granulation tissue, which extended to the periosteum and lateral surfaces of the vertebrae. In addition to granulation tissue, we were able to see here disintegrating masses forming a cold wandering abcess on the inner surface of the lower portions of the thorax.

Many calcareous inclusions could be seen in the much enlarged bifurcation nodes of the trachea and paratracheal nodes in the midst of caseous masses. Tuberculous foci in the lungs, liver, and spleen were small and comparatively few in number. Besides caseous,

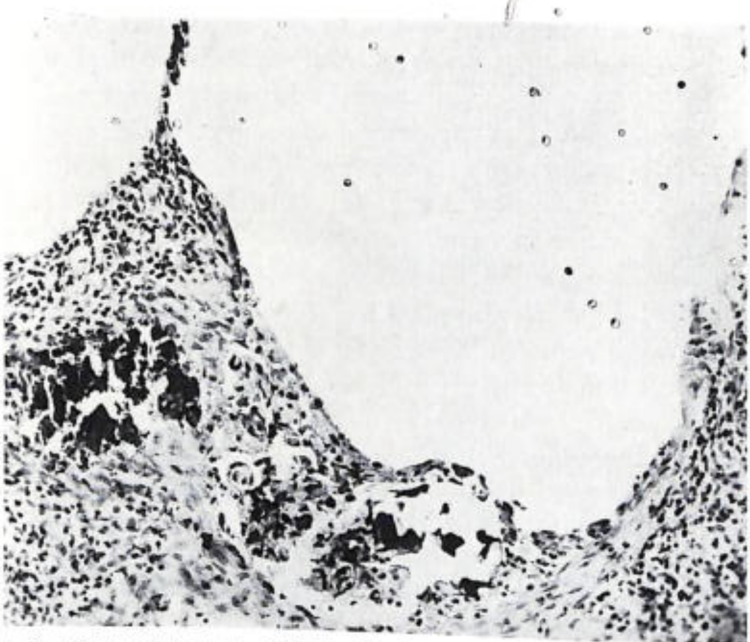


Fig. 43. Photomicrograph. Calcified foci in the lung of the rhesus monkey Robik. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

sometimes calcified foci (Fig. 43) the lungs were found to contain epithelioid tubercles surrounded on the periphery by a ridge of lymphoid cells. Many small foci were present in the cortex of both kidneys. Individual solitary tubercles were discovered in the pancreas. The granulation tissue commonly distributed around already calcified foci contained many multinuclear giant cells. A capsule of compact collagenous tissue was visible in most of the tubercles, except the fresh epithelioid tubercles. The bifurcation lymph nodes were caseous and full of calcium deposits and spreading sclerotic patches.

Thus, in these three cases the process, both clinically and morphologically, was chronic in nature. This was manifested by signs of sclerosis along the edges of the foci with indications of encapsulation accompanied by calcereous necrotic masses. The specific granulation tissue, unlike that in the acute cases of tuberculosis described above, contained many giant cells. It should, of course, be kept in mind that all the animals involved received antibiotics, but in the first two monkeys the period of treatment was so brief that it could scarcely have had any significant effect on the nature of the morphological manifestations of the tuberculous process in these animals. We must also emphasize that the chronic process in monkeys tends to affect the organs. In the cases of tuberculous spondylitis it is clear that from the beginning the process in the lungs was not widespread, but rather seemed to be limited to the formation of a primary complex. Moreover, the lymph nodes of the hili of the lung became much more involved than the lung tissue. In all the cases of chronic tuberculosis the process developed in wavelike fashion, ending in massive terminal dissemination.

In conclusion, we should like to point out that monkeys long resident in an animal house, contrary to the established view, may display considerable resistance when brought in contact with tuberculosis. However, this initial contact generally coincides with removal from their natural habitat and placing them in completely new surroundings. The development of progressive tuberculosis in monkeys is due, therefore, not to some susceptibility to the disease on the part of these animals, but to the fact that they may have been exposed to infection at an extremely unfavorable time, i.e., sudden captivity, different climatic conditions and food with resultant avitaminosis, dyspeptic disturbances, etc. As we tried to show before, even under these circumstances not all the animals infected become sick and die. It is primarily the weakened animals (those shipped under highly adverse conditions) that become sick. Other animals coming in contact with the infection become tuberculin-positive. It is quite possible that the monkeys that subsequently become tuberculin-positive start by developing a primary complex.

Besides a positive tuberculin reaction, another indication of an earlier tuberculous infection may be the presence of small sclerotic foci (in tuberculin-positive monkeys that die without symptoms of tuberculosis) of a calcified or ossified primary tuberculous complex in the bifurcation lymph nodes of the trachea. Two of the observations of S. G. Kaktin, who found tuberculous changes of productive character in the bifurcation lymph nodes of the trachea of a tuberculin-positive sacrificed monkey, likewise suggest that a tuberculin-positive monkey, even though completely healthy clinically, may have a primary complex. The fate of this complex tends to vary with the health of the animal, the conditions in which it is kept when the lesion develops, etc. One of the results may be a generalization of the process (sometimes like the primary pulmonary tuberculosis frequently observed in children).

In monkeys with greater resistance the primary complex may develop into a chronic process lasting years. However, it seems that the most frequent outcome of the infection is either healing of the primary complex with sclerosis and petrification or total disappearance of the primary complex. Moreover, the monkeys' contact with tubercle bacilli, regardless of whether the disease develops or not, is accompanied by immunological reorganization as reflected in a positive reaction to tuberculin. Even complete anatomical healing of the primary complex apparently does not mean biological sterilization, as shown by the fact that the tuberculin-positive reaction is virtually permanent. Neither petrification nor ossification of the healed primary focus signifies that the bacilli have disappeared from the animal.

Consequently, a positive reaction to tuberculin is indicative of a specific immunological reorganization following contact with a tuberculous infection. What then is the prognosis after such a reaction? Does it indicate that therapeutic and preventive measures (including sanitation) are in order? It is our opinion that the physician in charge should in each instance determine how the attendants are to be handled. Unlike Lubarsch (1917) and Hamerton (1936), who believed that it was impossible to detect the early symptoms of tuberculosis in monkeys, S. G. Kaktin (1958) worked out clinical techniques for detecting these symptoms. It would seem, therefore, that clinical observations are the decisive factor and that as soon as they indicate the presence of a tuberculous process, the latter should be treated the same way as an active form of the disease.

POLIOMYELITIS

It is a well known fact that infecting a rhesus monkey with the poliomyelitis virus can easily result in development of the disease with a typical clinical picture and pathoanatomical manifestations.

Monkeys can be infected in other ways than by intramedullary injection. For example, the disease has been reproduced in four animals by administering the virus orally (Horstman, 1952; Melnik and Ledinko, 1951; others). There are also a few reports describing spontaneous poliomyelitis in anthropoid apes (Müller, 1935; Schoen, 1936; Lindan, 1938; Tanaka, 1939; Howe and Bodian, 1944). In the cases described by Müller the disease developed in the paralytic form and it may have been the source of the disease in two children who had visited the zoo. Scott (1927) described three cases of "cage paralysis" which he considered comparable to poliomyelitis in man. He did not cite any data from actual investigations of these cases, but his reasons seem convincing to us. Hamerton (1936) states that "cage paralysis" is a collective term applied to various diseases including poliomyelitis. We agree with him.

We were unable to find any references in the literature to the disease arising spontaneously among the lower forms of apes.

During the fall of 1957 (between September 28 and October 8) six monkeys in the Sukhumi animal house came down with paralysis of the extremities. The disease broke out almost simultaneously in two cages fairly distant from each other (about 0.5 km). The first to be diagnosed were two adult female rhesus monkeys (Tolbi and Emba) in which flaccid paralysis of the hind limbs was detected during the course of the daily examination. These two animals along with four others in the same cage were isolated. The next day (September 30, 1957) a third adult female Gusikha was found to have flaccid paralysis of the left hind leg and tremor in the right hind leg when she moved. The animal's general condition was very poor. Three days later (October 2, 1957) the neuropathologist noted flaccid paraplegia, paresis of the trunk and thoracic muscles, and some drooping of the right corner of the mouth in facial movements. The condition steadily worsened and the animal was eventually unable to move, lying still on its side and scarcely breathing. Forced feeding induced vomiting. The animal died eight days after onset of the disease.

In the other two adult females (Neva and Khaya), who became sick on October 3 and 7, the disease started with the characteristic sluggishness and chills, tremor and flaccidity of the hind limbs. The animals moved their limbs with some difficulty. The second day of the illness Neva gave birth prematurely to an almost full-term dead fetus. Paralysis of all four extremities developed about this time and was soon followed by paralysis of the respiratory muscles. The animal died six days after onset of the disease. The disease lasted five days in Khaya who, besides paralytic symptoms similar to Neva's, had liquid stools the first few days. Khaya's baby, mostly breast-fed, developed on October 8 the symptoms of general depression in the form of sluggishness. Sneezing, mucous discharges from the nose, periodic tremor, mild digestive disturbances, and pulpy stools were also noted at the same time. The animal died on the second day of the illness.

Thus, six animals developed an infectious disease in a short period of time marked chiefly by clinical symptoms indicative of deep involvement of the spinal cord. Four of them died in less than ten days, i.e., on the second, fifth, sixth, and eighth days, respectively, after the disease was diagnosed. In the monkey dying on the second day the symptoms of paralysis were not noted during a general clinical examination.

The infectiousness of the disease was confirmed by a virological investigation (M. K. Voroshilova, N. N. Golubeva, Ye. A. Tolgskaya, I. K. Lavrova, and N. Ye. Gol'drin, 1958) in which the type II poliomyelitis virus was isolated from the brains of the dead monkeys. The authors demonstrated the pathogenicity of the isolated virus for monkeys by intramedullary infection of the animals. They were unable to determine the cause of the outbreak.

Macroscopically, the dead animals exhibited no significant abnormalities. There was marked plethora of the brain tissue, chiefly the gray matter of the spinal cord. Khada's brain was swollen. The autopsy revealed, in addition, moderate hyperemia of the internal organs and some hyperplasia in the mesenteric lymph nodes. In two of the animals (Khaya and Khada) the contents of the large intestine were semiliquid. Double focal pneumonia had developed in Neva. Microscopical examination of the animal that died two days after onset of the disease revealed pronounced hyperemia both of the brain membranes and of gray and white matter tissue with considerable dilatation of all the blood vessels down to the smallest of capillaries. Here and there tiny, chiefly perivascular, hemorrhages could be seen. A diffuse, pronounced swelling of the nerve cells, especially the small ones, was observed in the cortex of the various brain lobes (frontal, occipital, parietal, temporal) in preparations stained with thionine. The swelling was manifested in a rounding of the cell body which was sometimes so exaggerated that the cell lost its normal pyramidal form. Unevenly swollen, long cell processes were very prominent. The bodies of the nerve cells were pale and frequently possessed a very delicate, finely alveolate structure. The nuclei were frequently light-colored and vesicular with distinct nucleoli; there were, however, some cells with hyperchromatic nuclei. In the midst of the pale staining cells of the cortex were a few very pale staining cell shadows. Against this general background of swollen, pale staining cells could be seen single large pyramidal cells staining more intensely. Their processes were traceable for a considerable distance. There was no perceptible edema of the white matter.

Despite diffuse involvement of the nerve cells, we were unable to see any hyperplasia of glial elements. The neuroglia cells were somewhat hypertrophic, possessing large light-colored nuclei and small cell bodies with short fuzzy processes. Somewhat more extensive hypertrophy of glial elements was observed very close to the lateral ventricle, of which the lumen in the region of the anterior cornu was almost completely filled with desquamative cells.

Clearly pronounced hyperemia, swelling of nerve cells and lysis of individual cells were observed in the nodes of the base of the brain, but they were less distinct than in the cortex. There was no evident glial reaction. Swelling of the cell bodies and their processes with thorough staining of the latter for some distance together with lysis of individual cells could be readily seen in the nuclei of the cerebellum, especially in the dentate nucleus. The embolus was found to contain, in addition to the above, a large quantity of nerve cells whose protoplasm stained unevenly due to the presence of a few extremely hyperchromatic areas alternating

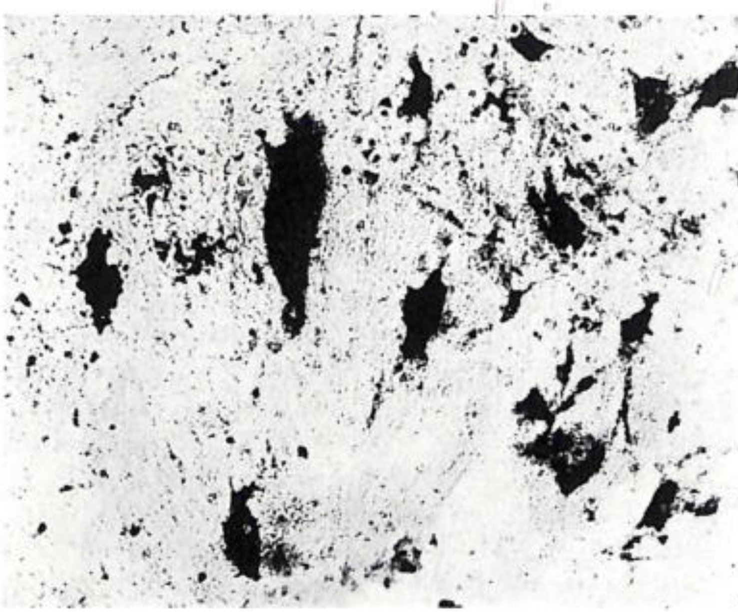


Fig. 44. Photomicrograph. Dying nerve cells in the anterior horn of the spinal cord. The rhesus monkey Khada. Stained with thionine. Obj. 60, oc. 10.

with individual pale staining portions of protoplasm. The contours of these cells were jagged as though eaten away. Their nuclei either could not be distinguished or were hyperchromatic with fuzzy outlines. The region of the embolus created the impression of some hyperplasia of glial elements and their bodies were moderately hypertrophic. The above-mentioned phenomena found in the nuclei of the cerebellum scarcely reached the cortex where we observed only the slightly staining processes of Purkinje cells.

The spinal cord was most affected as evidenced primarily by marked hyperemia, especially of the gray matter. Small hemorrhages, chiefly perivascular, were very frequent. They were particularly numerous in the region of the lumbar enlargement. Considerable swelling of the cells with staining of the processes for quite a distance was observed in the cervical, thoracic, and lumbar sections of the spinal cord. The relatively small cells seemed to be more affected. Many of them were in a pathological condition

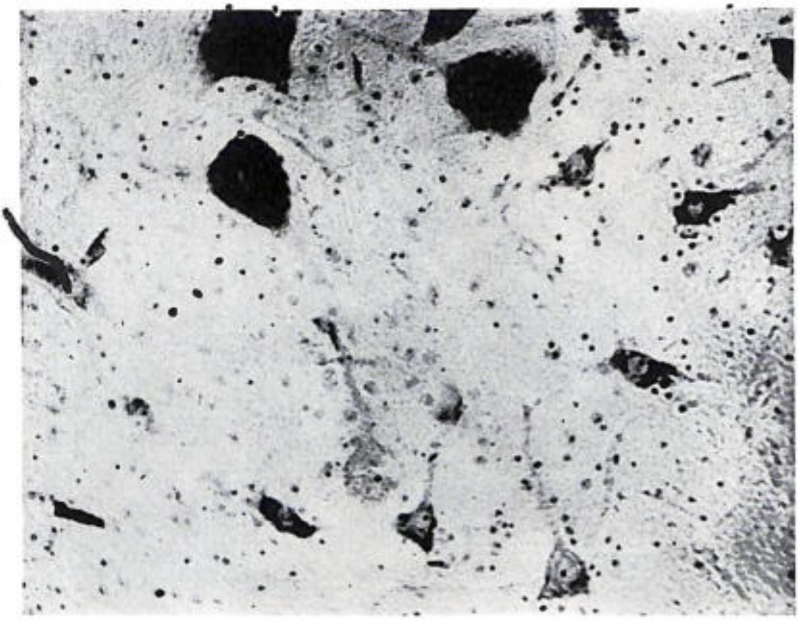


Fig. 45. Photomicrograph. Lysis of a nerve cell in the anterior horn of the spinal cord. The rhesus monkey Khada. Stained with thionine. Obj. 60, oc. 10.

with extremely uneven hyperchromatic protoplasm and nucleus (Fig. 44). Frequently the latter could not be discerned. The contours of the cells were very jagged as though eaten away. Some of the cells were undergoing lysis with the formation of shadows. Necrosis was particularly noticeable in the anterior cornua of the thoracic section of the spinal cord where there also was a distinct decrease in the number of nerve cells.

In the region of the cervical and thoracic enlargement we saw quite often large motor cells in satisfactory condition with light-colored nuclei and clearly outlined lumps of a chromophil substance. Among these cells were severely damaged cells with complete pulverization of the chromophil substance (Fig. 45). The contours of the nuclei could not be discerned; only the nucleoli were visible. The entire cell body was pale, apparently fine-grained and somewhat rounded. Individual, unevenly distended, pale staining processes branched out from it. Dying motor cells in

Fig. 46. Photomicrograph. Neuronophagia in the nucleus of the facial nerve. The rhesus monkey Khada. Stained with thionine. Obj. 90, oc. 10.

the anterior horn were somewhat more numerous in the lumbar section than in the cervical section. Pale staining cells undergoing lysis were found in the anterior horn of the spinal cord, in the central portions of the gray matter, and at the base of the posterior horn.

Pronounced hyperemia of brain tissue with individual small hemorrhages could be seen in all parts of the brain stem. In addition to involvement of the cell bodies, staining of the processes was regularly traced for a considerable distance. Some of the swollen cells were characterized by very pale staining up to the formation of cell shadows. Severely affected cells with the chromophil substance pulverized, outline of the nuclei blurred, and pale staining processes abnormally bloated were rather frequently encountered in the nucleus of the facial nerve. In addition, we were able to see here and there signs of neuronophagia with the introduction of glial elements into the body of the nerve cell (Fig. 46). Large cells with no perceptible pathology were found next to injured cells in

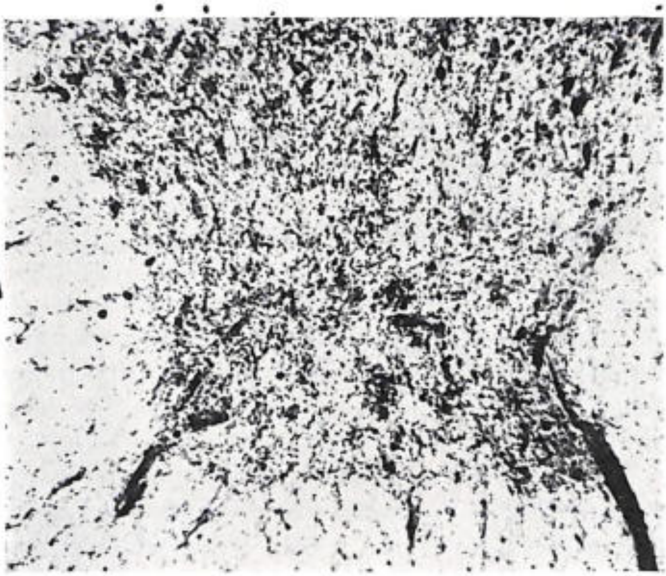


Fig. 47. Photomicrograph. Destruction and gliosis in the anterior horn of the spinal cord. The rhesus monkey Neva. Stained with thionine. Obj. 8, oc. 7.

the nucleus of the facial nerve. A great many dying cells were observed in Bekhterev's nucleus. Hyperplasia of the neuroglia was not marked either in the spinal cord or brain stem. There was little or no hypertrophy evident in the neuroglia. A narrow protoplasmatic body, sometimes with short processes, could be seen in the hypertrophic cells around a large light-colored nucleus.

The picture in the other three animals that died during later stages of the disease was similar. Severe spinal cord lesion was prominent. Signs of extreme destruction of brain tissue, chiefly in the anterior horn of the spinal cord, could be seen in the region of the lumbar and cervical enlargements (Fig. 47). No large motor cells could be seen. Surviving isolated small cells were generally in a poor condition. They were either very unevenly hyperchromatic with dark nuclei or they stained quite faintly, possessing a homogeneous or somewhat fine-grained structure. Occasionally neuronophagia was in evidence. Involvement of the nerve cells was not limited to the anterior horn. A few severely injured nerve cells were encountered in the central sections of the spinal cord and in the ventral sections of the posterior horn.

The destruction of nervous tissue was accompanied by a distinct glial reaction in the form of diffuse hypertrophy and hyperplasia of the tissue. These manifestations were so pronounced that it was often difficult to make out the boundaries of the greatly enlarged, ill-defined bodies of the nearby glial elements. Numerous neuroglial nodules were visible amidst the general hyperplasia of the neuroglia. The central portions of the nodules occasionally contained fragments of nerve cells. The glial reaction was sharply pronounced in the anterior horn and gradually diminished from front to back, but isolated neuroglial nodules could be seen at the base of the posterior horn.

The blood vessels were dilated both in the brain membranes and directly in brain tissue, especially in the region of the anterior horn. This was clearly seen in the monkey that died on the eighth day of the illness. Small hemorrhages were seen here and there. We frequently noted around the blood vessels of the gray and white matter a sharp reaction in the neuroglia, the cells and lymphoid elements of which formed massive cuffs. In some places these cells were round and fine-grained and looked like granular balls.

The central canal of the spinal cord was dilated. A mass of cellular elements was visible in the lumen. The picture in the thoracic section of the spinal cord generally resembled that just described, only here the destruction of the anterior horn was somewhat less marked, although the nerve cells frequently were severely injured. Many cells in Clarke's columns were also injured. Everywhere there was a distinct glial reaction. In one case (the monkey Khaya) hyperplasia of the neuroglia in Clarke's columns was unusually intense.

When the brain stem was stained with thionine, most of the nerve cells appeared to be swollen with deep staining of the processes for a considerable distance. The brain tissue was hyperemic. Glial cuffs of varying widths were generally seen around the vessels. Small hemorrhages were in evidence. Cells with varying degrees of injury were found in the reticular formation among the cells of the raphé and olives, especially in the nucleus of the facial nerve and vestibular nuclei. Besides injured cells the facial nerve included large cells with light-colored well-defined nuclei and chromophil substance possessing the usual structure. Diffuse hypertrophy of the neuroglia was noted near the nucleus of the facial nerve along with the formation of individual nodules.

In the cerebellum the nuclei were mostly affected, the emboliform in particular, where we noted marked hypertrophy and hyperplasia of the neuroglia with the formation of individual neuroglial nodules and cuffs around the blood vessels. Most of the nerve cells in this nucleus were severely injured with hyperchromatic nuclei and pulverized and pale staining chromophil substance. In places the protoplasm looked slightly alveolate. Pale staining cells with pulverized Nissl substance and somewhat hyperchromatic nuclei were also found in the nuclei; *dentatus, fastigii* and *globosus*. Cells in the cerebellar cortex were much less injured. We observed only the swollen processes of the Purkinje cells; the phenomenon was extremely marked in one monkey (Neva). The nodes of the base of the brain and cortex of the various cerebral lobes were found to contain some swollen processes of nerve cells, slight diffuse hypertrophy of the neuroglia, and hyperemia of the brain tissue along with isolated hemorrhages. Single dying brain cells with pulverized chromophil substance, swollen processes, generally pale staining fine-grained cells were noted among the large pyramidal cells in the ascending frontal gyrus (Fig. 48). Here too we found individual nodular acculations of neuroglia. In one case where we examined the olfactory bulbs (Khaya), we observed moderate swelling of the nerve cells with deep staining of their processes for a considerable distance as well as vacuolization of the protoplasm in isolated cells.

Thus, all the animals that we examined experienced severe injury to the central nervous system. One animal in which illness lasted less than two days without clinical symptoms of paralysis presented a picture chiefly of marked diffuse swelling and edema of the cells in the spinal cord and brain along with general hyperemia of the brain tissue and development of numerous hemorrhages. The almost total absence of a glial reaction is noteworthy. This was the background for more severe involvement of the spinal cord (than elsewhere) in which a great many cells were dying.

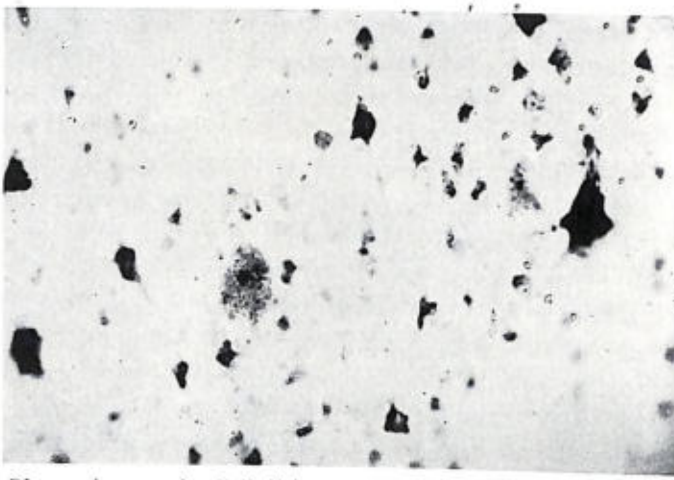


Fig. 48. Photomicrograph. Cell disintegration in the motor cortex. The rhesus monkey Neva. Stained with thionine. Obj. 40, oc. 7.

In the other animals that died at later stages of the disease spinal cord involvement was even more dominant. Necrosis of the basal mass of cells in the anterior horns resulted in their total destruction. This process was particuarly prominent in the region of the lumbar enlargement of the spinal cord; but it was also severe in the thoracic section. Death of the nerve cells was accompanied by a sharp glial reaction and by hyperemia of the brain tissue. Involvement of the nerve cells was observed in the anterior horns of the spinal cord, to a somewhat lesser extent in Clarke's columns, and least of all in the basal sections of the posterior horns.

The brain stem was also diffusely affected, but somewhat less so than the spinal cord. A great many dying cells were found in the nucleus of the facial nerve and in the reticular formation. In the cerebellum the nuclei, especially of the emboliform, were clearly injured. Injury to the cortex and nodes of the base of the brain was limited chiefly to manifestations of hyperemia. However, individual severely injured nerve cells were found in the motor zone of the cortex.

As for the other internal organs, abnormalities were much less pronounced than in the central nervous system. For example, hyperemia and small, mostly perivascular, infiltrates could be seen in the myocardium. Here and there in the large intestine were indications of epithelial desquamation and intensified production of mucus, some edema, and hyperemia of the submucosa. The monkey Neva, which died on the sixth day, had developed a focal, seromacrophagic type of pneumonia characterized by moderate adiposis of liver tissue and the presence of a few round-cell infiltrates.

It is evident from the above that the clinical manifestations and pathoanatomical structure of the disease are largely identical to those observed in human poliomyelitis and in monkeys experimentally infected with the disease (I. A. Robinzon and M. K. Voroshilova, 1949; M. P. Chumakov, I. M. Prisman, and T. S. Zatsepin, 1953; Rivers, 1955; M. K. Voroshilova, 1956; others). Typically the spinal cord is deeply involved; the process spreads to the brain stem leading to severe injury to the cells of the facial and vestibular nuclei, reticular formation, and cerebellar nuclei with involvement of the motor zone of the cortex.

PARASITIC DISEASES

Diseases caused by parasites are very common in monkeys. These diseases evidently make up almost the entire "monkey nosology" in their natural habitat. The pathology of monkeys in animal houses and zoos seems to be largely the result of invasions by a variety of parasites (chiefly helminths). This is convincingly shown by the comprehensive bibliography prepared by Halloran (1955), which familiarizes us with the diseases of wild animals and consists largely of reports describing helminths in monkeys.

From the various parasitic diseases affecting monkeys we have singled out tick invasion of the lungs for detailed description because of its highly stereotypic morphology and the fact that it is found in virtually all the monkeys brought from Asia.

Tick Invasion of the Lungs

There are comparatively few Soviet or foreign reports on that unusual lung disease of monkeys and man—tick invasion of the lungs. Schlotauer and Essex (1932), Wurm (1926), Fairbrother and Hurst (1932), Hamerton (1929), A. N. Sergeyev (1949), Grzimek

(1949), Kirsch (1950), Hill (1953), Innes, Colton, Jevick, and Smith (1954), B. A. Lapin (1956), B. A. Lapin and L. A. Yakovleva (1957), and A. P. Savinov and A. V. Tyufanov (1957) described parasitism in the respiratory system of the lower monkeys. Carter and Abrera (1946) mentioned tick invasion of the lungs in people living in Ceylon. Some of the above-mentioned reports (Innes, Colton, Jevich, and Smith, A. N. Sergeyev, and B. A. Lapin) note that even in pronounced forms of the disease clinical symptoms are frequently absent. In man, according to Carter and D'Abrera, the disease is characterized by heavy coughing with a copious discharge of sputum. Microscopic examination shows that the latter contains a fairly large number of adult tick specimens and larvae. This explains why tick invasion of the lungs in monkeys is so prevalent in certain regions.

While observing infested animals in the Sukhumi monkey house we were struck by the considerable viability and mobility of the ticks removed from lung tissue. The immature forms (nymphs) were exceptionally active; after removal from the bronchi to a slide, they moved up and down the slide for 30 to 60 seconds. When placed in a physiological solution at room temperature, they survived for about 30 minutes. They moved about for hours at a temperature of 30 to 35 °C.

This circumstance accounts for the spread of ticks from one person to another in a hot humid climate. The conditions at Sukhumi are apparently very favorable for the transmission of tick-borne diseases. The close quarters in which the monkeys live and the "searching" of one another also helps to spread the parasites.

We found ticks in the lungs of 381 monkeys that died of various causes. The vast majority of these monkeys had been brought to the animal house from India or China. Ticks were discovered in 22 animals born in Sukhumi. The percentage of animals infested with ticks, according to data from different sources, varies. This is apparently due to the fact that monkeys are shipped from different regions. However, all our cases involved rhesus monkeys from Asia. Fairbrother and Hurst say that 46% of incoming animals are infested. Innes and co-workers cite a figure of almost

100% infestation. It will be noted that in Sukhumi 80% of the total number of recently imported monkeys that died had ticks in the lungs. Most of the cases involved rhesus monkeys. However, ticks were found in Javanese macaques, green marmosets, geladas, pig-tailed macaques, and hamadryad baboons (in the latter two groups only among those born in the Sukhumi animal house).

The parasites were of two types—large, with four pairs of legs (adults), and small, with three pairs of legs (nymphs). The body was whitish, semitransparent under the microscope, and 0.3 to 0.5 mm long. Sometimes the ticks were brownish-red because of the considerable amount of blood elements present in their intestinal lumens.

After comparing this species of tick with that described by other investigators and using indirect evidence (nature of the pulmonary involvement, incidence among monkeys from certain regions, etc.), we classified our tick as *Pneumonyssus semicola,* first described in 1901 by its discoverers, de Haan and Griyns. Some references to the morphological features of the process can be found in Dorman (1939) and A. K. Sergeyev (1949). A more detailed description of the changes is given by Kirsch (1950), who made a careful histological study of four cases of tick invasion of the lungs in monkeys, and by B. A. Lapin (1956).

Dorman (1939), followed by Kirsch (1950) and Lapin, pointed out that pulmonary cirrhosis is highly characteristic of tick infestation. The development of bronchitis with bronchiectasis is also very common (Kirsch, Innes and co-workers, B. A. Lapin). A. N. Sergeyev held that the appearance of small cavities in the form of emphysematous vesicles is even more frequently associated with tick infestation. These vesicles are dilated alveoli surrounded by a zone of nonspecific inflammation.

The affected lung presents a fairly typical appearance, although there are some differences from case to case depending on the nature of the lesion and length of the process. The lung very frequently contains numerous yellowish, indistinctly outlined foci the size of a pinhead or smaller situated beneath the pleura (Fig. 49). Most of these foci are beneath the pleura, but there are a few in the lung proper. In some cases they are flat, light gray in

Fig. 49. Bronchitis with bronchiectatic areas. A rhesus monkey.

color, and do not protrude over the pleura. The former are the more common. They appear on the surface of the lung in the form of yellowish-gray tubercles frequently resembling tuberculous foci. In cross section these foci are rigid cavities with rather thick walls covered with grayish friable masses of detritus. Similar masses fill the lumen of the cavity wholly or partly. The flat whitish foci immediately collapse when cut and their lumens cannot be discerned without great difficulty. After the foci are cut, the live parasite can be extracted fairly easily with a teasing needle.

The openings of the draining bronchi can often be seen in the rigid cavities, which shows that the above-described cavities are bronchiectatic. Cavities with thick rough walls containing dry friable masses of detritus are associated with a more protracted process. The yellowish foci, which look like stearin spots and collapse when cut, are the acute initial changes that take place when ticks enter the terminal branches of the bronchi. Hemorrhages are occasionally found around these foci. Sometimes on the surface of the lung parenchyma one can see, with or without the above-mentioned changes, small vesicles the size of a pinhead or less that collapse as soon as they are cut. It is often difficult to distinguish the site of a cavity after it has been cut because the tissue has collapsed. However, individual ticks can be drawn out of these cavities too with the help of a teasing needle.

It is evident from a study of the history of the disease in monkeys that died naturally or were sacrificed in experiments and from observations of live monkeys reported in the literature that tick invasion of the lungs does not produce a clear-cut clinical picture. It is only in an occasional monkey that the slight coughing can be attributed, with some assurance, to ticks. The macroscopical changes in the lungs noted above closely resemble those in tuberculosis, although the correct diagnosis is easily established by histological examination of the lungs.

Microscopical examination reveals that when the infestation is characterized by the appearance of yellowish foci (flat or in the form of small tubercles elevated above the lung tissue) we are dealing with bronchiectatic cavities, sometimes acute, sometimes of longer duration. In the acute cavities there is diffuse infiltration of the bronchial wall by leukocytes and lymphoid cells, desquamation of the epithelial lining of the bronchus, accumulation of an exudate in the lumen of the bronchus, and slight peribronchial infiltration. A tick can frequently be seen in a microscopical section (Fig. 50).

The picture looks different in the case of older cavities. The noteworthy thing here is marked hypertrophy of the muscle fibers of the bronchial walls. Frequently the circular arrangement of the sharply hypertrophic muscle fibers found in the midst of wildly proliferating granulation tissue is almost the only indication that the existing formation is associated with the bronchus. There is no epithelial lining and the granulation tissue is heavily infiltrated with lymphocytes, plasma cells, and macrophages. The protoplasm of the latter contains a substantial amount of brown pigment, which produces a positive aniline blue reaction. Some hemosiderin is present in the granulation tissue outside of the cells. The lumen contains an exudate. Parasites cut up in various ways are often

Fig. 50. Photomicrograph. Acute ulcerative panbronchitis. A tick is in the lumen of a dilated bronchial tube. The hamadryad baboon Sampur. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

found in the preparations. Sometimes hypertrophic muscle fibers in the walls of the dilated bronchi branch outwards, forming a thick growth of muscle fibers nearby. The alveolar septa around these foci are somewhat thickened, their lumens constricted. The epithelium lining the alveoli and fissures between the strands of muscle fibers tends to grow tall, which sometimes creates the impression that they are adenomatous structures.

Muscle fibers become hypertrophic elsewhere than in the bronchiectatic areas. The muscles of the bronchial walls some distance away from the affected bronchi also undergo hypertrophy, frequently in the small bronchi and bronchioles. Muscles with thick ridges protrude into the lumens of the latter (Fig. 51). There is also hypertrophy of the muscle fibers in the alveolar septa, especially at the edges of the alveolar pores (Fig. 52). The epithelial

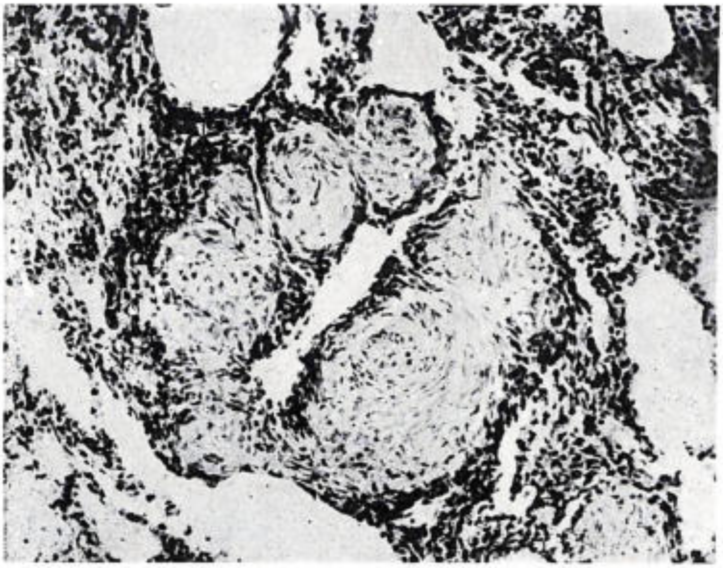


Fig. 51. Photomicrograph. Marked hypertrophy of the smooth muscles of the wall of a small bronchus. The rhesus monkey Ruta. Stained with hematoxylin-eosin. Obj. 20, oc. 5.

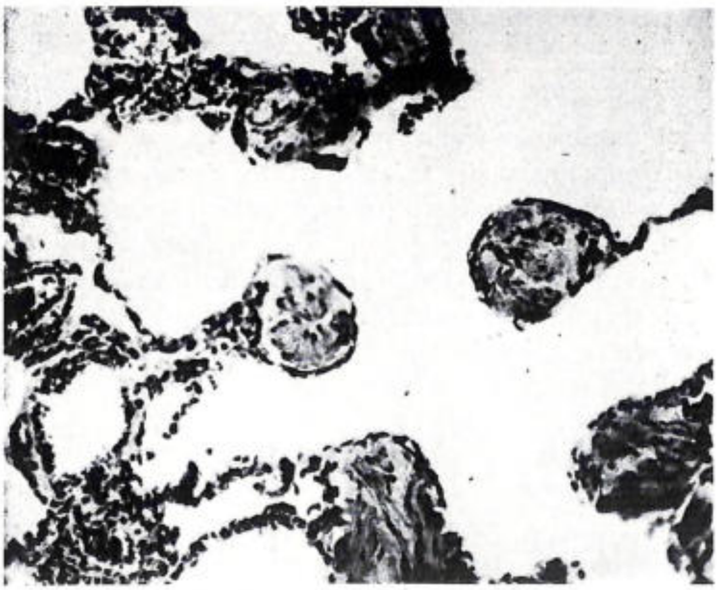


Fig. 52. Photomicrograph. Hypertrophy of the smooth muscles in the margins of the alveolar pores and in the septa. A rhesus monkey. Stained with hematoxylin-eosin. Obj. 20, oc. 10.

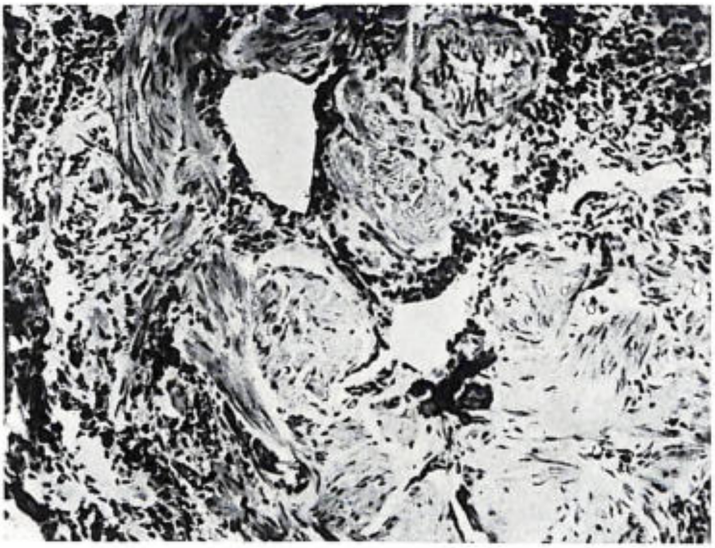


Fig. 53. Photomicrograph. Hypertrophy of the smooth muscles of the wall of a small bronchus with spreading of the muscles into the adjacent areas. The epithelial lining of the bronchus is preserved. A rhesus monkey. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

lining of these small bronchi is generally preserved although it is lower than usual and cuboidal in form (Fig. 53).

Less commonly the ticks settle in the alveoli rather than in the bronchi. Grossly, as described above, this is frequently marked by small cavities developing under the pleura and collapsing when cut. Microscopical examination reveals the presence of ticks in sharply dilated alveoli. Sometimes a narrow zone of lung tissue near the ticks is diffusely infiltrated with leukocytes and lymphoid cells. There is an exudate admixed with macrophages and plasma cells.

This description of isolated newer or older changes caused by ticks invading the bronchi or alveoli is somewhat arbitrary in that they are often found together. The existence of acute bronchiectatic cavities along with old ones as well as the presence of ticks in alveoli surrounded by a zone of nonspecific inflammation testify, in our opinion, to spread of the process within the same lung. Tick

Fig. 54. Chronic nonspecific tuberculosis. The rhesus monkey Tartas.

lesions are occasionally accompanied by the formation of delicate thin fibrous adhesions between the pulmonary lobes and between the lungs and the costal pleura.

We observed in two cases a far-reaching process which looked morphologically like nonspecific pulmonary tuberculosis (Fig. 54). X-rays made while one of the animals was alive led the clinicians to suspect tuberculosis. Coughing and slight dyspnea were symptoms. However, allergic tests for tuberculosis proved to be negative. The monkey was sacrificed in an acute experiment and the lungs at necropsy were extensively changed. The lungs were attached to the parietal pleura and mediastinal pleura by widespread fibrous adhesions. The lungs were shrunken and somewhat wrinkled with a thick fleshy consistency. The marked dilatation of the main bronchi at the roots of the lungs immediately caught our eye. These bronchi were surrounded by yellowish-gray cuffs. A liquid puriform exudate filled their lumens. The mucosa lining the main bronchi was cyanotic. The bronchi proceeding toward the pe-

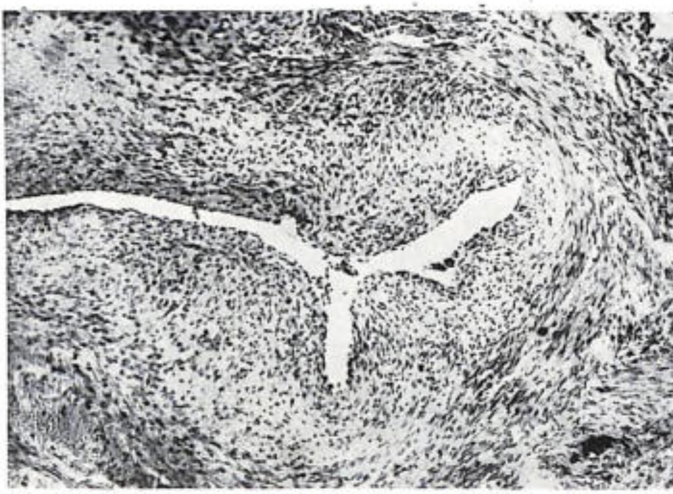


Fig. 55. Photomicrograph. Marked hypertrophy of a vascular wall. The muscle fibers branch from the outer layers of the wall into the adjacent areas of pulmonary parenchyma. The rhesus monkey Tartas. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

riphery were also surrounded by a cuff of very compact yellowish-gray tissue. The tissue formed fairly large continuous areas in the region of the upper lobes. They alternated with areas of comparatively unchanged lung tissue, producing a rather variegated picture. However, the most typical and striking phenomenon was the multitude of large, irregularly shaped cavities that were likewise surrounded by the compact yellowish-gray tissue. These changes were highly reminiscent of tuberculosis, but the openings of the draining bronchi found in each cavity showed that they were bronchiectatic.

Microscopical examination enabled us in principle to identify this process with the mild course of tick bronchitis described above, the main difference being that quantitatively all aspects of the process were much more pronounced. The massive areas of yellowish-gray tissue in the upper lobes of both lungs and the yellowish-gray cuffs around the bronchi were shown by microscopical examination to be areas of muscular cirrhosis. It was virtually impossible to find any connective-tissue fibers in the dense airless fields described above. Here and there in the areas of muscular cirrhosis could be seen a fairly large number of fissures lined with epithelium along with pseudoadenomatous structures.

The origin of the muscle fibers in the cirrhotic areas was clearly traced from the layers of muscle in the bronchial and vascular walls (Fig. 55). There was marked hypertrophy of the muscles in the pulmonary vessels found both in the cirrhotic area and in places some distance from it. A substantial number of arteriovenous anastomoses, normally almost imperceptible, was in evidence.

Hypertrophy of muscle fibers was universal and affected all regions of the lungs, including those distant from the bronchiectatic cavities. Muscle fibers of the bronchi and blood vessels as well as fibers in the alveolar septa and, in particular, on the edges of the alveolar pores were undergoing hypertrophy. Marked hypertrophy of the muscles was observed in the walls of the small bronchi and bronchioles. The hypertrophy muscle fibers of the latter were thicker than the lumens. The bronchiectatic cavities were full of ticks.

In the second case involving a severe extensive bronchiectatic process we noted marked signs of bullous emphysema in addition to the changes mentioned above (Fig. 56). The emphysema was caused by cirrhotic changes in the lungs.

Masses of round lymphoid cells sometimes forming real follicles are generally found both in the walls of the dilated bronchi and in the cirrhotic foci. I. K. Yesipova (1951) proved that this is caused by disruption of the outflow of lymph for which it may be regarded as a compensation.

To sum up, the most characteristic feature of tick invasion of the lungs is the presence of the parasites in the bronchi (chiefly in their terminal, subpleural branches) followed by severe destructive bronchitis and then bronchiectasis. Localization of the ticks in the alveoli is much less common and is accompanied by emphysematous dilatation of the alveoli containing the ticks and appearance of foci of inflammation. We should add, however, that the latter is not pneumonia in the nosological sense.

The second and perhaps even more characteristic feature of tick invasion of the lungs is the devlopment of muscular cirrhosis

Fig. 56. Bullous emphysema. The rhesus monkey Umnitsa.

of the lungs. "The development of so-called muscular cirrhosis . . . is essentially a collective term referring to any excessive proliferation of smooth muscle fibers in the lungs. It may be due to impaired bronchial and lymphatic drainage of the lungs. Accordingly, the bundles of smooth muscle fibers are overly abundant in the walls of the bronchi and lymph vessels" (Yesipova, 1952). However, despite the fact that the symptoms of muscular cirrhosis are nonspecific, we encounter them quite regularly in tick invasion of the lungs. We therefore agree with Dorman and the others who maintain that muscular cirrhosis is the most characteristic feature of lung tick infestation. We must nevertheless point out that marked hypertrophy of the smooth muscles of the lung also occurs in dictyocaulosis and in helminthiasis of the lungs of cattle, sheep, and horses (Nieberle and Kohrs, 1954). It is our view that hypertrophy of the lung muscles is typical of the pathological processes set in motion by the presence of the parasites.

Tick invasion of the lungs is by itself rarely fatal. Wurm (1926) and Gay and Branch (1927) also state that death from a tick infestation is very rare (and even then it is not the direct cause). Apparently an animal may die if the process is particularly far-reaching (like that described above) when cardiac insufficiency is added to pulmonary insufficiency. The case described by Grzimek (1951) is extremely uncommon. We therefore doubt that Hamerton (1939) and Hill (1952) were right in attributing the death of several monkeys directly to this condition. Since no details were given by the authors, we are inclined to believe that the animals died of some other disease, the tick infestation being intercurrent.

Helminths

Helminthiasis is very prevalent among animals. The available literature indicates that monkeys are quite specific carriers of many species of parasites—*Trichocephalus cynocephalus Khera* (Ye. N. Pavlovskiy, 1934), parasites of the genus *Odantorobius* (K. I. Skrjabin and N. P. Schichobalova, 1948). *Termidens deminutus, Ascaris lumbricoides, Ascaris cebi* (in capuchins), *Clolascaris Baylis* (Skrjabin and Schichobalova, 1948) have been found in the intestines of gorillas and monkeys. *Oesophagostomum apiastomum* has been found in the large intestine of anthropoid apes, Javanese macaques, and rhesus monkeys (Ye. N. Pavlovskiy, 1934; Tan Kok Siang and Lie Kian Joe, 1953). The tapeworms *Bartiella satyri Stil* and *Hiss* have been found in the intestine of anthropoid apes and macaques. The flatworm *Watsonius Watsoni Stibes* is a parasite in the cecum of macaques (Ye. N. Pavlovskiy, 1934).

Various species of filariae have been found in Old World and New World monkeys (Rudolphi, 1809; McCoy, 1936). However, the authors do not give a detailed description of the course of the disease and the pathological changes caused by entrance of the worm into the body. In Soviet literature we found only the short report of M. F. Nesturkh and O. I. Grigorova (1931) who described microfilariae (the larvae of an unknown form of adult filariae) in the blood of chimpanzees. The papers of the Moscow Zoo mention the discovery of worms in the lung of a white-shouldered capuchin without mentioning the species (N. P. Tsvetayeva, 1941).

Isolated observations made years ago in the Sukhumi animal house indicate that it is by no means uncommon for monkeys to be carriers of helminths. P. E. Butning (1948) investigated the feces of monkeys in a search for intestinal parasites and found only the nematodes *Trichocephalus* and *Trichostrongylus*. Some 63%

of the rhesus monkeys and 79% of the hamadryad baboons, the main species of monkeys in the animal house, were found to be carrying these parasites. P. E. Butning and B. A. Kacharava (1948-1949) mention finding at necropsy the polycystic *Echinococcus* in the lung of a green marmoset. In the abdominal cavity of four other marmosets the same authors came across what they regarded as cystercerci clinging to various parts of the peritoneum. However, they did not make any microscopical examination.

Examining the animals of the London Zoo for parasites, A. Porter (1954) found in newly arrived anthropoid apes the following: *Trichomonas, Balantidii, Entamoeba, Trichuris trichura, Enterobius sp., Strongyloides larva, Schistosoma typeova,* and *Oesophagostomum.* She found the same parasites in the same animals upon re-examining them the following year.

We do not propose to enumerate all the investigations of parasites in monkeys. Wiegert (1928) described the death of an orangutan in a zoo from ascariasis. Stadie (1930) mentioned finding parasites of the family *Strongyloidea.* Fairbrother and Hurst (1932) observed intramural intestinal parasites that they could not identify. Hill (1952) reported on filariasis in monkeys. He also described esophagostomiasis in monkeys with the formation of diverticuli in the intestine. Hamerton (1932) described round helminths in the bronchi of the (white-shouldered) squirrel monkey. Schultz (1938) while studying monkeys in their natural habitat observed that many of the animals were infested with helminths. Even these few selective references indicate that helminths are extremely prevalent among monkeys.

Since we are not helminthologists and are not concerned with elucidating the nature of the worm carrier state in monkeys, we shall confine ourselves to the data obtained from pathoanatomical examination of monkeys that died of a variety of causes in the institute. The parasites were identified at our request by the Zoological Institute of the Academy of Sciences USSR (M. N. Dubinina) and by the Helminthological Laboratory of the Academy of Sciences USSR (Prof. A. I. Spasskiy).

We found *Oesophagostomum apiastomum* to be a common parasite in the intestine of monkeys. It was almost invariably

Fig. 57. Hemorrhagic cysts in the submucosa of the large intestine at the invasion site of the parasite *Oesophagostomum apiastomum*. The redfaced macaque Lamela.

present in the large intestine of Indian and Chinese macaques chiefly in the wall of the cecum. Fairbrother and Hurst frequently observed "chocolate cysts" with unidentified nematodes in the submucosa of the large intestine of macaques. A. P. Savinov and A. V. Tyufanov (1957) also mentioned that they frequently saw these cysts in macaques.

Grossly, the invasion sites of the parasite look like irregularly rounded cysts about the size of a pea and filled with semiliquid masses of a reddish-coffee color (Fig. 57). A pathohistological examination clearly shows that the cysts are located in the submucous layer of the intestine. The lumens of the cysts are filled with clotted blood being resorbed by numerous macrophages grouped along the periphery of the cysts. The cysts have capsules of delicate collagenous fibers interspersed with many lymphocytes, segmentonuclear leukocytes, macrophages, and plasma cells (Fig. 58). Round-celled infiltrates and masses of macrophages loaded with lumps of brown pigment are present in all the coats of the intestine near the cysts. With the exception of the aforementioned, the mucous, muscular, and serous coats have no visible lesions.

Fig. 58. Photomicrograph. A hemorrhagic cyst in the submucosa of the large intestine. A parasite can be seen in the lumen of the cavity. The red-faced macaque Lamela. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

Nematodes (*Trichocephalus cynocephalus Khera,* 1951) are often found in the cecum of baboons. They are usually in groups of a few parasites each. Occasionally the infestation is very heavy. Only a few nematodes are found in macaques and much more rarely. The head end of the helminth is attached to the intestinal mucosa and is removed with difficulty; the filiform anterior part makes up two-thirds of its length. The places in the cecal mucosa where the worms penetrate, especially if the invasion is extensive, seem somewhat edematous and moderately hyperemic (Fig. 59). Histological examination reveals that the parasites bore into the surface layers of the intestinal mucosa without reaching the submucosa.

In the small intestine of a Chinese macaque we discovered 10 roundworms (7 female, 3 male) which in external appearance closely resembled the ascarid (*Streptopharagus armotus Blanc,* family *Spiruridae*). They were in the lumen of the ileum. The helminths were elongated and spindle-shaped, their bodies taper-

Fig. 59. *Trichocephalus cynocephalus* in the large intestine of a hamadryad baboon.

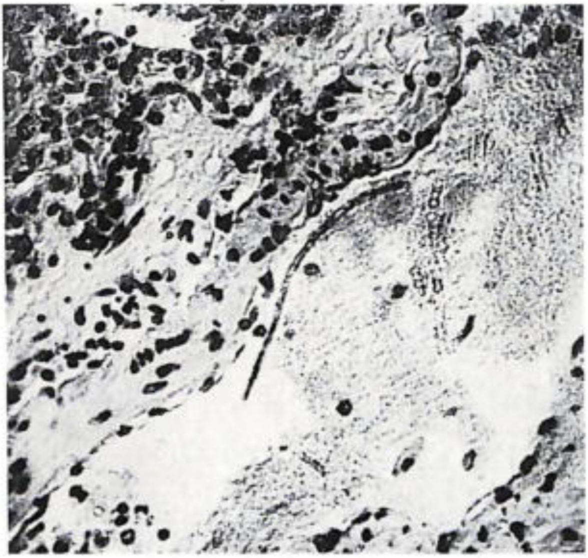
ing more toward the head than toward the tail. The tail end of the male was curled like a corkscrew. The parasites were covered with a distinct cuticle on which could be seen very delicate, uniform cross striations in addition to folds of various sizes. The body of the female was 4.4 to 6.1 cm long, averaging 1.5 mm at the widest part and 0.5 mm in the region of the head. The body of the male was 2.5 to 2.8 long and 0.8 to 1 mm wide. The intestinal mucosa appeared to be unchanged in the section where the helminths were found.

We also noted filariasis in six capuchins shortly after they reached the institute's animal house. The presence of microfilariae in the blood of these monkeys enabled us to make an early diagnosis and to examine clinically carriers of filariae over a period of five months. Two of these six monkeys were not given a clinical examination because one of them died of pyogenic meningitis soon after arrival while the other was sacrificed in an experiment involving poliomyelitis. A careful clinical examination of the other four animals failed to turn up any abnormalities; they seemed to be completely healthy. Their body temperature fluctuated considerably from 37 and several tenths to 39° C, a common phenomenon in monkeys of various species (S. G. Kaktin, 1958). There was no noticeable pattern either for the temperature curve or for the indicators of morning and evening temperatures.

To detect and count the microfilariae, we examined either smears usually stained by Giemsa's method or (to observe live filariae) plasma or citrated blood in a dark field. The number of microfilariae in the blood when counted in an ordinary smear varied from monkey to monkey. There were 15 to 30 of them in Chilik and Orchik, sometimes 100, and 200 or more in Orchik. Very few—one, two, or three—were discovered in the other two animals examined clinically. More or less the same amount was found in the blood at different times during the day. They were particularly numerous in blood taken from the ear. Only isolated microfilariae were present in venous blood and none at all in urine or cerebrospinal fluid.

The microfilariae were of different kinds. Some were coarse looking about 162 to 165 μ long and about 4 μ wide; they showed up in various shades of violet when stained by Giemsa's method. Others were thinner and more delicate (108 μ long and 2 μ wide), staining light blue in the same smears. When stained by the hematoxylineosin method, the bodies of the microfilariae looked finegrained. One end, apparently the head, was blunt. This end, which was quite noticeable in the larger specimens when the blood was examined in a dark field, was used for forward locomotion. The tail end was pointed.

The pathological changes noted in the organs and tissues of monkeys infested with filariae are mostly caused by adults. We examined six animals that died of various diseases or were sacrificed in acute experiments. The morphological picture at necropsy looked more or less uniform. There was some degree of emaciation, maximally exhibited by those monkeys most infested (Orchik, Chilik). The skin and visible mucosa were in all cases clear. The serous leaflets lining the cavities were also clear, smooth, and shiny. In some cases we were struck by the increased amount of fluid in the abdominal cavity, somewhat viscous but quite transparent. In the abdominal cavity of all the monkeys but one, in whose blood there were only isolated microfilariae (Kaperts), we found live,



ZOOLOGICAL GARDEN CALCUTTA

Fig. 60. Photomicrograph. Microfilariae in the lung of a capuchin. Stained with hematoxylin-eosin. Obj. 40, oc. 7.

filiform, round parasites *Dipetalonema gracile,* which were 9.2 to 24.6 cm long and about 0.2 to 0.5 mm wide. The number of worms ranged from three to nine and they moved about freely in the abdominal cavity between the intestinal loops. There were none at all in the pleural or pericardial cavity. Histological examination revealed the presence of microfilariae in the blood vessels of all the internal organs, including those of the brain (Fig. 60).

Four of the capuchins mentioned above had filariae in the abdominal cavity as well as in the lungs. In the more severe cases the lungs were unevenly dense. Areas of distended lung tissue alternated with more compact airless areas. Irregularly outlined grayish-pink foci with tuberous surfaces could be seen in all the lobes directly under the pleura, mostly on the outside of the lungs. In cross section these foci appeared to be small coalesced cavities and ducts containing live, round, very thin filiform helminths 4 to 8.5 cm long (*Dipetalonema* (?) *sp.* family *Filariidae*).

Histological examination revealed the presence of worms in the lumens of the alveoli and small bronchi forming elongated

Fig. 61. Photomicrograph. *Filaria sp.* in the lumens of alveoli and bronchi. The alveolar septa are thickened and infiltrated. A capuchin. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

cavities. The alveolar septa here were for the most part quite thickened due to proliferation of connective-tissue cells and infiltration, chiefly by lymphocytes (Fig. 61). There were a great many eosinophils among the cells of the infiltrate. The lung tissue outside the zone where the worms were also appeared changed in some degree. Numerous small atelectatic areas were found everywhere as well as excessive hemorrhages in the lumens of the alveoli, less commonly in the lumens of the bronchi. Some of the lumens of the alveoli were filled with a serous exudate abounding in alveolar macrophages. Occasional bronchial lumens were filled with an exudate rich in segmentonuclear leukocytes thoroughly admixed with blood. The blood vessels of the lungs were markedly dilated.

The entire group of capuchins had ulcerative lesions in the small intestine due to penetration of the intestinal wall by the parasite *Molineus torulosus,* family *Trichostrongylidae.*

Changes in the intestine were manifested in varying degree and mostly localized in the duodenum. In some cases macroscopical examination revealed the presence of numerous round formations

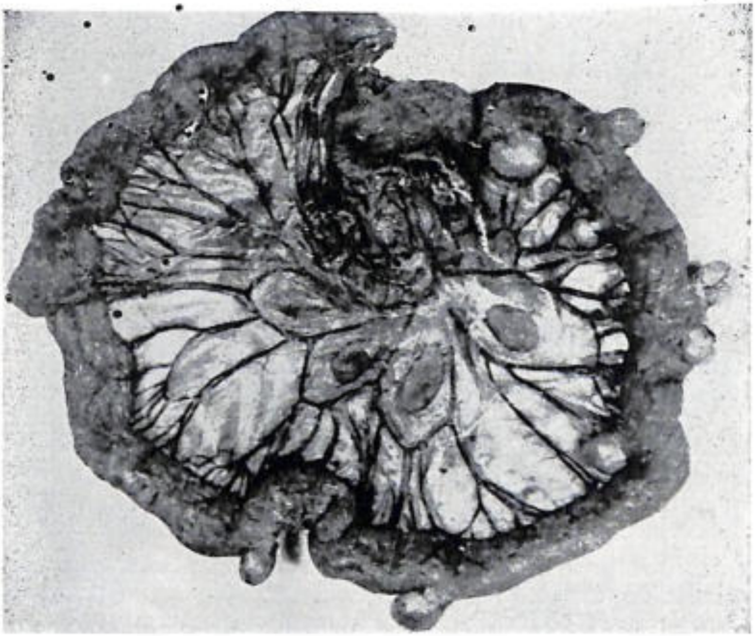


Fig. 62. Diverticula of the intestinal wall (jejunum) caused by penetration of the wall by *Molineus torulosus*. A capuchin.

the size of a large pea in the lower sections of the duodenum and in the large intestine under the serous membrane. On closer scrutiny these formations turned out to be intestinal diverticula (Fig. 62). The cavities of the diverticula communicated with the intestinal lumen through a narrow pore and (Fig. 63) were filled with live, small, round, filiform parasites 0.4 to 1.1 cm long. The latter were surrounded by a puriform exudate and they were easily forced into the intestinal lumen when the diverticula were squeezed. In other cases eventration of the wall was slight and the diverticula were not so prominent on gross inspection. Here the intestinal lumen contained numerous ulcers with infiltrated margins; live helminths were also found deep in the ulcers. Microscopical examination of the walls of the diverticula in the small intestine revealed the proliferation of compact fibrous tissue forming the base and margins of the ulcers with marked infiltration by lymphoid and

Fig. 63. Opening connecting a diverticulum with an intestinal cavity. A capuchin.

plasma cells (Fig. 64). These infiltrates were particularly noticeable around the blood vessels where they formed here and there circumvascular cuffs. Ordinarily within the diverticula proper there were several cavities with necrosed walls saturated with leukocytes and lymphocytes. The lumens of these cavities were always full of parasites. The structure of the intestine at the sites of the ulcers was broken and the serous membrane generally somewhat thickened. The intestinal mucosa and submucosa around the ulcers were undergoing necrosis almost everywhere. We counted 10 to 16 parasites in a single cavity. A rough count in the small intestine of one capuchin came to 184. Isolated live helminths were also found moving about freely in the duodenum and jejunum. There were no live parasites in the lower divisions of the intestine. The mucosa of the small intestine near the ulcers with the parasites was inflamed with indications of edema, congestion of the blood vessels, and numerous hemorrhages. Numerous small hemorrhages were noted away from the zone of the ulcers in the mucosa of the small intestine and, in particular, of the large intestine.

Hill (1952) observed similar diverticula in the monkeys Red. Colob. and Monkey; in two of the animals the intestine was perforated.

Fig. 64. Photomicrograph. Sclerotic capsule in a diverticulum with signs of infiltration by lymphoid and plasma cells. A capuchin. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

The autopsy of a young imported rhesus monkey revealed that a small section of the gastric wall was thickened. At this place in the submucosa there were several small round cystoid communicating formations in whose lumens was found the short, bright red filiform parasite *Nochita nochti*. The mucosa here was hypertrophic and protruded for a considerable distance into the lumen of the stomach. The glandular tubules in this area were markedly dilated in places and somewhat irregularly distributed, which made the tissue resemble a tubular polyp. A similar phenomenon was observed by Bonne and Sandground (1939) in Javanese macaques. The authors describe the appearance of adenomatous gastric tumors caused by penetration of the gastric wall by *Nochtia nochti*.

We very rarely found flat helminths in monkeys. We came across *Echinococcus* (cystic form) in two cases. One animal (a hamadryad baboon) had echinococcus cysts in the lungs. The polycystic *Echinococcus* was found in the subcutaneous tissue and muscles of the scapular region in a gelada. Microscopical exam-

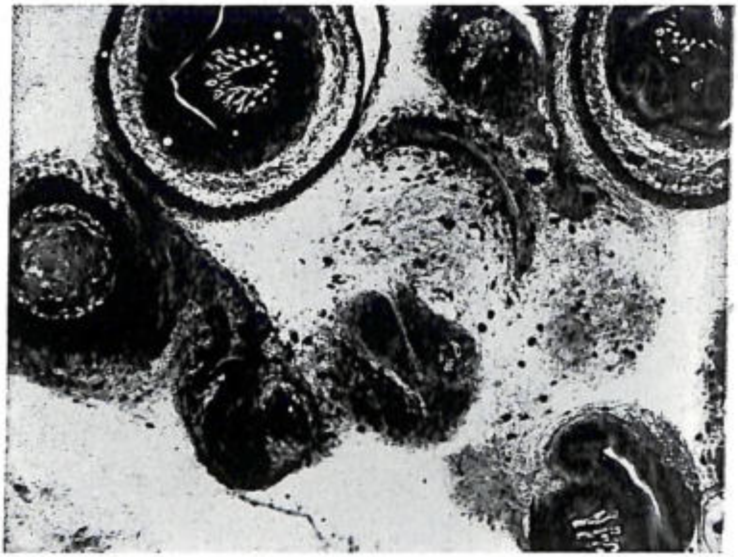


Fig. 65. *Echinococcus* in the subcutaneous tissue of the scapular region. The gelada Yamal.

ination of the infested area revealed numerous round cavities filled with a pale fluid. The lumens of the cavities contained groups of scolices of the parasites somewhat eccentrically arranged (Fig. 65). The scolices had a typical structure. The mouth openings possessed numerous chitinous hooks. The inner membrane of the cavity was thin and structureless. The outer capsule consisted of connective-tissue fibers interspersed with numerous round cell infiltrates containing substantial numbers of plasma cells and, not infrequently, eosinophils. Isolated multinuclear giant cells could also be seen. In the tissue surrounding the echinococcus cysts were areas of various sizes undergoing necrosis and suppurative liquefaction. Here and there calcium deposits were noted in the necrotic masses.

Five adult Javanese macaques arriving in a single small batch in 1956 were found at necropsy to have a great many long flat inarticulated parasites (the plerocercoids *Diphyllobothrium erinacei*) lying about in small groups in the connective tissue of various parts of the abdominal cavity. A thin connective-tissue capsule sur-

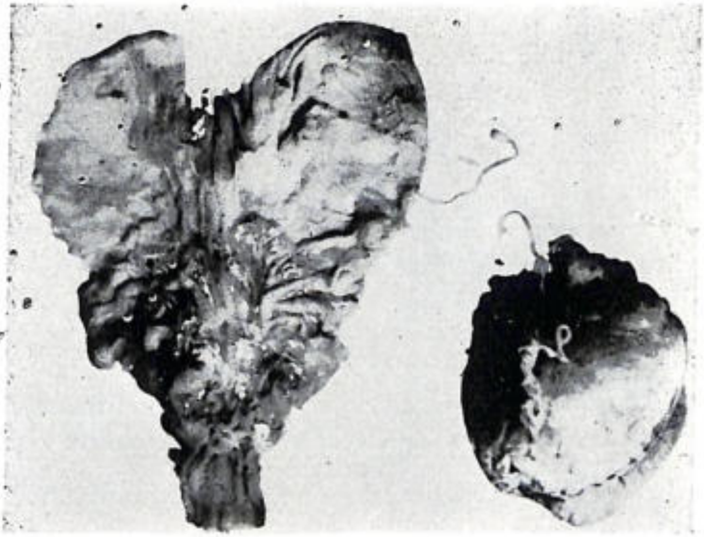


Fig. 66. Flat helminths in the gastric wall (left) and between the membranes of the testis (right). A Javanese macaque.

rounded the worms. They were present in the gastric wall, in cellular tissue of the kidneys, and between the membranes of the testes (Figs. 66 and 67). All the monkeys harboring the parasites were very emaciated.

In other cases of parasitism flat helminths were found in the intestinal lumen. The mucosa remained unchanged. We saw flat filiform helminths in only three animals. A brown capuchin that died soon after reaching the animal house in 1953 was found to have two flat parasites that were quite alike, the larger being 16.5 cm long. It had a distinct irregularly rounded head, short thin neck, and a long articulated body consisting of 352 segments. The head measured 0.3 mm at its widest. It had small oval suckers and a tiny proboscis that protruded only slightly. The segments gradually increased in size toward the end so that the last ones were 1 to 1.2 cm in diameter. The species to which the parasite belongs has not been determined. One specimen each of long articulated helminths (*Bertiella specii*) similar to those described above was found in two Indian macaques. Single *Bertiella studeri* were noted

Fig. 67. Photomicrograph. Capsule around a cavity in the gastric wall containing a flat parasite. A Javanese macaque. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

in a few rhesus monkeys. The cecal lumen of two other Indian macaques were found to contain a great many trematodes—small racket-shaped bright red parasites tightly attached to the intestinal wall by the narrow end. Besides the above, an autopsy occasionally revealed the presence of numerous small calcareous nodules (mainly in the liver) in completely healthy monkeys. This may have been the result of multiple cysticercosis of the liver when calcium was deposited in the dead parasites.

Thus, published material as well as our own data indicate that a variety of helminths very frequently infest monkeys. However, many of the species typically cause only moderate pathological changes. Exceptions are *Oesophagostomum* and *Strongyloides*, which exhaust the monkeys and may produce severe complications. We are not discussing here the helminths that infest the anthropoid apes. Although the lower apes are heavily infested with helminths, only certain species are prevalent. *Oesophagostomum* is common among macaques, *Trichinelloidea* among baboons, filariae and *Strongyloides* among capuchins. These worms are essentially parasites of monkeys, despite the fact that under certain conditions they may infect man. Parasites common to man and to monkeys (we are speaking here of helminths) seem to be extremely rare. Cameron (1929) wrote that the parasites of man and monkeys are for the most part different. This is borne out by our material, which indicates, in turn, that the helminths are peculiar to monkeys in their natural habitat.

It is likely that conditions in the Sukhumi animal house are not favorable for completion of the developmental cycle of most of the parasites enumerated above, as evidenced by the fact that they are found only in imported monkeys, and not in those born in the animal house. The only exception is *Trichinelloidea*, which are found with equal frequency in imported and in native-born monkeys.

NONINFECTIOUS DISEASES

DISEASES OF THE CARDIOVASCULAR SYSTEM

Hypertension

Experiments performed under the supervision of D. I. Miminoshvili (1956, 1957) demonstrated the theoretical possibility of experimentally reproducing hypertension in monkeys by creating severe neurotic disorders in them. The use of natural stimuli and interference of natural reflexes (sexual and protective), which are very strong in this species of animals, achieved results unattainable by earlier investigators who followed the methods that had been successfully employed to produce persistent neuroses in dogs (S. D. Kaminskiy, 1935; L. Bam, 1936, 1939; others).

Relying on I. P. Pavlov's data indicating that stimuli applied to various cortical and subcortical points negatively reinforce one another and exert much greater influence than does the interference of stimulatory and inhibitory stimuli elaborated on the basis of food conditioned reflexes, Miminoshvili made successful use of the method to produce neuroses in monkeys. The method of creating conflict situations by means of natural stimuli enabled him in a short time to produce severe neurotic disorders with persistent somatic disturbances in the form of continuously elevated blood pressure. D. Masserman and K. Pachtel (1953) also produced experimental neuroses in monkeys using the same approach. In principle, G. M. Cherkovich (1956) accomplished more or less the same thing when she altered the daily routine (thereby changing the normal rhythm of physiological functions). The method proved to be even more successful because neurotic disorders set in sooner and more severely impaired the activity of the cardiovascular system.

An investigation of blood pressure in the monkeys of the Sukhumi animal house (G. O. Magakayan, 1953) and of normal electrocardiograms (G. Ya. Kokaya, 1954, 1958) turned up a great many animals suffering from persistent high blood pressure with electrocardiograms similar to those of persons with coronary insufficiency. After analyzing the material, we have come to the conclusion that monkeys used over a long period of time in different experiments and kept in regular cages tend to have hypertension and coronary insufficiency. Animals in open-air cages almost never develop these diseases.

Experimental reproduction of neuroses and associated hypertension and coronary insufficiency enabled us to elucidate the mechanism of comparable conditions arising in monkeys kept in the animal house for a long time. Cardiovascular pathology is the commonest somatic manifestation of a neurosis. Hypertension occasionally develops after a neurosis. Coronary insufficiency arises at the same time or a little later. This condition may precede hypertension, arise independently, or be absent altogether (D. I. Miminoshvili, G. O. Magakayan, and G. Ya. Kokaya, 1956). These diseases have no clinical symptoms and they can be detected only from blood pressure and electrocardiographic data. The usual sequelae for man—myocardial infarct and cerebral hemorrhage—seem to be the rarer in monkeys.

In this section we plan to discuss chiefly the pathoanatomical changes in monkeys caused by hypertension. We studied a total of 14 animals (6 rhesus monkeys and 8 baboons) which had elevated blood pressure while alive. Thirteen monkeys died of various causes or were sacrificed in experiments; only one died of cerebral hemorrhage, a direct complication of hypertension. Three of the 14 animals, as revealed by an electrocardiogram, exhibited symptoms of coronary insufficiency in addition to hypertension. The animals ranged in age from five to 25 years. Eleven, with elevated blood pressure, were used over a long period of time in different experiments and only three were never used or were used briefly.

In nine of the animals elevation of blood pressure persisted one, two, five years or more within these limits: maximum, 150 to 180 mm mercury column; minimum, 90 to 105 mm mercury column. Five animals exhibited substantial fluctuations with a periodic drop to normal values in an occasional animal (e.g., Forum) the fluctuations were quite substantial, rising periodically to large values (170/95 mm) and then dropping to subnormal figures (100/50 mm). The fluctuations in these five animals resembled those in persons with a transient form of hypertension.

Morphological changes in hypertension are regularly marked by hypertrophy of the myocardial fibers, which become enlarged with big, vesiculate nuclei. However, hypertrophic changes in muscle fibers are not invariably present. Hypertrophy of the myocardial fibers was pronounced in seven animals with persistent high blood pressure and in one animal (Robik) whose hypertension was transient. In the other cases myocardial hypertrophy was weakly pronounced (Boltun'ya, Yasen', Banan) or could not be observed at all (Forum, Blokha). There is some correlation between the extent of myocardial hypertrophy and the duration and degree of elevated arterial blood pressure. For example, the monkey Vasilek consistently showed a very high pressure for six years. Hypertrophy of the muscle fibers was quite pronounced. Considerable hypertrophy of the myocardial fibers was observed in Beluga, who suffered from persistent hypertension for at least three years (the condition was discovered in 1955 and the animal died three years later).

Fairly uniform changes were noted in the kidneys of three animals. Mostly the glomerular apparatus was affected. Changed glomeruli were generally found in the area of the focus of sclerotic changes in the kidneys and along their periphery.

The lumens of the glomeruli contained solid homogeneous masses of albumin staining pink with eosin. Less common were glomeruli in which the albuminous masses were deposited between the wall of the capsule and the retracted loops of the glomerular arterioles. Solid homogeneous masses of albumin invaded the arterioles of the glomeruli, but the path of the individual arterioles could be traced (Fig. 68). Heavier accumulations of pink-stained albumin still allowed tracing the nuclei of the arteriole endothelium, although the individual loops could not be discerned. The final stage of the process was total homogenization of the glomeruli, disappearance of the nuclei in the albuminous masses, and transformation of the glomeruli into hyaline nodules.

In one instance changes in the glomerular apparatus developed in a different way. Obliteration of the glomeruli was caused both

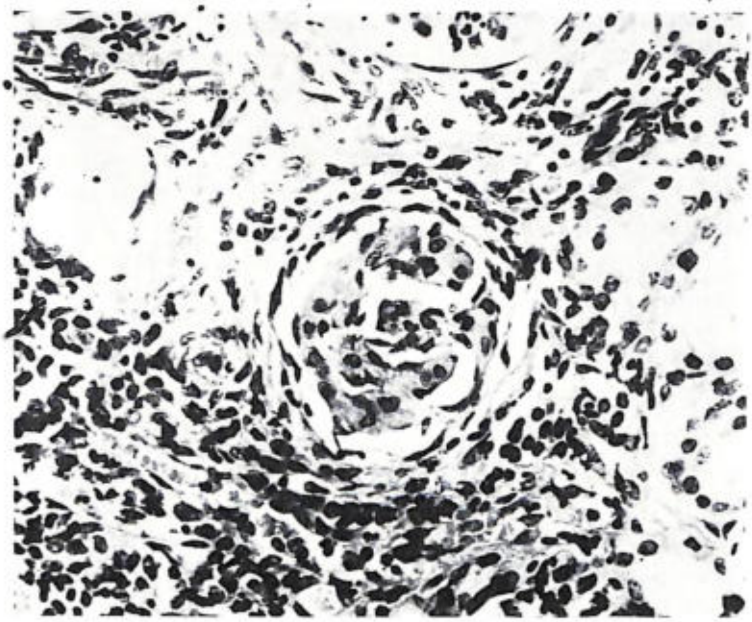


Fig. 68. Photomicrograph. Deposition of albuminous masses along the arterioles of the glomeruli. The rhesus monkey Yakhta. Stained with hematoxylin-eosin. Obj. 40, oc. 7.

tension (Vesta, Yakhta, Beluga, Grubiyanka, Vasilek) and one monkey with irregularly elevated blood pressure (Yasen') exhibited in the myocardium varying numbers of small and larger scars in the central portions of which the muscle fibers had atrophied and died. Two of these monkeys (Vesta and Vasilek) had atherosclerotic plaques near the orifice of the left circumflex artery of the heart. The plaques were flat and thus unable to block the supply of blood to the myocardium. As mentioned above, the animals did not die of hypertension, but as a result of an experiment or some other disease. In only one case (the rhesus monkey Yasen') was death due to cerebral hemorrhage. This was about the only death from hypertension, i.e., from one of its most typical complications. Let us therefore examine the case a little more closely.

Yasen' came to the animal house in 1953 when it was quite young. In 1954 it was used in the laboratory of experimental by the exudation of albumin into the lumens of Bowman's capsule and by sclerotic processes. The glomeruli were converted into connective-tissue nodules. The kidney scars were wedge-shaped in places, the base facing out toward the surface of the kidney. Slight contractions were noted there, imparting a granular appearance to the kidney. The small scars (area of contraction) were usually marked by the proliferation of young cell-rich connective tissue containing changed and unchanged glomeruli. Most of the glomeruli in the region of cicatricial contraction were wholly or partly obliterated. A few tubules surviving near the scar were also changed. Some of their lumens were small and barely discernible. Others were greatly enlarged. The intima of the main blood vessels was smooth, with no signs of atherosclerosis, in those cases where wedge-shaped scars formed in the kidney.

In two monkeys with persistently elevated blood pressure (Beluga, Mississippi) sclerosis in the kidneys was diffuse. In addition to changes in the kidneys, five monkeys with persistent hyperoncology which inserted an ampul of radium into a bone to reproduce an osteoma. Thereafter the animal was periodically injected with methylcholanthrene. It was a carrier of Flexner's dysentery bacteria for a long time and was repeatedly treated with antibiotics.

The animal's maximum blood pressure in 1956 was found to be elevated for the first time—135 to 140 mm mercury column. However, the minimum pressure was not elevated, tending rather to lower values. In 1957 the pressure rose to 145 to 170 mm. The minimum pressure also rose, but slightly—from 60 mm to 80 to 85 mm. This comparatively slight increase in arterial pressure was nevertheless fairly high for this animal in view of the low original minimum pressure. No further measurements were taken. On July 28, 1958 the monkey suddenly became paralyzed in the left extremities. Its condition remained satisfactory for three weeks when it unexpectedly died (August 19).

The autopsy revealed the dura mater to very turgid. Removal of the dura mater exposed the asymmetry of the cerebral hemispheres caused by perceptible swelling of the right hemisphere where the gyri were considerably smoothed out. The frontal lobe of the right hemisphere contained a massive hemorrhage extending to the parietal region and embracing the right subcortical ganglia

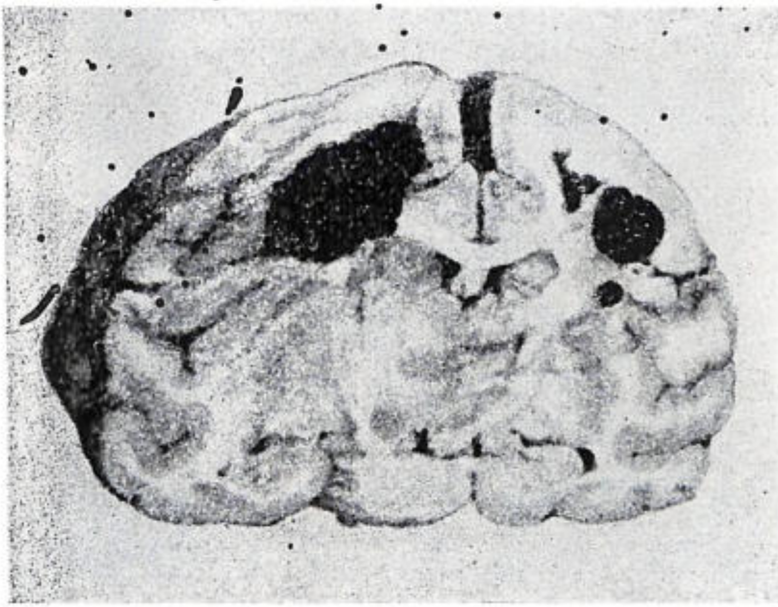


Fig. 69. Cerebral hemorrhage. The rhesus monkey Yasen'.

surrounded along the edges by brain tissue staining pale yellow. Fresh hemorrhages varying in size from a pinhead to a pea were scattered about the white matter of the left hemisjhere and in the cortex and frontal and parietal regions (Fig. 69). The blood vessels of the base of the brain were thin and transparent. Their lumens were clear. No changes were observed in the other organs except for acute hyperemia of the internal organs.

Microscopical examination of the medulla revealed hemorrhages that were here and there delaminating the medulla while cavities filled with erythrocytes were being formed. Sometimes we noted diffuse infiltration of the brain tissue by erythrocytes with the medulla destroyed for a considerable distance. The small arteries of the brain showed signs of plasma saturation. The vascular walls were thickened, homogenized, and structureless (Fig. 70). In addition to signs of marked plethora in the kidneys, we noted the transudation of albuminous masses into the lumens of the glomeruli which at times tended to crowd the arterioles of the

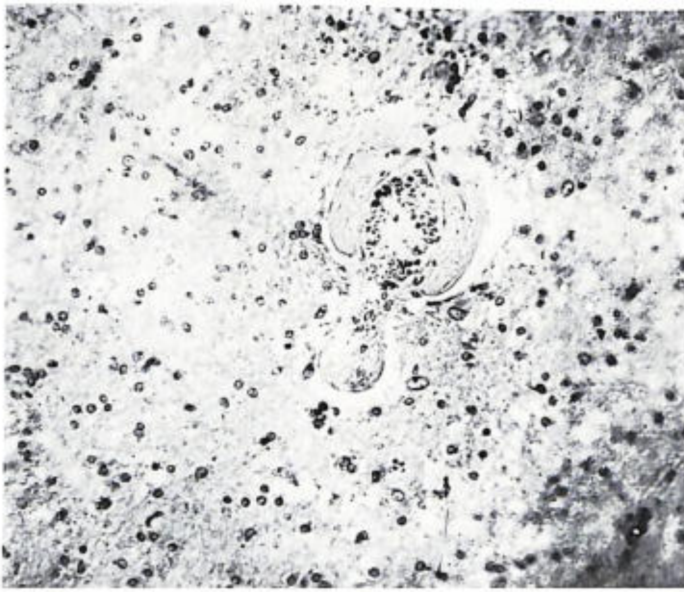


Fig. 70. Photomicrograph. Plasma saturation of a vascular wall in the brain. The rhesus monkey Yasen'. Stained with hematoxylin-eosin. Obj. 20, oc. 10.

glomeruli to the periphery. Individual glomeruli were completely obliterated. Some of the small blood vessels showed signs of plasma saturation of their walls, resulting in thickening of the latter and constriction of the vascular lumens. There were indications of hypertrophy of the myocardial fibers with occasional sclerotic foci of varying sizes. The signs of myofibrosis were diffuse in isolated areas.

In this instance the morphological changes were quite typical of hypertension and analogous to the plasmorrhage followed by homogenization of the vascular wall described in hypertension.

Consequently, the morphological manifestations of hypertension in monkeys, as may be judged from the small amount of material cited, are marked by involvement of the small blood vessels in the process—another point of similarity between the disease in monkeys and that in man. Typically, the kidneys, heart, and brain are also involved.

Our research and clinical observations conducted for several years in the Institute (G. O. Makagayan, 1953, 1958; M. A. Grigoliya, 1957) indicate that hypertension in monkeys follows a comparatively benign course. We have not been able to calculate the frequency and nature of cerebral crises in hypertensive monkeys and our meager material does not permit us to make any generalizations.

Coronary Insufficiency and Cardiosclerosis

Coronary insufficiency is rightly considered a disease found only in man. Textbooks of pathological anatomy and of therapy describe it not as an independent disease, but as a common complication of hypertension or atherosclerosis. It is more often linked with atherosclerosis of the coronary vessels and subsumed under coronary atherosclerosis or vice versa. The interrelation of hypertension and coronary insufficiency stems from the fact that both originate from a single pathological condition in the form of a neurosis. The two diseases quite often arise together (either one may follow the other). However, coronary insufficiency frequently arises without the subsequent development of hypertension.

The term "coronary insufficiency" is not applied to animals, but there are references in the literature to cardiosclerosis in certain animals (particularly work horses) following "neurogenic impairment of the coronary blood flow" (Nieberle and Kohrs, 1954).

Myocardial infarction should be regarded as a form of coronary insufficiency when manifestations of the latter have become pronounced. In its classical form myocardial infarction is known to us only in monkeys, but there are just a few descriptions of the cases. Hamerton (1941) described a myocardial infarct accompanied by atherosclerosis and thrombosis of the coronary vessels in a mangabey. He also described (1946) the sudden death of a mangabey which at necropsy was found to have a massive red infarct of the left ventricle of the heart. No stenosis of the coronary arteries was observed, and atherosclerotic plaques were present only around the orifice of coronary vessels. We believe that in the first case the infarct was not the result of thrombosis of a coronary vessel; rather, it originated at the same time as the latter due to vasomotor disturbance of the coronary blood flow. There may be some justification for assuming a causal relationship between the infarct and involvement of the coronary vessels in this case, but not in the second case. Atherosclerotic plaques around the orifice of coronary vessels cannot be explained either by the degree of disturbance of the coronary blood flow or by the insult factor in the genesis of a myocardial infarct. In both instances the infarct was noted in aged monkeys that had lived for a long time in the London zoo. Despite the lack of any data on the condition of their nervous systems, we have no doubt that they were neurotic due to prolonged captivity. We know from experience that most monkeys in zoos are neurotic.

Returning to the interrelation of atherosclerosis, coronary insufficiency and myocardial infarction, we maintain that if the presence and degree of coronary insufficiency in animals were related to atherosclerosis of the heart vessels, we ought to find very often disturbances of the coronary blood flow in certain species of birds which have exhibited atherosclerotic vascular changes possibly just as pronounced as those in man. In point of fact, however, we were unable to find in the available literature even a single reference to myocardial infarction in birds.

Signs of coronary insufficiency in monkeys not experimentally induced were recorded electrocardiographically by G. Ya. Kokaya between 1954 and 1958 during a mass examination of the main group of monkeys in the Sukhumi animal house. Experimental research on hypertension and coronary insufficiency performed under the direction of D. I. Miminoshvili (1956-1957) demonstrated the connection between the above-mentioned cardiovascular diseases and neurotic conditions and laid the foundation for elucidating the mechanism underlying the development of spontaneous coronary insufficiency in monkeys.

An analysis of the material shows that coronary insufficiency is frequently associated with hypertension, both being somatic manifestations of a neurosis. We had at our disposal for morphological investigation five adult monkeys (one hamadryad baboon, two rhesus monkeys, and two green marmosets), which died at various ages (from 8 to 25 years). Electrocardiograms indicated the presence of coronary insufficiency in all these animals. We were unable to tell how long they suffered from coronary disturbances since they showed up during a mass examination on an average of one to one and one-half years before the animals died. In three of the monkeys coronary insufficiency was combined with hypertension (as mentioned in the preceding section). No elevation in arterial pressure was observed in two (the green marmosets Rio and Paragvay).

A morphological examination of four animals (two hypertensives and two with normal arterial pressure) revealed numerous scattered sclerotic foci of varying extent and age in the myocardium. No traces of coronary insufficiency were detected in the myocardium of one of the monkeys. Coronary insufficiency in monkeys is apparently due to functional impairment of the coronary blood flow. The insignificant flat plaques found in the intima of the coronary arteries of two monkeys (Vesta, Rio) were too small to have served as mechanical blocks to circulation. Nor is coronary insufficiency attributable to lipidosis of the intima of the coronary arteries, which is more frequent in monkeys. In one case (the rhesus monkey Robik), despite the coronary disturbances recorded electrocardiographically while the animal was alive and periodic elevation in arterial pressure, histological examination failed to reveal any signs of cardiosclerosis.

The cause of cardiosclerosis in monkeys, according to our observations (as mentioned in the preceding section), may be hypertension, even in those cases where the electrocardiogram of the animal does not show any indications of coronary disorders. Similar phenomena are known in human pathology, for not infrequently an investigation of the myocardium of hypertensive patients reveals clear signs of cardiosclerosis.

In this connection we should like to point out that cicatricial changes can be observed in the myocardium of monkeys that do not have hypertension or coronary insufficiency documented electrocardiographically.

We examined the hearts of 90 monkeys of various ages, from two and one half years old to senility. In nine animals the walls of the left ventricle and interventricular septum contained scattered sclerotic foci varying in age and extent. We believe that cardiosclerosis in some of the cases was the consequence not of coronary insufficiency, but of myocarditis. For example, in two cases there were faint indications of myocarditis besides scattered foci of connective tissue. This supports our view that the signs of cardiosclerosis here resulted from an earlier myocarditis.

However, it is very difficult to differentiate coronary cardiosclerosis from myocarditic cardiosclerosis when symptoms of myocarditis are absent.

Coronary insufficiency in monkeys outwardly follows a benign course. Yet the development of a myocardial infarct is theoretically possible even in monkeys. We have already described a case of chronic aneurysms in the left ventricle of the heart after a previous myocardial infarct (B. A. Lapin, 1956). These chronic aneurysms could not be interpreted as being other than the consequence of previous myocardial infarcts. They apparently developed with very few clinical symptoms because a careful study of the history of the animal revealed no indications of any disease that could have been regarded as acute myocardial infarction. This was the cause of the animal's death, developing as cardiac insufficiency with hemostasis in the systemic circulation and general edema.

The autopsy revealed marked edema of subcutaneous tissue in the region of the trunk and extremities plus accumulation of an edematous fluid in the pleural and pericardial cavities. The heart was enlarged with dilated cavities. On the rear wall of the left verticle in the area of the posterior longitudinal sulcus was a round protrusion about 2.1 cm in diameter. Near the protrusion the rear wall of the left ventricle was very thin, a delicate film of connective tissue. Whitish connective-tissue strands stretched from the eventration to the adjacent portions of the myocardium. A large white dry thrombus lay alongside the endocardium (Fig. 71). Another protrusion of the left ventricle with a very thin wall and covering an area approximately 1 x 0.5 cm was noted on the front wall of the left ventricle in the upper section of the anterior longitudinal sulcus. The endocardium near the aneurysms was thick, milky-white in color. There were a great many mural, intertrabecular thrombi in the left antrium and ventricle. The intima of the aorta and initial part of the innominate artery contained numerous flat yellow spots and atherosclerotic plaques. The coronary vessels were clear, their intima smooth and apparently unchanged. The

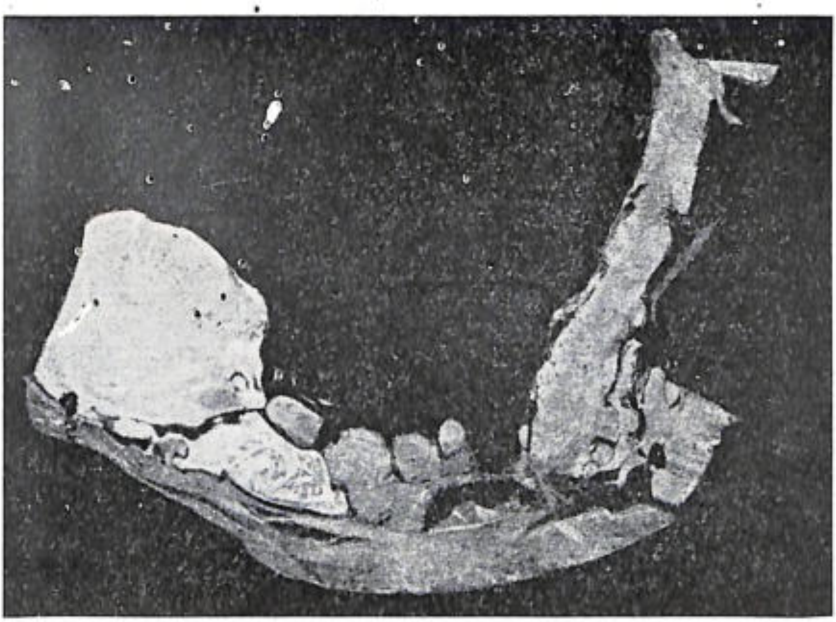


Fig. 71. Chronic aneurysm with mural thrombosis in the posterior wall of the left ventricle of the heart. Natural size. The lapunder macaque Zuzya. Stained with hematoxylin-eosin.

liver was somewhat enlarged, compact, its surface fine-grained, in cross section showing a nutmeg pattern. There were cyanotic induration of the spleeen and kidneys and congestion in all the tissues and organs.

Thus, the autopsy revealed chronic aneurysms of the left ventricle of the heart with signs of cardiac insufficiency, edema, nutmeg liver, and cyanotic induration of the organs. A microscopical examination did not show any changes in the coronary vessels. The initial symptoms of nutmeg cirrhosis were visible in the liver while the kidneys and spleen showed distinct signs of congestion.

We stated above that the two large aneurysms of the left ventricle were caused not by myocarditis, but apparently by earlier myocardial infarcts. However, we also want to stress that this was the only case in our material in which death resulted from cardiac insufficiency. This condition had existed for a fairly long period of time, as indicated by cardiac cirrhosis of the liver. Decompensation developed for reasons unknown to us and was the cause of the animal's death. A study of the anamnesis of the monkey disclosed that it had been used every day in a long series of highly complex experiments on higher nervous activity. The experimenters and physicians detected the symptoms of a neurosis, which resulted in a myocardial infarct.

To sum up, we have found that coronary insufficiency in monkeys is generally combined with hypertension, originating in vasomotor disturbances caused by a natural neurosis. More rarely, a vasomotor neurosis may show up as an isolated disorder of coronary blood circulation without any signs of hypertension. The indications of cardiosclerosis found in the myocardium of half the hypertensive monkeys apparently are to be regarded as the morphological manifestation of undiagnosed coronary insufficiency. It is a fair assumption that a number of cases of coronary insufficiency escape the notice of physicians.

The existence of coronary insufficiency in monkeys despite the rarity of atherosclerosis of the coronary arteries suggests that coronary insufficiency is caused by functional disorders of coronary blood circulation. This view is further reinforced by the fact that atherosclerotic changes in the coronary arteries, whenever they are present, are usually so slight that they cannot mechanically hinder the coronary blood flow. Some of the cases of cardiosclerosis must have been caused by earlier myocarditis.

Atherosclerosis

Atherosclerosis has been the object of extensive research. Much effort has been directed at modeling this pathological process through the production of alimentary hypercholesteremia and at investigating the conditions under which atherosclerosis may arise. The reproduction of atherosclerosis in rabbits by feeding them cholesterol enabled Acad. N. N. Anichkov to formulate his infiltration theory of atherosclerosis.

Hypercholesteremia, although it is easily reproduced in rabbits (the animals do not normally receive cholesterol with their food) and leads to the deposition of lipids on the vascular walls, does not seem to be the cause of atherosclerosis in man. Man normally eats a good deal of cholesterol with his food. The substance is usually involved in a variety of metabolic processes. Efforts to reproduce atherosclerosis in animals, specifically in monkeys, by creating alimentary hypercholesteremia have not been successful (Hueper, 1946; Kawamura, 1927; others). Other experimental factors besides hypercholesteremia (lowering metabolism by the use of methylthiouracil to depress the functioning of the thyroid gland, setting up diets lacking in this or that vitamin, etc.) enabled some investigators to reproduce atherosclerosis in dogs, monkeys, and other animals (Rinehart and Greenberg, 1949; Mann, Andrus, McNelly, and Stare, 1952; T. A. Sinitsyna, 1957; others).

Atherosclerosis is a major disease of people over 50 years old. The pathology of the organs involved is quite familiar. Most frequently affected are the aorta, blood vessels of the heart, brain, abdominal organs, and kidneys. The process begins with the deposition of cholesterol in the intima of a vessel followed by sclerotic phenomena, which are considered a secondary reaction to deposition of the lipids. The latter takes place in wavelike fashion, alternating with phenomena of resorption. Old atherosclerotic plaques frequently contain deposits of calcium salts, which are not a precondition of atherosclerosis, being probably a form of dystrophic calcification.

Domestic animals (old dogs, horses, pigs, cattle) exhibit vascular lesions, which outwardly resemble atherosclerosis in man. Sclerotic involvement of the blood vessels of animals is chiefly of two kinds. The commoner is deposition of calcium salts in the middle coat of the vessels, mainly the aorta (K. G. Bol' and B. K. Bol', 1954; Nieberle and Kohrs, 1954; Pallaske, 1955; others). A similar phenomenon is also known in people over 50 years old (N. N. Anichkov, 1947; others). In man, however, this process appears to be primary and is not as pronounced as primary calcinosis of the middle coat in animals. In addition to the above, there is another process in animals closely resembling atherosclerosis in man. We are referring to lipid infiltration of the intima accompanied by moderate sclerotic changes there. However, unlike that in man, the process in animals involves the deposition chiefly of neutral fats. This is very common in cows (V. D. Tsinzerling, 1913; V. D. Tsinzerling and Sh. I. Krinitskiy, 1925; K. G. Bol' and B. K. Bol', 1954; Nieberle and Kohrs, 1954; Pallaske, 1955; others). Nieberle and Kohrs emphasize that this process in animals cannot be equated with atherosclerosis in man due to the neutral character of the fats deposited. Lipid infiltration of the intima of vessels in animals usually proceeds in benign fashion without significant sclerotic changes and, as a rule, without signs of atheromatosis.

Pigs exhibit arteriosclerotic changes, in addition to the above-mentioned processes, which closely resemble atherosclerosis in man. Gotlieb and Lalich (1954) studied the aortas of 2,000 pigs ranging in age from four months to three years and found a great many compact white plaques 0.5 to 10 mm in size in the lower part of the arch and in the thoracic aorta. In isolated cases the plaques contained small calcium deposits. Cholesterol or neutral fats were not found either between the cells or in intercellular tissue. Thus, this process too only outwardly resembles atherosclerosis in man, differing from it in absence of the main symptom—infiltration of the intima by cholesterol.

We have only scattered reports on sclerotic vascular lesions in wild animals. Krause (1939) mentioned atherosclerosis in kangaroos and giraffes living in zoos. Hamerton (1930, 1933) described atherosclerosis (sometimes accompanied by calcinosis) in badgers and squirrels and in one lizard and one iguana. However, neither Hamerton nor Krause went into details on the vascular lesions so that we cannot fully picture them.

Atheromatosis of the blood vessels in birds is apparently quite similar to atherosclerosis in man. In the London Zoo reports, Hamerton and Hill (1929, 1930, 1933, 1934, 1935, 1936, 1937, 1939, 1941, 1943, 1944, 1946, 1953) described atheromatous changes in the vessels of a variety of birds—parrots, pheasants, birds of paradise, sea gulls, peacocks, mandarin ducks, teals, toucans, ibis, geese, and many others. These changes were associated with sclerotic processes in the intima. The organopathology of vascular changes in birds often resembles that in man. We have repeatedly come across descriptions of atherosclerosis of the coronary arteries and vessels of the extremities. Gangrene of the lower extremities and cicatricial changes in the kidneys accompanying atherosclerosis of the corresponding arteries have been noted in a number of cases.

There have been some recent investigations of delaminating aneurysms in turkeys which resulted in rupture of the aorta. These lesions were due to atheromatous changes in the aorta with the deposition of cholesterol rather than neutral fat in the vascular wall (Gibson and de Cruchy, 1955). However, other investigators do not classify these vascular lesions as proper atherosclerosis, but they do consider atherosclerosis in parrots close to human atherosclerosis morphologically and in respect to the lipids deposited (K. G. Volkova, 1924; Dobberstein, 1936; Pallaske, 1954; and many others). The morphology of atherosclerosis in birds is very much like that in man except that the manifestations of atheromatosis are very pronounced and those of sclerosis less so.

Spontaneous atherosclerotic vascular changes have also been described in monkeys (Fox, 1933; Hamerton, 1934, 1935, 1936, 1941, 1943, 1946; L. A. Yakovleva, 1954, 1956). All these reports deal with animals long resident in monkey houses and zoos. There is no direct reference in the literature to the possibility of atherosclerosis developing in monkeys in their natural habitat. It is quite possible that the disease does not exist there. This is indirectly confirmed by the observations of A. P. Savinov and A. V. Tyufanov, L. A. Porubel', I. A. Prokhorova, A. N. Sergeyev, and Yu. M. Shavin who dissected thousands of newly arrived monkeys killed in connection with the manufacture of poliomyelitis vaccine but failed to find a single case of atherosclerosis. The atherosclerosis noted by Fox and Hamerton was in monkeys that had been living in zoos for many years.

Before describing the atherosclerotic vascular lesions that we observed, we should like to discuss some changes in the blood vessels of monkeys related to their age. N. N. Anichkov (1941) pointed out that age and senility changes in man must be carefully distinguished from injuries to the vascular wall resulting from atherosclerosis. Vascular changes with age are now well known. And they occur throughout the arterial system. The intima is most heavily involved. The process consists of a thickening of the intima due to the ingrowth of smooth muscle, elastic, and collagenous fibers. Ye. P. Feringer (1952), who studied this process in the coronary arteries, pointed out that changes in the intima begin in early childhood as shown by separation of the inner elastic membrane and appearance of smooth muscle fibers in the vascular intima. Between the ages of three and five elastic and precol-

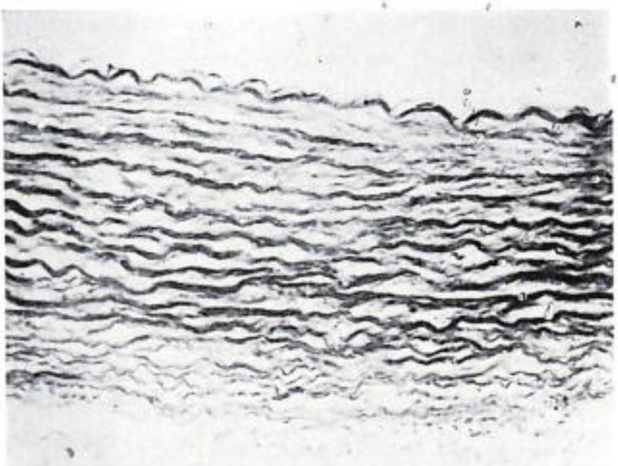


Fig. 72. Elastic framework of the aorta. The rhesus monkey Gizar, one-half year old. Stained with hematoxylin-eosin. Obj. 5, oc. 7.

lagenous fibers begin to grow in the intima followed by collagenous fibers. Similar changes in the aortic intima can also be noted at an early age. In the opinion of some investigators (K. G. Volkova, 1923; N. Ye. Levin, 1935; Ye. P. Feringer, 1952; others), age changes in the vessels take place throughout life. Others (L. O. Vishnevetskaya, 1935) believe that differentiation and growth of the arterial wall occur mainly during the first 12 years of life.

We made an histological examination of the aorta, coronary vessels of the heart and brain of 30 monkeys of varying ages to obtain a clearer idea of the changes occurring with age in the arterial system.

During the first six months of life the aorta of a monkey is an elastic vessel, the main mass of which in cross section is constituted by the middle coat (Fig. 72). The latter is made up of delicate, closely packed, moderately twisted elastic membranes averaging 25 to 35 in number in a transverse section of the ascending portion of the aorta. The membranes next to the lumen and on the outer circumference of the middle coat are often coarser than the others. Smooth muscle and precollagenous fibers are invariably found between the membranes. Preparations impregnated with silver show that the fibers form a fairly even, delicately fibrous frame.

There are comparatively few collagenous fibers. They are found for the most part in the outermost portions of the middle coat where it passes into the adventitia. The latter is very narrow and contains, in addition to collagenous fibers, precollagenous fibers and a few delicate elastic fibrils. The intima of the aorta is very thin, consisting of a layer of endothelium generally found almost next to the internal elastic membrane. Cells with large light-colored nuclei appear here and there under the endothelium. Distally, the aortic wall tends to thin out due to attenuation of the middle coat in which the number of elastic membranes gradually decreases.

The coronary arteries of the heart are vessels of the muscular type, differing from one another chiefly in the thickness of the middle coat. The smooth muscles of the middle coat usually consist of five to seven layers near the orifice of the vessel. Between the middle coat and intima is a very distinct, twisted internal elastic membrane. The intima of a vessel like the aorta consists mostly of endothelium located almost on top of the internal elastic membrane. The middle coat contains smooth muscle fibers, just a few precollagenous and some very delicate elastic fibers. These last are somewhat more numerous in the outer third of the middle coat. The number of elastic fibers increases sharply near the boundary of the adventitia. There are a great many delicate intertwined elastic fibers in the adventitious membrane of the vessel where they alternate with collagenous and precollagenous fibers.

The arteries in the base of the brain are very thin vessels of the muscular type whose middle coat consists of two or three layers of smooth muscle fibers. The outer coat is very narrow. It consists of delicate elastic and precollagenous fibers admixed with collagenous fibers. The vessels have a very well defined, wavy, twisted internal elastic membrane lined with endothelium.

The above-described vascular structure changes somewhat at the place where the lateral branch leaves the main trunk. Around the orifice of the branching vessel on the inner surface is a ridge-like thickening slightly protruding into the lumen. In cross section this thickening of the vascular wall appears to be an irregular triangular formation inside the internal elastic membrane. The intima thus thickened is composed of thickly intertwined precollagenous, collagenous, and elastic fibers. The elastic fibers are crowded together next to the vascular lumen and at the place where the thickening joins the intima, being intertwined here with the internal elastic membrane.

In time the structure of the intima changes. The main change in the other coats is gradual thickening with age. After six months (sometimes a little earlier) one can see the detachment of the thinner fibers, initially in the form of small loops and bows, from the elastic membrane in the coronary arteries and aorta. Then delicate precollagenous fibers and smooth muscles begin to appear at the internal elastic membrane and inwards.

At the age of four or five there is another still thinner membrane (internal border lamina) in the narrow intima of the vessel inwards from the internal elastic membrane with even more delicate elastic fibers, arranged here and there in several rows, separating from the lamina. Delicate collagenous and precollagenous fibers are found along the internal elastic membrane and the other more delicate membranes. Just a few smooth muscle fibers are visible between the fibrous connective-tissue structures, chiefly in the basal portions of the intima. The innermost zone of the intima is for the most part almost devoid of fibrous structures. It has only a few delicate precollagenous fibers. Subsequent changes in the vascular intima consist largely of an increase in the number of precollagenous and collagenous fibers and growth of elastic tissue.

At the age of seven or eight one can see in preparations of the intima impregnated with silver that the precollagenous fibers are quite uniformly distributed in the intima, forming a delicately reticulate frame. When stained with fuchsilin the intima reveals the presence of a great many delicate, twisted elastic fibers (Fig. 73).

In older monkeys as the aortic intima thickens, collagenous tissue comes to dominate perceptibly over the other structural elements. This is most marked in the innermost zone of the aortic intima.

Changes in the coronary arteries are similar to those in the aorta and they take place generally at the same time. The difference is that the elastic tissue of the vascular intima is much less developed than that of the aorta. In addition, the process is not uniform all over the vessel. Frequently in adult monkeys 12 to

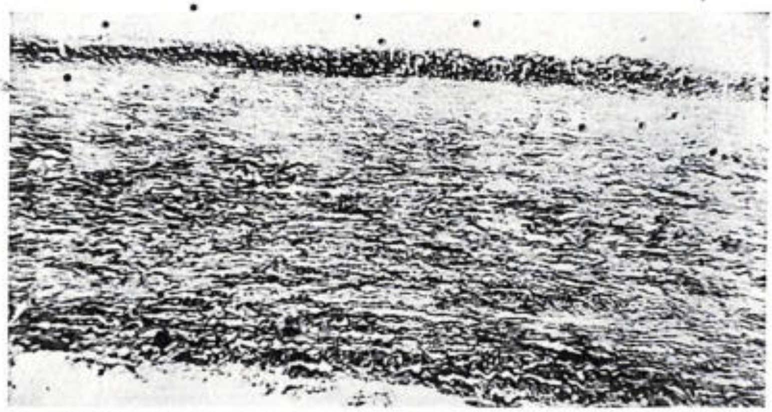


Fig. 73. Photomicrograph. Increased amount of elastic fibers in the aortic intima. The anubis baboon Borneo, eight years old. Stained with fuchsilin. Obj. 20, oc. 7.

14 years old, when the intima in the proximal portions of the main arteries of the heart thicken significantly due to the growth of elastic and collagenous tissue, the distal portions of the arteries exhibit only slight separation of the internal elastic membrane accompanied by moderate growth of collagenous fibers.

Age changes in the vessels of the base of the brain were much less pronounced in our material. Only in monkeys seven years and older could we see sporadic separation of the internal elastic membrane and growth of collagenous and precollagenous tissue in the arterial intima. These processes were not constant, and sometimes in old monkeys (Vesta—25 years old, Ruina—20 years old) the internal elastic membrane in the arteries of the base of the brain had not separated. Our observations of these cerebral vessels tend to accord with those made of vessels in man. Gekkel' (1923) showed that while these changes are fairly distinct, they are not as pronounced as elsewhere in the human arterial system.

Just as we did in the case of atherosclerotic changes with age, we investigated the aorta, coronary arteries, and blood vessels of the base of the brain of all the animals that died.

Out of the 1,179 monkeys dissected in the Sukhumi animal house during the past six years, we observed varying degrees of atherosclerotic involvement of the aorta in 30 animals of all species from 5½ to 27 years old (Table 6).

TABLE 6

TOTAL SUDAN-STAINING OF THE AORTA OF MONKEYS

Name of monkey	*Species*	*Monkeys born in the animal house*	*Monkeys brought into the animal house*	*Age, in years*	*Years of living in the animal house*	*Aorta* Presence of athero-sclerotic plaques	*Aorta* Presence of lipid spots
Nura	hybid macaque	+		½	½	—	—
Riga	rhesus monkey	+		½	½	—	—
Muzar	hamadryad baboon	+		½	½	—	—
Gizar	rhesus monkey	+		½	½	—	—
Kazan	hamadryad baboon	+		1 yr., 1 mth.	1 yr., 1 mth.	—	—
Pekos	" "	+		1 yr., 3 mths.	1 yr., 3 mths.	—	—
Bapina	" "	+		1 yr., 5 mths.	1 yr., 5 mths.	—	—
Kacha	" "	+		1 yr., 5 mths.	1 yr., 5 mths.	—	—
Malka	" "	+		1 yr., 5 mths.	1 yr., 5 mths.	—	—
Yezh	rhesus monkey		+	3	2	—	+ —
Utkonos	" "	+		2½	2½	—	—
Tunis	" "	+		3	3	—	—
Tsaplya	" "	+		3½	3½	—	+ —
Chibis	" "	+		3½	3½	—	+ —
Skvorets	" "	+		3½	3½	—	+ —
Monus	" "		+	5	4	—	+
Kashtanka	green marmoset		+	5	4	—	+
Kadril'	capuchin		+	5	1	—	+ —
Prima	hybrid baboon	+		5½	5½	+	+
Shalfey	rhesus monkey		+	5½	5	—	—
Kuznechik	hybrid baboon	+		6	6	—	not investigated
Pigmey	rhesus monkey	+		6	6	—	+
Lamela	red-faced macaque		+	6	7 months	—	+ —
Mokh	rhesus monkey		+	6	4	—	+
Mok	" "		+	6	4	—	+
Mik	" "		+	6	4	—	+
Meksika	" "		+	adult	4 months	—	+ —
Ufa	red faced macaque		+	adult	9 months	—	+
Loza	rhesus monkey		+	adult	4 months	—	+
1639	red faced macaque		+	adult	4 months	—	+ —
Rio	green marmoset		+	7	6	+	+
Gindukush	" "		+	7	6	+	+
Kokon	hamadryad baboon	+		7	7	—	+
Saklalin	" "		+	7	6	—	+
Kuznechik	" "	+		7	7	—	+

Zeland	anubis baboon		+	8	7	+	+
Ipatiya	rhesus monkey	+		8	8	−	+
Paragvay	green marmoset		+	8	6	+	+
Yamal	gelada		+	8	6	−	+
Lang	anubis baboon	+		8	8	−	+
Borneo	" "	+		8	8	−	+
Dafniya	hamadryad baboon	+		8½	8½	+	+
Ishim	green marmoset		+	8½	6	−	+
Levan	" "		+	7	6	+	−
Izobar	rhesus monkey	+		9	9	+	+
Oktava	green marmoset		+	9	8	+	+
Mirnyy	hamadryad baboon		+	9	7	−	not investigated
Verbena	" "	+		10	10	−	+
Formosa	gelada		+	10	8	+	+
Izumrud	rhesus monkey	+		10	10	−	+
Kipr	gelada		+	10	8	+	++
Ket'	green marmoset		+	10	8	+	++
Zevs	hamadryad baboon	+		11	11	+	−
Iva	" "	+		11	11	+	−
Labrador	" "		+	11	8	+	+
Iskra	" "	+		11½	11½	−	−
Chemga	rhesus monkey		+	12	4	−	−
Yuola	" "	+		12	12	−	+
Lev	hamadryad baboon	+		12	12	+	−
Banan	" "	+		13	13	+	−
Yakhta	rhesus monkey	+		13½	13½	+	−
Irtysh	hamadryad baboon	+		14	14	−	−
Kanareyka	rhesus monkey	+		14	14	++	+ −
Yana	green marmoset		+	14	9	−	+
Barabul'ka	hamadryad baboon	+		15	15	+	−
Nal'ma	*lapunder* macaque	+		15	15	+	+
Fata	rhesus monkey	+		15	15	++	+ −
Yukka	" "		+	15	5	−	+
Rantik	" "	+		16	16	−	+
Undina	" "		+	17	15	−	+
Angara	hamadryad baboon	+		18	18	++	+
Lovkaya	*lapunder* macaque	+		19	19	+	+
Beluga	hamadryad baboon	+		19	19	++	+
Vasilek	" "	+		20	20	+	+
Ruina	rhesus monkey		+	20	18	+	+
Mississippi	anubis baboon		+	20	9	++	+
Ruta	rhesus monkey		+	21	19	−	+
Zyuzya	*lapunder* macaque	+		22	22	+	+
Vesta	rhesus monkey		+	25	20	+++	+
Malysh	" "		+	27	23	+++	+

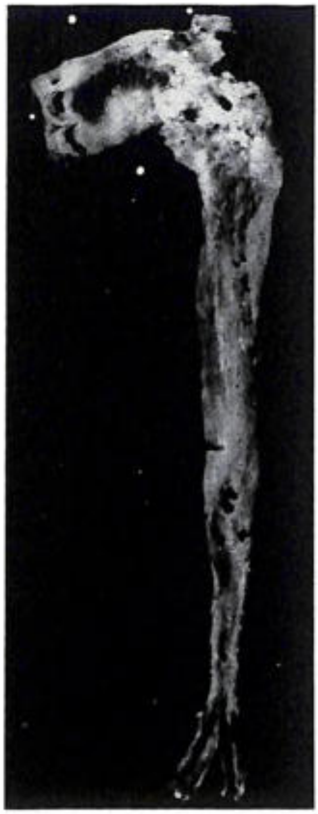


Fig. 74. Atherosclerosis of the aortic arch. The hamadryad baboon Vesta, 25 years old.

In most of the animals plaques in the aortic intima were very small and comparatively few in number. They were irregularly rounded, flat formations light gray or yellowish in color and no more than 2 to 3 mm in diameter. In seven animals (the baboons Vesta, Angara, Mississippi, the green marmoset Rio, and the macaques Kanareyka, Fata, and Yakhta) the plaques were numerous, merging together to form spots 2 to 3 cm wide or more (Fig. 74). The location of the plaques in the aorta differed from animal to animal. In five of them (the baboons Vesta, Zevs, Zeland, Prima, and the macaque Nal'ma) they were found chiefly in the arch and in the distal part of the descending portion of the aorta near the

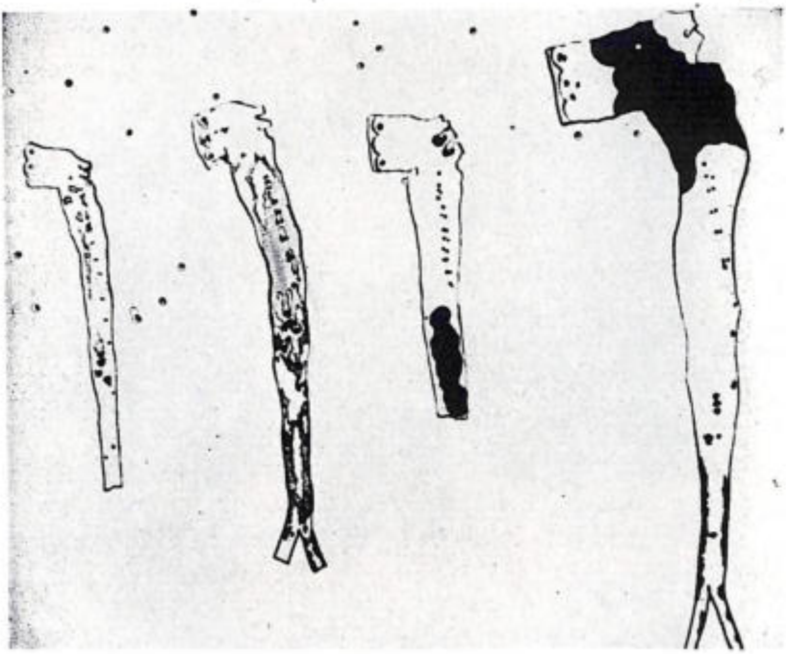


Fig. 75. Different arrangements of lipid spots (first two) and atherosclerotic plaques (second two) in monkeys.

bifurcation. In the other monkeys they were mostly in the abdominal section of the aorta. When the process was indistinct, a plaquelike thickening of the intima was usually observed near the orifices of the vessels branching from the aorta (Fig. 75).

Histological examination revealed that the intima of the aorta had changed most. Plaquelike thickenings consisting mainly of collagenous tissue admixed with a few elastic fibers were in evidence (Figs. 76 and 77). In between the fibrous structures could be seen accumulations of drops of fat, which sometimes included isolated crystals. Macrophages loaded with drops of fat were frequently found near the place where the lipids had accumulated. Some places inwards from the dense fibrous plaques next to the vascular lumen contained lipid deposits within which there was no perceptible development of fibrous tissue. Deposits of calcium salts were noted in cases of very pronounced atherosclerosis (Vesta,

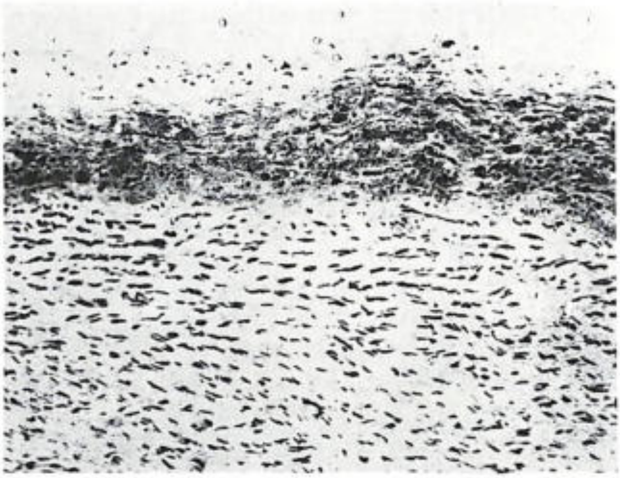


Fig. 76. Photomicrographs. Initial stage in the formation of a sclerotic plaque. The green marmoset Ket'. Stained with Sudan III-hematoxylin. Obj. 10, oc. 7.

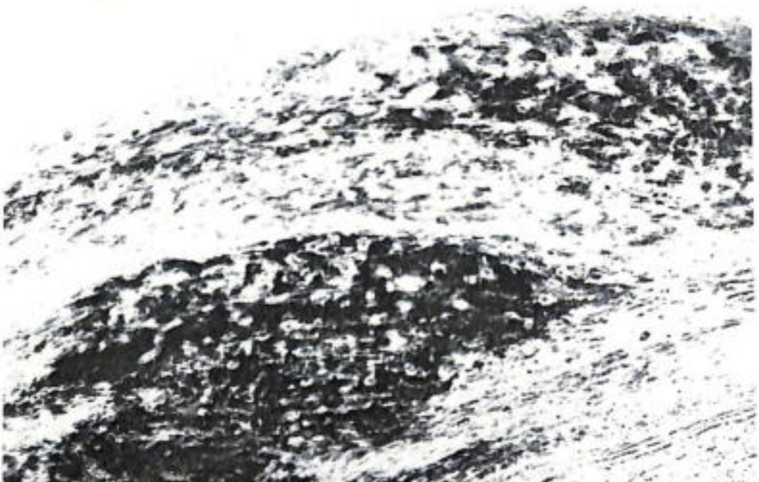


Fig. 77. Photomicrograph. Atherosclerotic plaque in the aorta. The hamadryad baboon Vesta. Stained with Sudan III-hematoxylin. Obj. 8, oc. 7.

Fig. 78. Photomicrograph. Calcium deposits in an atherosclerotic plaque. The hamadryad baboon Vesta. Stained with hematoxylin-eosin. Obj. 8, oc. 7.

Malysh) in the aortic intima in addition to the development of lipid plaques (Fig. 78). A chemical analysis of the aortic wall (lacking in the external coat) at the site of the plaques revealed a high cholesterol content (about 6.7%). The middle coat at the same site was atrophied, with round-cell infiltrates found here and there. In the midst of the infiltrates were large numbers of macrophages loaded with fat. Single macrophages were invariably found between the fibers of the middle and external coats of the vessel.

In almost all the monkeys the aortic intima, when the vessel was totally stained with Sudan III, showed lipid spots of varying size and spread in addition to fibrous plaques. However, in nine cases, despite the presence of fibrous plaques, total staining of the aorta failed to disclose any lipid deposits in the intima at all, or they were slight and less extensive than the plaques. Histological examination revealed that the plaques consisted mainly of dense connective tissue. Delicate elastic fibers were invariably present among the collagenous fibers. Very small quantities of lipids were noted only in the most basal portions of the plaques along the internal elastic membrane. Macrophages loaded with fat were frequently seen either in groups or alone.

Besides the 30 animals referred to above, we stained with

Sudan III the aortas of 50 more monkeys of different species that died of one cause or another (cf. Table 6). Lipid spots of varying extent were readily discerned in the aorta. None could be found in 9 animals dying before the age of three or in 12 adult monkeys of different ages.

In the aorta of monkeys from two to five years old we found only a few very small lipid spots in the thoracic portion, chiefly around the orifices of the vessels branching from the aorta. Lipid spots in the intima of adult monkeys were noted mostly in the thoracic portion of the aorta. They were fairly extensive with irregular contours.

In the ascending section of the aorta, in the arch, and in the abdominal aorta the lipid spots tended to be sparse, located for the most part around the vessels branching from the aorta. Small lipid deposits were frequently noted at the base of the aortic valve. Spots in large quantities were found in the ascending section of the aorta and in the arch in only one monkey (Izumrud). The main mass of spots appeared in the abdominal section of the aorta in two monkeys (Prima and Rio). These two animals also had numerous atheromatous plaques in the same section of the aorta. Five animals (six to eight years old) had small lipid spots in the orifices of the coronary arteries.

Histological examination revealed an accumulation of lipid drops in the area of the lipid spots in the vascular intima next to the internal elastic membrane. Fibrosis of the intima near the lipid spots beyond that normally accompanying age changes was not in evidence.

An investigation of the coronary arteries of the heart showed small plaquelike thickenings of the intima in five animals. They were generally flat (1 to 2 mm in diameter), barely reaching the lumen of the vessel. In just one animal (Malysh) did an atherosclerotic plaque, located near the orifice of the left coronary artery, constrict the vascular lumen markedly. In all the monkeys the plaques were generally found near the orifice of the coronary artery or right in it.

Microscopical examination of the coronary arteries in the region of the plaques revealed the complete similarity of the picture with that observed in connection with atherosclerotic plaques in the aorta. The inside of the plaques was composed of dense fibrous tissue; the basal portions generally had lipid deposits in varying quantities. In only one case (Malysh) were there virtually no free lying lipid drops present in a plaque in the orifice of the right coronary artery. The intimal plaque was solidly fibrous. Macrophages loaded with lipids were detected in the basal portions near the internal elastic membrane.

Due to the very small lumen of the coronary arteries in most of the animals, we could completely stain with Sudan the intima of these vessels in only 27 monkeys up to 27 years old. No lipid deposits were found in the intima of the coronary arteries of animals under seven years old (10 monkeys). Lipid deposits were discovered in eight animals (including those mentioned above with atherosclerotic plaques in the coronary arteries) seven years and older (Table 7).

Lipid spots in the coronary arteries were generally few in number and located, as a rule, near the orifices of the main trunks or at the place where the small branches start. They were not distributed evenly throughout the vessels. Lipid deposits were found in the intima of the left coronary artery of eight animals and in the anterior descending branch of only five animals. Small lipid spots were noted in the right circumflex artery of only two animals (Vasilek, Malysh) where the process of lipid infiltration of the coronal intima was generally more pronounced; atherosclerotic plaques were also in evidence.

A detailed examination of the intima of cerebral blood vessels after total staining with Sudan III proved to be exceptionally difficult owing to their small lumens. An histological investigation revealed the presence of a small quantity of lipids in the intima of the anterior and posterior cerebral arteries of only one animal (the green marmoset Rio). These extracellular deposits were in the form of small drops in the outermost portions of the intima next to the internal elastic membrane. There was no perceptible growth of fibrous tissue in the region of the lipids.

We have concluded from our data that in monkeys as in man the aorta, coronary arteries of the heart, and arteries of the base of the brain may undergo a series of changes. As in man, these

TABLE 7

TOTAL SUDAN-STAINING OF THE CORONARY ARTERIES OF THE HEART

Name of monkey	*Species*	*Monkeys born in the animal house*	*Monkeys brought into the animal house*	*Age, in years*	*Years of living in the animal house*	*Coronary arteries of the heart:* *Presence of athero-sclerotic plaques*	*Coronary arteries of the heart:* *Presence of lipid spots*
734	hamadryad baboon	+		stillborn			
Magra	" "	+		10 months	10 months	–	–
Pik	rhesus monkey	+		1	1	–	–
Kacha	hamadryad baboon	+		1½	1½	–	–
Slavka	" "	+		2½	2½	–	–
Nitsa	Chinese macaque		+	3	2	–	–
Yulka	rhesus monkey		+	3	2	–	–
Zelim	hamadryad baboon	+		3	3	–	–
Korsar	rhesus monkey		+	5½	2	–	–
Kuznechik	hamadryad baboon	+		6	6	–	–
Kameliya	" "		+	7	6	–	–
Rio	green marmoset		+	7	6	+	+
Zeland	anubis baboon		+	8	8	–	–
Onga	rhesus monkey		+	9	7	–	–
Mirnyy	hamadryad baboon		+	9	7	–	–
Verbena	" "	+		10	10	–	+
Kipr	gelada		+	11	8	–	–
Iva	hamadryad baboon	+		11	11	–	–
Labrador	" "		+	11	8	–	+
Lev	" "	+		12	12	–	+
Banan	" "	+		13	13	–	+
Yana	green marmoset		+	14	9	–	–
Rantik	rhesus monkey	+		16	16	–	–
Angara	hamadryad baboon	+		18	18	–	–
Lovkaya	*lapunder* macaque	+		19	19	–	–
Vasilek	hamadryad baboon	+		20	20	+	+
Malysh	rhesus monkey		+	27	23	+	+

changes can be divided into changes due to age and changes in the vascular wall caused by atherosclerosis. The former involve thickening of the arterial wall as the animal grows older. This process, in addition to gradual thickening of all the coats of the vessel, results in alteration of the inner wall of the artery through the growth there of smooth muscle elastic, precollagenous, and, afterwards, of collagenous fibers. The process is most pronounced in the aorta, less so in the coronary arteries, and least of all in the arteries of the base of the brain. The gradual reorganization and complication of the structure of the arterial intima begins very early, during the first six months of the animal's life.

Lipid deposits in the intima could be traced in all the vessels that came under our scrutiny (aorta, coronary arteries, arteries of the base of the brain). The process of lipid infiltration of the aortic intima, as is evident from Table 6, is not due only to the age of an animal. We found lipid spots in the aortas of animals under two years of age. From then on, especially from the third, fourth, and fifth years, lipid spots were almost invariably found in the aortic intima. This phenomenon is apparently of physiological nature, analogous to that noted in the human aorta, as shown by V. D. Tsinzerling and his co-workers.

Reflecting to some extent general lipid exchange, the lipid spots in the aortic intima may be absent in monkeys 14 years and older.

Since we do not have enough data on the adult monkeys that died soon after reaching the animal house, we cannot form any judgment about the process of lipid infiltration of the aortic wall in monkeys living in their natural habitat. We can only say that a considerable number of lipid spots have often been found in monkeys after four to nine months in Sukhumi.

Lipid spots are much rarer in the coronary arteries than in the aorta. We encountered them only in monkeys over 10 years old. Lipid spots can be resorbed from the intima of the aorta and coronary arteries, as shown by the fact that we found fibrous plaques almost wholly lacking in lipids in nine animals. A great many macrophages could be seen at the base of these plaques resorbing the remnants of lipid deposits.

Atherosclerosis of the aorta is not common in monkeys, if we take into account all the dead animals. Atherosclerosis was noted in 2.6% of all these examined (1,179 necropsies). However, if only monkeys over five years old (the age when atherosclerosis begins) are considered, the rate rises to 19.6% of the animals in the main group (158). It will also be noted that we did not discover a single manifestation of atherosclerosis in 81 animals 6 to 17 years old that died soon after reaching the monkey house (during the first two years).

Thus, the rate of atherosclerosis in monkeys of the main group examined by us is somewhat higher than that in Fox' materials. This discrepancy is possible due to the fact that monkeys, as a rule, do not live too long in zoos. It seems that atherosclerosis develops in monkeys kept in captivity, which involves a whole set of factors, e.g., restrictions on movement, changes in diet, etc.

Atherosclerosis in monkeys is obviously quite close to the disease in man. In monkeys, unlike other mammals, it is cholesterol rather than neutral fats that is deposited in the vessels. Just as happens in man, atherosclerosis in monkeys develops in wavelike fashion with alternation of the processes of lipid deposition and resorption. The difference is that in monkeys resorption is often very pronounced so that in addition to plaques containing varying amounts of lipids there are often plaques containing little or no lipids. The number of these plaques increases with age. Atherosclerotic changes in monkeys, unlike those in man, very rarely affect the cerebral or cardiac vessels, tending to be localized mostly in the aorta.

Age Changes in the Valves, Endocarditis, and Cardiac Defects

Endocarditis in man is generally caused by rheumatism. Endocarditis due to streptococcal infection is second in frequency. In domestic animals endocarditis is usually accompanied by chronic infections (chronic swine erysipelas, the chronic form of infectious anemia of horses, etc.). K. G. Bol' and B. K. Bol' (1954) distinguish erysipelatous endocarditis of swine principally involving the mitral valve, pyogenic endocarditis of cattle (sometimes found in sheep and swine), and streptococcal endocarditis of cattle, horses, and swine principally involving the aortic and pulmonary valves. These diseases are ulcerative in character and are frequently recurrent. Recurrent endocarditis is also found in dogs (Nieberle and Kohrs, 1954).

Pallaske (1955) states that endocarditis arises in animals after infections: in swine after erysipelas, in cattle, sheep, and swine after a pyogenic infection, in horses and cattle after a streptococcal infection. However, he stresses that endocarditis never develops in an acute process, only in chronic infections. He also says that endocarditis is very likely to arise in animals rendered hyperimmune in order to obtain serum. Recovery from endocarditis generally leaves traces in the form of some damage to the valves (in valvular endocarditis) or thickening of the parietal endocardium after parietal endocarditis. The latter very rarely occurs in the pure form and it normally accompanies valvular endocarditis. The resultant heart damage may lead to cardiac insufficiency.

Isolated instances of endocarditis in monkeys have been described by Scott (1927) and Hamerton (1929). The first was a case of polypous ulcerative endocarditis of the mitral valve with involvement of the parietal endocardium. Scars were noted in the kidneys after infarcts resulting from an embolism. The second case involved the parietal endocardium as well as the valves. The direct cause of death was a cerebral embolism. Hamerton (1934, 1935) described substantial sclerosis of the heart valves in two old baboons. Since he furnished no details on the morphology of the areas affected or history of the animals, we have found it difficult to evaluate the cases. The fact that the diseases were observed in old monkeys suggests that the changes in heart valves were linked to age.

In studying the valves of the heart, pulmonary artery, and aorta of monkeys with heart damage and endocarditis, which generally represents a fairly rare pathology in these animals, we found it necessary to determine the nature of the changes in the valves due to age. Our classical textbooks of histology contain no description of the normal histological structure of the heart, aortic, and pulmonary valves of man. A detailed description of the valves of the heart and major blood vessels is given by A. V. Walter (1948), G. A. Chekareva (1950), and Sh. I. Krinitskiy (1950). These authors also studied senile changes in the valves; so too Gross and Kugel (1931).

We investigated the valve structure of 39 monkeys of different ages—bicuspid, tricuspid, aortic and pulmonary valves. The valves were excised lengthwise together with adjoining portions of the myocardium, aorta, and pulmonary artery. The following animals were involved: two monkeys under one, eight monkeys one to five years old, 14 monkeys five to 10 years old, and 15 monkeys over 15 years old.

Our research on healthy valves has led us to make the following formulation of their structure in monkeys and the general features of the changes arising in senescence. The valve structure is fairly close to that in man, although there are some significant differences. The aortic and pulmonary valves of monkeys are more or less similar. In young animals the cuspate valves contain dense collagenous fibers protruding like wedges into the base. Strands of collagenous fibers stretch from the base of the valves into the adjacent portions of the myocardium. A few fibers proceed from here into the valve tissue, passing with the elastic fibers just under the atrial and ventricular surfaces. Somewhat larger numbers of collagenous fibers can be seen on the side facing the ventricle (we could not see the thick fibrous leaflet characteristic of human valves). The valve consists mainly of loose connective tissue resembling embryonic tissue. This tissue is composed of the main substance staining metachromatically and is rich in stellate and elongated cells. The areolar tissue contains a few very fine collagenous and elastic fibrils thickly intertwined. Fissures looking like sinusoids and lined with endothelium can be seen in the distal section of the cuspate valves (chiefly the mitral) in monkeys of all ages, including those under one. Just below the endothelium are several layers of very thin elastic fibers (Fig. 79). The abovementioned vessels, as can easily be seen when they are stained with picrofuchsin, appear to be surrounded by packs of intertwined, concentrically arranged collagenous and elastic fibers.

The elastic framework of the valves is a continuation of the elastic layer of the auricles and ventricles. The cuspate valves contain a great many elastic fibers on the side facing the atria where the elastic layer is much thicker than in the ventricles. There are several layers of elastic fibers somewhat pulled away from the endo-

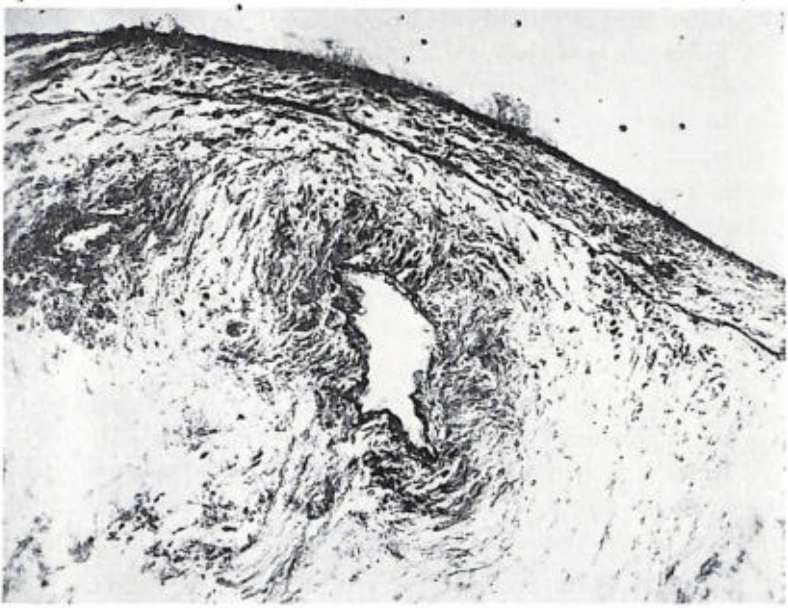


Fig. 79. Photomicrograph. Elastic fibers surrounding vascular cavities. Proliferation of elastic fibers and granules of elastin. The rhesus monkey Dama, 8½ years old. Stained with fuchsilin. Obj. 20, oc. 10.

thelium on the side facing the atria. Tapering elastic fibers stretch between the mid-point and top of the valve into the adjoining tissue. At the free edge of the valve a considerably attenuated layer of elastic fibers bends toward the ventricular surface, interlocking with a very thin elastic layer passing under the endothelium along the ventricular side of the valve. When impregnated with silver, all portions of the valve show numerous argyrophil fibers forming a delicate even framework. A somewhat larger quantity of precollagenous fibers are present in the central portions of the valve.

We have described the structure of the cusps of the mitral valve. The structure of the tricuspid valve is essentially the same. Its cusps are somewhat thinner because the middle layer of loose connective tissue is not so thick.

The aortic and pulmonary valves have the following structure. The cusps consists mainly of loose connective tissue. On the side facing the atria under the endocardium is a fairly wide elastic layer composed of thin elastic fibers parallel to one another. These fibers are a continuation of the elastic layer of the atria. This layer, which gradually becomes attenuated and constantly gives off thin elastic fibers within the valve, proceeds to the surface of the valve facing the sinus of the aorta (or pulmonary artery) and in the form of a very fine strand passes under the endothelium of the valve. On the side facing the sinus thin connective-tissue fibers arranged lengthwise can sometimes be seen under the endothelium. The aortic valves differ from the pulmonary valves only in having much coarser structural elements in the cusps. Both have a delicate framework of precollagenous fibrils.

Age changes in the valves are varied. They are manifested in hyperplasia of the loose connective tissue sometimes all over the valve, more frequently in the distal section. There is transformation of fibrous tissue (usually at the base of the valve) in the form of swelling and homogenization of collagenous fibers with sporadic fibers turning into completely uniform masses staining pink with eosin. Sometimes homogeneous yellow areas appear among the basic masses of collagen when stained red with picrofuchsin. In some cases there is moderate diffuse (occasionally focal) fibrosis of areolar tissue accompanied by the development of a delicate network of intertwined collagenous fibrils (Fig. 80).

Metachromasia of loose connective tissue becomes more pronounced with age. Indications of fibrosis may also show up in the form of focal sclerotic patches in different parts of the valves. Sometimes they are horizontal strands of coarse collagenous fibers. Sclerosis is occasionally manifested in the development of foci of twisted collagenous fibers, but in focal sclerosis the collagenous bundles may also lie lengthwise. The very delicate elastic network found in loose connective tissue usually disappears in the sclerotic areas. Another manifestation of age changes in the valves is the formation of focal thickenings and partial deformations in the distal sections of the valves. Several sinusoids lined with epithelium are frequently found in the areolar tissue of the thickened distal sections.

Small focal excrescences described by Lambl (1856), V. S. Devitskiy (1908), A. V. Walter (1948), and others and classified by M. A. Baron (1949) with the reactive structures of the endocardium appear in isolated cases on the atrial surface near the closing line of

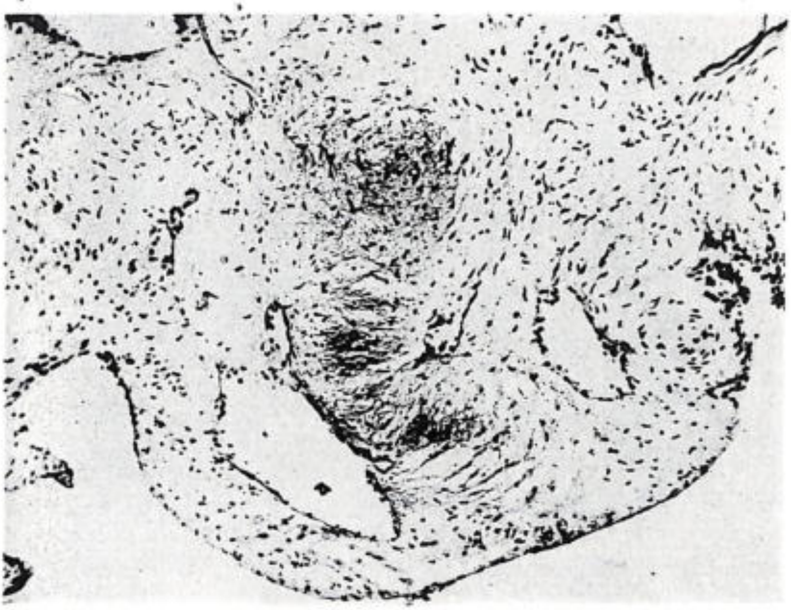


Fig. 80. Photomicrograph. Marked thickening and deformation of valve cusps. Areas of delicate intertwined collagenous fibrils are formed by individual islets. The hamadryad baboon Lev, 12 years old. Stained with hematoxylin-eosin. Obj. 10, oc. 10.

the valves. Grossly, they look like small semitransparent outgrowths. They are composed of nonnuclear masses containing collagenous and elastic fibers and are covered with endothelium on the exterior. Plaquelike thickenings may also develop in the valves due to focal increases in the amount of collagenous substance in the subendothelial layer. The other layers of the cusps are not involved in the formation of these thickenings. This can be easily traced on preparations stained with fuchsilin when the continuous elastic layer separates it from the other part of the valve without reaching the plaquelike thickening.

Age changes may show up in different combinations. They may differ from valve to valve in the same animal. Changes in the bicuspid valve are manifested chiefly in sclerosis of the proximal section with enlargement of the distal section due to hyperplasia of areolar tissue, sometimes combined with the focal growth of

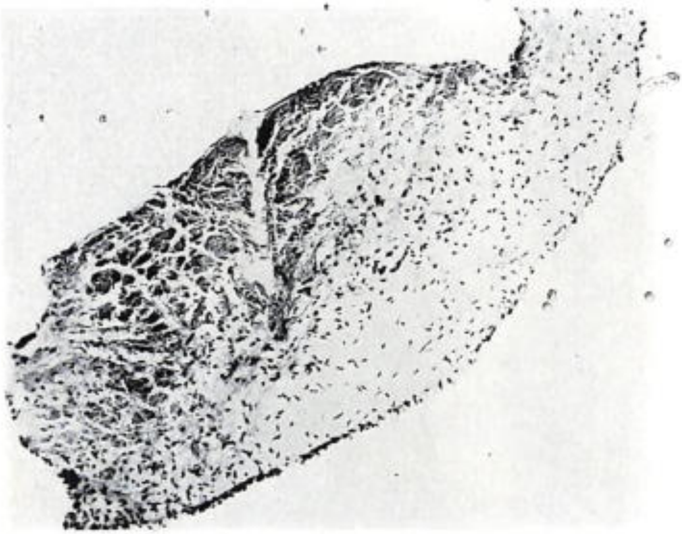


Fig. 81. Photomicrograph. Senile change in a valve. Proliferation of collagenous fibers in the distal section of the valve. A rhesus monkey. Stained with hematoxylin-eosin. Magnifying glass.

collagenous fibers into the subendothelial layer. It was these valves alone that contained the above-mentioned reactive structures in the form of Lambl's excrescences. Thickening of the distal portions of the cusps caused by the growth of collagenous fibers into the subendothelial layer may also occur in the tricuspid valve. However, this valve rather tends to show signs of diffuse sclerosis of the cusps (more often when the aforementioned changes are present in the bicuspid valve). In such cases the loose connective tissue is wholly or partly displaced by collagenous fibers (Fig. 81). Age changes in the aortic and pulmonary valves most frequently take the form of diffuse fibrosis.

We were sometimes unable to explain the differences in valvular changes among the various monkeys in a single age group. For example, in the 10 to 25 year old group we found no sclerosis in the mitral valves of six animals; the valves were composed of loose metachromatically staining connective tissue. In five animals the proximal section was sclerosed whereas the distal section was composed of areolar tissue. The valves of four animals consisted almost entirely of collagenous tissue. Two of these animals had been hypertensive for a long time. A study of the anamnesis of two monkeys failed to turn up anything that could be linked with the nature of the changes found in the valves. The tricuspid, aortic, and pulmonary valves were characterized chiefly by diffuse sclerosis or, more rarely, by sclerosis of the proximal section.

In the five to 10 year group we found no evidence of sclerosis in the mitral valves of only two animals. The valves of four monkeys were composed principally of dense collagenous tissue. There was sclerosis of the proximal section in eight cases along with hyperplasia of areolar tissue in the distal section. In all these cases we noted uneven thickening of the distal section of the valve due to abnormal growth of the subintimal layer frequently resembling plaques. Almost every valve had several vessels of the sinusoid type within the cusps. Deformations arising with age in the cusps, especially of the mitral valve, may impair the functioning of the valve. This is manifested clinically by a systolic murmur at the apex of the heart. The latter enabled the physicians to diagnose mitral valve failure in two monkeys (the rhesus monkey Undina and the hamadryad baboon Vesta).

Morphological changes in the valves are occasionally very pronounced, resulting in senile heart failure that is scarcely distinguishable from postrheumatic failure. One monkey that died when 16 years old (the rhesus monkey Rantik) exhibited thickening of the subendothelial layer in the distal section of the valve with the formation of a plaque in addition to gross signs of sclerosis and hyperelastosis, which by virtue of its magnitude could simulate postendocarditic valve failure. Here the bicuspid valve was thin up to the mid-point and consisted of collagenous fibers arranged lengthwise. The distal section on the side facing the atrium had a large plaquelike thickening mostly of dense collagenous tissue considerably lacking in fibrous structure and containing thick strata of hypertrophic elastic fibers. In the most distal section, in the stratum of coarse collagenous fiber, was a small area of areolar tissue of the middle layer. There was a vascular fissure lined with endothelium in the mass of collagenous tissue. The massiveness of the plaques (three to four times as thick as the valve at this point) and the presence of gross sclerosis with indications of hyperelastosis

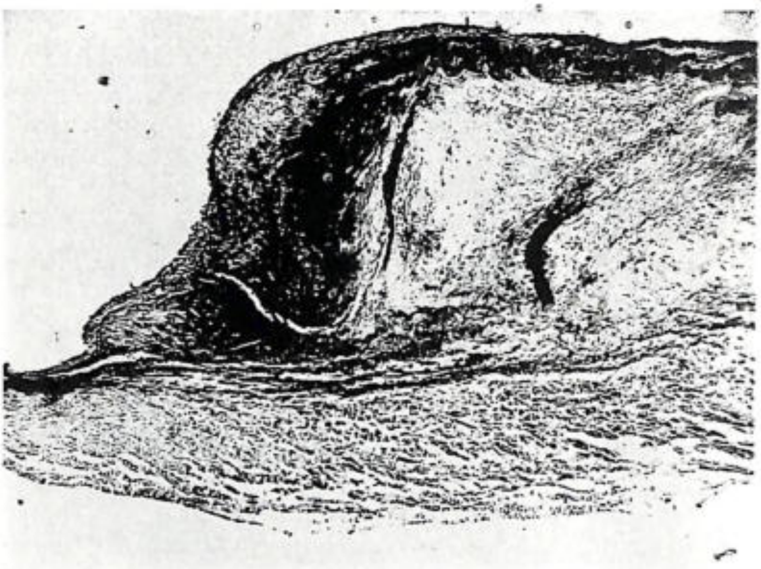


Fig. 82. Photomicrograph. Subendothelial sclerosis of a valve. Hyperelastosis. The rhesus monkey Rantik, 15 years old. Stained with fuchsilin. Obj. 3, oc. 7.

suggested that the changes in the valves were the result of a previous inflammation. However, it was immediately obvious from examination of an histological preparation that the changes were localized in the subendothelial layer outside the layer of elastic fibers proceeding through the entire valve under the layer of endothelial cells on the atrial surface of the valve. Fibers branched out from this layer into the mass of the plaque, but the main bundle of elastic fibers continued to go in the same direction, separating the plaque from the tissue of the valve. This feature, in our opinion, differentiated the senile from the inflammatory changes (Fig. 82).

While examining 40 hearts, we found a different pathology in six of them that was unrelated to possible senile changes in the valves. In two instances the valve failure was apparently the result of an earlier endocarditis, although the anamnesis failed to disclose any clear-cut evidence of this. The autopsy of one of these animals showed heart damage, but there were no clincal symptoms that could be linked to an earlier endocarditis or cardiac failure that developed while the monkey was alive. More likely these changes had existed without being recorded on the animal's card. The reason is that the monkey (Ruina) had lived in the animal house about 22 years, most of the time in an open-air cage so that symptoms of the condition were not observed by the attendants. These changes affected only the mitral valve and were characterized by marked thickening and deformation of the cusps with partial adhesion at the base. The failure might be described morphologically as a combination of valvular insufficiency with stenosis of the left ostium venosum.

Microscopical examination of the cusps of the mitral valve reveals that they consist almost entirely of dense collagenous tissue in which homogeneous albuminous masses staining yellow with picrofuchsin can be discerned between collagenous strands and amorphous lumps of collagen. The areolar tissue of the middle layer can be seen in very small patches between masses of collagen. A little appears at the base of the valve and in the form of islets along the valve between strands of collagenous fibers. There is an islet of areolar tissue under the endothelium in the distal section of the valve (near the line of closure) at the place where the valve is thickest. The distal section of the valve is greatly thickened with coarse strata of collagen (here and there losing its fibrous structure) between which one can make out very thick hypertrophic strands of elastic fibers and coarse grains of elastin. The direction of the strands of elastic fibers follows that of the strata of collagenous tissue (Fig. 83).

The second case of valve failure involved a young hamadryad baboon that died of an injury when 14 months old. The animal was kept under careful observation in a crib from the time it was two weeks old until it died. When two weeks old it developed a serious disease featured by intense cyanosis, panting when it moved, and vomiting from time to time. While in the crib the animal had recurrent pneumonia, dyspepsia, and colitis. It suffered from rickets and was extremely irritable.

After the animal died of a skull injury, the autopsy revealed mitral valve failure with thickening of the cusps along the edge, shortening of the cusps, and adhesions. The chorda tendinea were

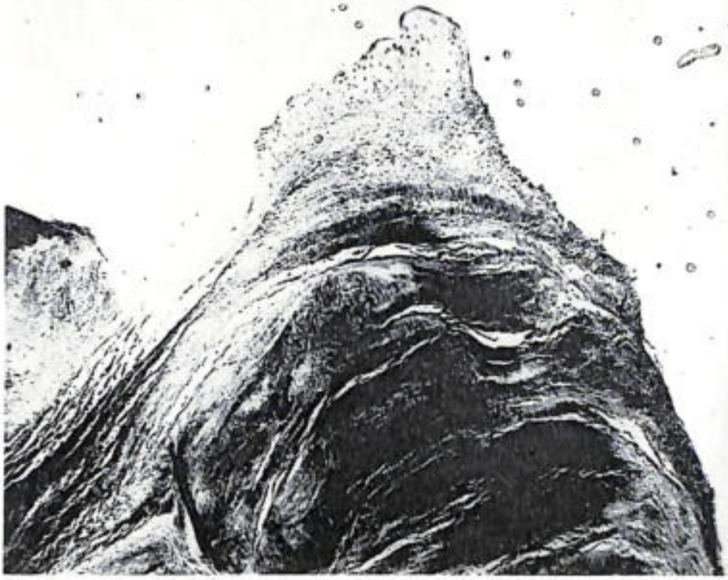


Fig. 83. Photomicrograph. Valve damage after endocarditis. Thickening of the valve, sclerosis, and hyperelastosis. The rhesus monkey Ruina. Stained with fuchsin. Obj. 5, oc. 7.

markedly thickened, shortened, milky-white in color (Fig. 84). There was a considerable milky-white thickening of the epicardium in the region of the left ventricle. There were extensive sclerotic foci in the myocardium of the left ventricle and pronounced sclerosis of the endocardium of the left atrium. Thus, the young monkey had suffered from cardiac failure, widespread cardiosclerosis, sclerosis of the endocardium and epicardium, the consequences of earlier pancarditis. The latter may well have developed soon after birth as manifested by pathological symptoms in the cardiovascular system in the form of cyanosis and dyspnea after moving about.

Besides the comparatively persistent valvular changes due to age or previous endocarditis, we observed acute valvular changes in four animals. In three animals the changes were endocarditic in nature; in two of them endocarditis developed because of and during sepsis, although there were some differences. In Malysh the

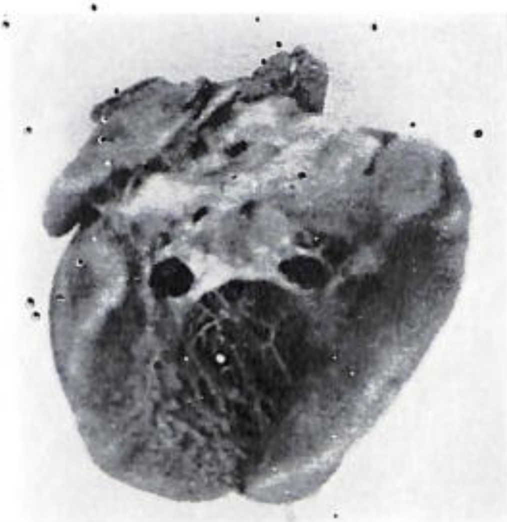


Fig. 84. Mitral valve damage. The rhesus monkey Venta.

endocarditis was a typical septic endocarditis. Morphological examination revealed that it was essentially a polypous ulcerative endocarditis (Fig. 85). Microscopically, there was marked infiltration of the valve by leukocytes and sporadic necrotic areas, especially on the surface, containing rich deposits of fibrin and indications of suppurative liquefaction of tissue. In the other animal (the rhesus monkey Yukka) the endocarditis, which likewise developed during sepsis, was much less pronounced, being characterized by leukocytic infiltration of the base of the mitral valve on the side facing the atrium. The third case of acute endocarditis developed in a monkey with exacerbation of hitherto chronic tuberculosis (the rhesus monkey Robik). This was characterized morphologically by edema and albuminous saturation of the base of the mitral valve on the side facing the atria and by moderate leukocytic infiltration of the valve in this area.

In the cases of Robik and Malysh endocarditis was diagnosed while they were alive on the basis of a systolic murmur at the apex of the heart.

Besides the cases of endocarditis referred to above, there was another in which hemorrhage was noted in the tissue of the valve.

Fig. 85. Polypous ulcerative endocarditis of the mitral valve. The rhesus monkey Malysh.

The animal, which died of dysentery at the age of one and a half, had a hemorrhage in the distal section of the pulmonary valve on the side facing the ventricle. The valve consisted of loose connective tissue diffusely infiltrated by erythrocytes (Fig. 86). No such changes were in evidence in the other valves.

Thus, an investigation of 39 hearts for senile changes showed that in general the histological structure of the heart valves of monkeys closely resembles that of man. One major difference is that the middle layer of loose connective tissue, which at times makes up virtually the entire mass of the valve, is much more pronounced in monkeys, whereas the fibrous layer is extremely faint and sometimes cannot be discerned at all. The valves often have numerous blood vessels of sinusoid structure. The vessels lie in different parts of the valve and possess a clearly defined two- or three-layered elastic membrane just under the endothelium.

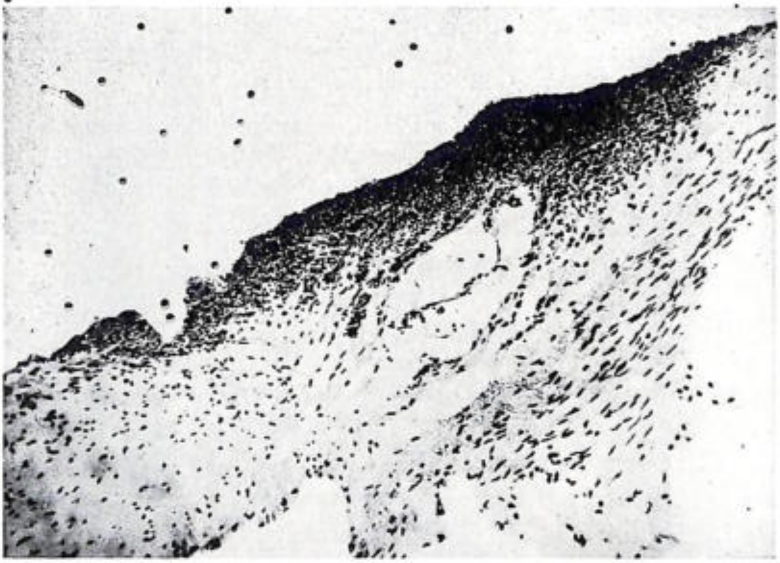


Fig. 86. Photomicrograph. Hemorrhage in the valve flap of a rhesus monkey. Stained with hematoxylin-eosin. Obj. 20, oc. 7.

Age changes in the valves of monkeys, as in human valves, are manifested by fibrosis of the middle loose connective-tissue layer and solid collagenization of the valves (chiefly in the proximal sections), sclerotic foci, and subendothelial thickening of the valves, sometimes resulting in marked deformity of the cusps. Collagenous tissue, especially at the base of the valves, changes considerably with age, turning into homogeneous amorphous masses of collagen. The increase in collagen (especially amorphous collagen) may be partly due to direct sclerosis. Indirect confirmation of this view comes from the occasional increase of metachromasia in loose connective tissue caused by the increased content of mucopolysaccharides. Homogeneous nonnuclear masses staining yellow with picrofuchsin occasionally accumulate between the collagenous fibers.

A previous endocarditis may lead to diffuse thickening of the valve with pronounced sclerosis and hyperelastosis, i.e., to the development of valve failure. Infectious diseases (sepsis or tuberculosis) may cause a limited endocarditis manifested by focal infiltration of the valves by leukocytes. A septic polypous ulcerative endocarditis may develop as a general manifestation of sepsis. Hemorrhage in the valve (along with exposure of the blood vessels) indicates that the valve is a formation with more than a purely mechanical function. It suggests that the valves have vessels which are involved in the general reactions of the body.

DISEASES OF THE BLOOD-FORMING SYSTEM

Blood diseases—particularly the leukoses—are widespread among people. Leukemia also occurs in domestic animals and birds, but is virtually nonexistent in wild animals. Individual incidences of leukosis in monkeys have been mentioned by Hill (1952, 1953, 1954). In four monkeys he observed lymphatic leukemia; two of them were marmosets—one wooly Gumboldt and one Senegal Galago. Hill obsreved lymphogranulomatosis in a lion marmoset. Other blood diseases mentioned by the author included pernicious anemia in a Chinese macaque and anemias in marmosets with intestinal diseases. The latter probably often develop in monkeys and were observed by us repeatedly in intestinal diseases.

We observed three cases of leukosis in green marmosets: the monkey Oktava developed reticulosis, Paragvay developed hemocytoblastic leukemia and Jutland lymphogranulomatosis. All three diseases were acute; both the leukoses (reticulosis and hemocytoblastic leukemia) were aleukemic variants. Because of the late discovery of the disease and the acute course of illness, the clinical picture of the leukoses was almost unstudied. Blood tests that were made for several days prior to death revealed no changes except for pronounced hypochromic anemia. The reticulosis was characterized by an enlargement of the spleen, with clearly marked yellowish-gray islets against a background of dark-red pulp, and enlargement of the liver, the parenchyma of which contained a small number of distinctly outlined yellowish-gray foci. There was also an enlargement of the kidneys and a slight enlargement of the lymph nodes.

Microscopical examination revealed a proliferation of reticular cells (Fig. 87) in the bone marrow, spleen, lymph nodes, liver and kidneys. The reticular cells in the bone marrow nearly com-

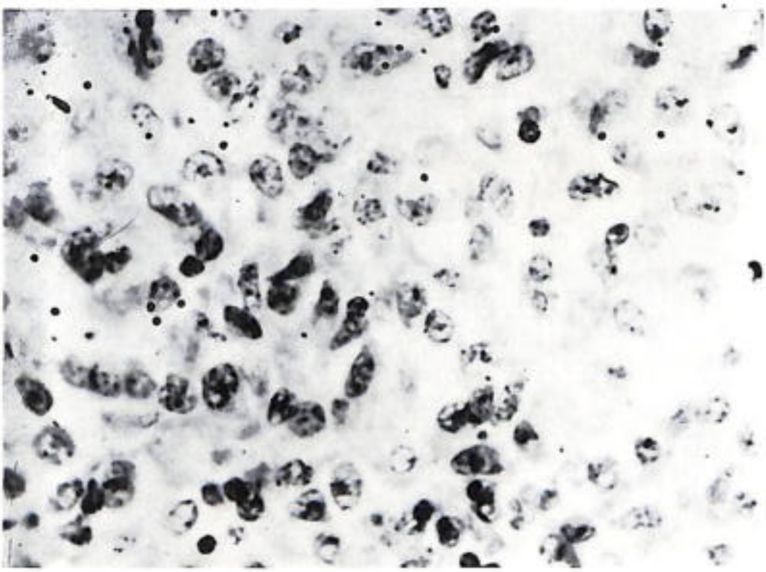


Fig. 87. Photomicrograph. Reticular cells in lymph node. Green marmoset Oktava. Obj. 40, oc. 10.

pletely displaced the lymphoid tissue. There was a proliferation of endothelial cells in the hili of the lymph nodes, with formation of complexes of reticular cells in the vascular lumens. The present observation is very reminiscent of acute aleukemic reticulosis in man. Kh. Kh. Vlados and N. A. Krayevskiy reported in 1953 that the characteristic features of acute aleukemic reticulosis included an acute initial period, the absence or weak manifestation of hyperplasia of the lymph nodes, and marked enlargement of the liver and spleen within a very short period of time.

In acute hemocytoblastic leukemia there was a fairly significant enlargement of the lymph nodes, enlargement of the spleen, slight enlargement of the liver and hyperplasia of the bone marrow in the tubular bones. Microscopical examination of the bone marrow revealed a proliferation of hemocytoblasts, forming a cellular syncytium. The lymphoid tissue in the lymph nodes was displaced by hemocytoblasts. The morphology of the given case is very similar to hemocytoblastic leukemia in man. The third case concerned

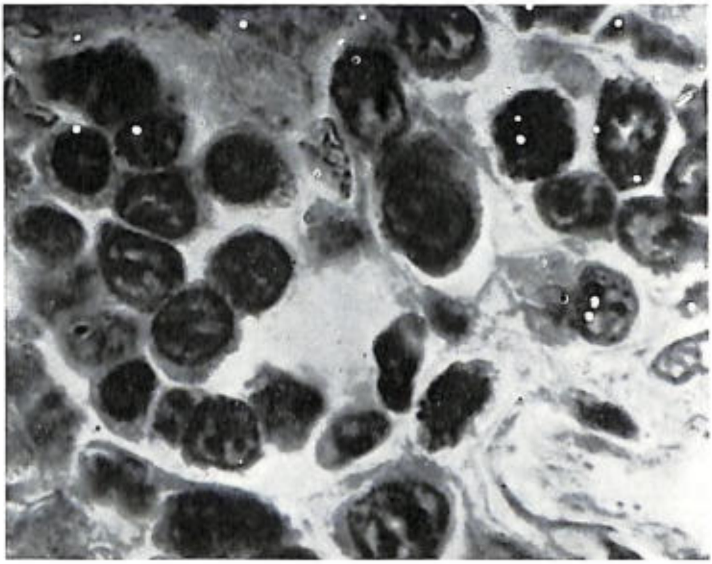


Fig. 88. Photomicrograph. Nondifferentiated blood formation in bone marrow. Hamadryad baboon Dingo. Hematoxylin-eosin stain. Obj. 90, oc. 10.

lymphogranulomatosis and was previously described by us (B. A. Lapin, 1956). It was characterized by a systemic enlargement of the lymph nodes and spleen, having a "porphyritic" appearance. The microscopical picture was similar to that of human lymphogranulomatosis.

Regarding diseases of the red blood cells, we observed anemias of the hypochromic type, usually connected with intestinal disorders. In two monkeys, the anemia was progressive in character and accompanied by a significant drop in hemoglobin, resulting in death. We noted the development of foci of extramedullary blood formation which, however (as in bone marrow), was nondifferentiated in character (Fig. 88). Thus, the blood diseases observed by us included nondifferentiated leukoses and anemias that were progressive in character. It is noteworthy that the leukoses that we observed developed only in green marmosets. It would seem that the number of cases of leukosis was small; however, the death rate among green marmosets during the past six years (47 dead) indicates a considerable morbidity rate (6.3%) A comparison of the diseases observed by us with analogous nosological forms in man and animals shows that the leukoses of monkeys resemble human leukoses, being much closer to the latter than to leukoses of other animals.

TUMORS

Human malignant neoplasms are among the most prevalent diseases. At the present time, tumors hold second place as the cause of death—next to cardiovascular diseases. According to N. N. Petrov (1947), the most common sites of human tumors are the stomach, 44%; esophagus, 13.3%; lungs, 7.8%; uterus, 7%; and liver, 5.6%. According to Dobberstein's statistical data of 1955, the most common sites of human tumors are the stomach, 30%; female genital organs, 15%; mammary glands, 8%; lungs, 7%; and skin, 7%.

In 1954, K. G. Bol' and B. K. Bol' reported that tumors of domestic animals develop most often in horses and dogs. The authors attribute this to the fact that these animals—in distinction to other domestic animals—live to old age. Horse tumors are localized most often in areas in which human tumors seldom occur, i.e., the penis, 14%; oral cavity, 14%; nasal accessory sinuses, 13.5%; and conjunctiva, 12%.

The data regarding the most common dog tumors varies. Dobberstein reported in 1955 that the most common site of neoplasms of dogs was the thyroid gland, 41%; the next in frequency of dog tumors was mammary carcinoma, 14%. Approximately the same data for tumors of the thyroid gland was reported by Krook in 1954; his figure at that time for the rate of mammary carcinoma was 35.2%. Other data was contributed by Mulligan in 1948, T. S. Verevkina and N. I. Zubova in 1952, Kotchin in 1954. Kotchin and Mulligan reported that the most common site of dog tumors was the skin, the next in frequency being mammary carcinoma. Verevkina and Zubova reported that one of the most common dog tumors was mammary carcinoma (44%). These authors made no mention at that time of the number of thyroid tumors that occurred in the dogs they had observed. The discrepancies between the given data and that of Dobberstein and Krook must evidently be connected with the fact that the researches were conducted in different countries, where both the conditions under which the dogs were kept and the specific effects which could induce tumors varied.

Dobberstein reported in 1955 that squamous-cell carcinoma of the stomach was most common (14%) in cattle, followed by tumors of the skin (12%) and uterus (9%).

The most common localization of cat tumors is the oral cavity, 33.6%; followed by the common bile duct, 22.2%; and pancreas (T. S. Verevkina and N. I. Zubova). According to the above-mentioned authors, the rate of tumor development in cats is 3.1%, and in dogs 3.6%.

Tumors are very widespread in rodents (rabbits, mice, rats). The most frequent localization of tumors of rabbits is the uterus; the most common tumor of rats and mice is mammary carcinoma. The relatively high rate of malignant growth in rodents and the high possibility of inducing tumors by artificial means renders these animals the most suitable objects for the experimental study of cancer.

Tumors of wild animals are known to us principally from materials from various zoos. The latter brings us to speak not about tumors of wild animals in general, but tumors that develop under conditions of prolonged captivity. According to the material of N. P. Tsvetayeva (1941), who investigated the death rate of animals in the Moscow Zoological Park from 1935 to 1939, tumors rarely occurred in the animals at the zoo, constituting 1% in mammals and 1.9% in birds. Tumors occurred very rarely in the primates; in 110 dissected monkeys not one malignant tumor was found, and only one had adenoma of the liver. The comparatively high rate of bird tumors was due to the high rate of tumors in crimped parakeets. A significant number of tumors were also observed in the latter by Fox in 1929 and Schlumberger in 1953. The latter discovered tumors—most of which were malignant—in 80 out of 200 crimped parakeets. According to Ratcliffe's data of 1933, tumors were found in nearly all the mammals of the Philadelphia Zoo. However, their rate of occurrence varied sharply in different species. In bears, tumors were found in approximately 6%; in rodents, 3.5-4%; in marsupials, 2.1%; raccoons, 2.4%; primates, 0.4%; ungulates, 0.16%. Comparing the localization of tumors in birds and in mammals, Ratcliffe reported that the predominant site of tumors in the former was the genitourinary tract, and in the latter the gastrointestinal tract.

Despite the biological similarity of monkeys to man, in whom neoplasms occur extremely often, an analysis of data in the literature shows that monkey tumors hold a modest place in the statistics of diseases. The cases described in the literature hardly exceed 30 to 40 in number. Tumors of primates are described, up to now, as very rare. In the prosectorial report (1913) of the London Zoological Park, Plimmer reported the discovery of monkey sarcoma of the head (?). In 1915, he also reported the occurrence of sarcoma of the kidneys in monkeys. In 1914, Schmey described adenocarcinoma of the stomach, with metastases. Fox reported on several tumors of monkeys: cancer of the esophagus, 1932; cancer of the kidneys, 1934; cancer of the uterine cervix, 1936; cancer of the esophagus, 1937. In 1939, Bonne and Sandground described gastric polyps of Javanese macaques, which were induced by the introduction of *Nochtia Nochti* nematodes into the wall of the stomach. Having introduced the aforesaid helminths into the stomach cavity, the authors succeeded in getting similar tumors in a short period of time.

A series of reports on monkey tumors were contributed by the London Zoo. Besides the above-mentioned tumors which Plimmer described, Scott described (in the prosectorial report of the London Zoological Park for 1928) cancer of the kidneys in a capuchin monkey, with metastases in the pericardium and pleura. In 1930, Hamerton described adenomatous polyp of the stomach in the pyloric region. In 1930, Zuckerman contributed a report on squamous-cell carcinoma of the oral cavity with intergrowth of tissues, but no metastases. He also mentioned six cases of monkey tumors out of 530 dissections at the London Zoo. However, four of these six tumors were described earlier by Plimmer, Scott and Hamerton, and have been discussed above in connection with the report of the London Zoo, the year 1957 included.

In 1940, Engle and Stout described a prostatic tumor of monkeys, which they treated as cancer. However, both morphologically and clinically, the tumor was quite benign and should have been classified as adenoma. In 1942, Steiner reported on his discovery of two malignant tumors of monkeys, one of which was metastatic. In 1947, Kluver and Brunschwig discovered cancer of the tongue and cancer of the buccal mucosa in two monkeys. In 1955, N. N. Blokhin and co-authors described a disintegrating skin cancer in a monkey. In 1956, A. M. Antonov described two kidney tumors in macaques. We have already mentioned the work of N. P. Tsvetayeva, who discovered only one benign tumor of the liver after dissecting 110 monkeys. In 1933, Ratcliffe discovered four malignant tumors and four benign tumors in 971 dissections of monkeys; this corresponds to 0.4 or 0.8%, counting the benign tumors.

There are different opinions in the literature on the rate of monkey tumors. In Krause's work (1933) on diseases of wild animals and analysis of data on the whole in the literature, he arrived at the conclusion that monkey tumors were rare. The same opinion was held by P. P. Dvizhkov and N. P. Tsvetayeva in 1946. A. P. Savinov and A. V. Tyufanov (1958) did not find a single malignant tumor in more than 800 dissections. However, these authors discovered polyps of the stomach, caused by parasitism of the stomach wall with slender, short helminths. The question in the given cases apparently concerns the phenomena described by Bonne and Sandground. L. A. Porubel', I. A. Prokhorova, A. N. Sergeyev and Yu. M. Slavin (1958) conducted dissections of 8,500 monkeys that died from infections or were killed for purposes of obtaining poliomyelitis vaccine, and made no mention of finding tumors.

In 1933, Ratcliffe suggested that the incidence of tumors in animals could be higher if they survived to a greater age in zoos.

An analogous viewpoint was held by A. V. Vadova and V. I. Gel'shteyn (1956). They expressed the opinion that tumors frequently occurred in monkeys, and expressed regret that a number of statistical reports on monkey tumors did not include the age of the dead animals. The insignificant rate of tumors in the reports of P. P. Dvizhkov, N. P. Tsvetayeva, Ratcliffe and others are considered by Vadova and Gel'shteyn to be the probable result of the young age of the dead monkeys. The authors analyzed material pertaining to 660 dissections of monkeys at the Sukhumi monkey-breeding farm from 1927 to 1952 and discovered 11 instances of tumors, four of which were malignant. After 1952, we continued to observe tumors of monkeys. We believe that the description of neoplasms in the monkeys at the breeding farm is of definite interest, especially for comparison with the data on age (Tables 8 and 9), the diseases contracted, etc.

TABLE 8

AGE OF AND PRESENCE OF TUMORS IN DEAD MONKEYS OF INITIAL HERD

	Macaques				*Baboons*				*Green marmosets*			
Age of dead monkeys, years	*female*	*male*	*total*	*with tumors*	*female*	*male*	*total*	*with tumors*	*female*	*male*	*total*	*with tumors*
Up to 1	23	29	52	—	17	34	51	—	9	8	17	—
1-2	7	21	28	—	5	22	27	—	1	2	3	—
2-3	10	19	29	—	3	10	13	—	1	4	5	—
3-4	3	7	10	—	—	7	7	—	—	3	3	—
4-5	2	6	8	—	—	3	3	—	1	1	2	—
5-6	2	5	7	—	4	3	7	—	1	—	1	—
6-7	4	10	14	1	2	2	4	—	—	—	—	—
7-8	3	7	10	—	2	7	9	—	2	1	3	—
8-9	6	4	10	1	1	5	6	—	—	2	2	—
9-10	5	2	7	—	2	3	5	—	—	2	2	—
10-11	4	4	8	2	1	1	2	—	—	2	2	—
11-12	1	—	1	—	2	3	5	1	—	—	—	—
12-13	3	2	5	2	1	2	3	—	1	—	—	—
13-14	5	2	7	—	—	1	1	—	—	—	—	—
14-15	3	—	3	—	1	1	2	—	2	—	2	—
15-16	5	—	5	—	4	—	4	—	2	1	3	—
16-17	2	1	3	—	1	—	1	—	1	—	1	—
17-18	1	1	2	—	—	—	—	—	—	—	—	—
18-19	1	—	1	1	1	—	1	—	—	—	—	—
19-20	1	—	1	2	1	—	1	1	—	—	—	—
20-21	—	—	—	—	2	1	3	1	—	—	—	—
21-22	—	—	—	—	—	—	—	—	—	—	—	—
22-23	2	—	2	1	—	—	—	—	—	—	—	—
23-24	1	—	1	—	—	—	—	—	—	—	—	—
Total	94	120	214	10	50	105	155	3	21	26	47	—

TABLE 9

AGE OF AND PRESENCE OF TUMORS IN IMPORTED MACAQUES

Age of dead monkeys, in years	*Females*	*Males*	*Total*	*With tumors*
Up to 1	9	6	15	----
1-2	218	350	568	----
2-3	28	35	63	2
3-4	9	8	17	----
4-5	9	9	18	----
5-6	10	11	21	----
6-7	16	6	22	----
7-8	12	2	14	----
8-9	6	4	10	----
9-10	3	1	4	----
10-11	4	----	4	----
11-12	2	----	2	----
12-13	1	2	3	----
----	----	----	----	----
----	----	----	----	----
----	----	----	----	----
16-17	----	1	1	----
----	----	----	----	----
----	----	----	----	----
----	----	----	----	----
Total	327	435	762	2

Malignant Tumors

From 1952 until 1959, in 1,179 dissections (excluding stillborn animals), we found a total of two malignant tumors and 13 benign tumors located in different areas. We present below a detailed description of these cases.

In the first case the tumor occurred in an anubis baboon called "Mississippi"—a female approximately 20 years of age. She had been brought to the breeding farm as an adult animal in 1948 and lived there for eight years. During this period of time she contracted no diseases and had eight pregnancies, four of which terminated in stillbirth. In the latter part of 1956, a tumorous node

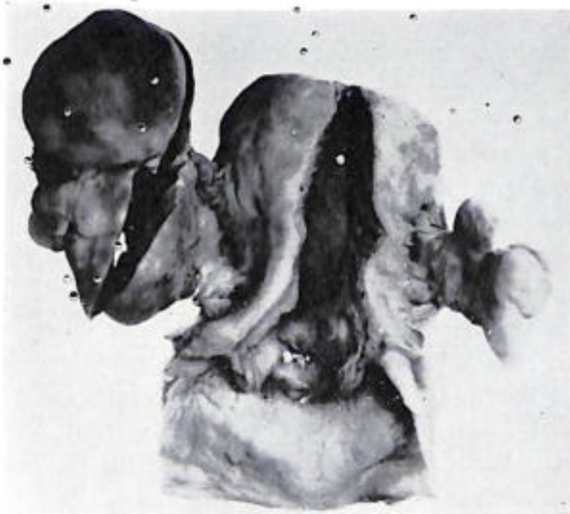


Fig. 89. Ovarian tumor. Growth of broad ligament of uterus. Anubis baboon Mississippi.

about the size of a walnut was found in the animal's right axillary region. Approximately during this period she incurred a pathological fracture of the lower jaw. She died within a month after increasing cardiac weakness.

A pathoanatomical study revealed marked enlargement of the right ovary, reaching the size of a walnut. The tissue of the ovary on the surface and in section was mottled, grayish pink, with a bluish tint in some areas. The right broad ligament was irregularly thickened and tuberous; sections of the thickened areas revealed fairly compact grayish-pink tissue (Fig. 89). The pericardium was distended with hemorrhagic exudate. Delicate fibrous deposits were defined on the epicardium and pericardium. Numerous grayish-pink tumorous growths were found in the regions of the posterior and anterior ventricular grooves, along the anterior surface of the left ventricle and in the region of the apex of the heart. The tissue of the tumorous growths had grown into the thickness of the myocardium. Fine-tuberous tumorous growths were seen between the travecular muscles in the region of the apex on the anterior wall of the left ventricle and the interventricular septum. This area also contained clearly outlined yellowish-gray nidi with irregular, scalloped margins (myocardial infarct). The left arch of the lower jaw was markedly thickened. Section revealed an intergrowth of pinkish-gray tumorous tissue in this region, the bony tissue was almost completely destroyed. The surface of the lower jaw contained an ulcerous lesion, approximately 7 cm long, exteending into the oral cavity. The base of the ulcer had undergone decomposition and was covered with dirty dark-gray masses.

In addition to the above-described features, dissection also revealed a marked enlargement of the para-aortal lymph nodes, the nodes located in the bifurcation of the aorta and in the area where the renal arteries branch off. The largest of them was the size of a large plum. Sections of the nodes showed the tissue to be juicy, grayish pink, with the appearance of fish meat. Individual nodes had undergone decomposition, their tissue had become transformed into a dirty-gray pulp. There was also a marked enlargement of the nodes of the right axillary region, forming a mass approximately the size of a goose egg, adhering to the surrounding cellular tissue. The sections of the axillary lymph nodes seemed analogous to the para-aortal.

Histological examination revealed almost no normal tissue in the right ovary. Only single primordial follicles were seen along the periphery of the organ; individual columns of the rete ovarii were retained in the hili of the ovary. Everywhere around the vessels, in the form of muffs, were proliferations of cells of incorrect oval form (Fig. 90) arranged in a fine connective-tissue stroma. The tumor cells varied in size, and frequently included multinuclear giant cells. In the majority of cells the nuclei were dark, sometimes pycnotic. Part of the cells possessed light-colored nuclei with large clumps of chromatin. Very often, there were pictures of mitotic division of the cellular elements (Fig. 91). Often the distribution of tumor cells was not limited to the perivascular zone. Outside the large vessels the tumor cells were usually located in small alveoli. The stroma of the tumor was very loosely arranged throughout, fine-fibrous, very rich in its capillary network. Occasionally, there were areas of the tumor which possessed

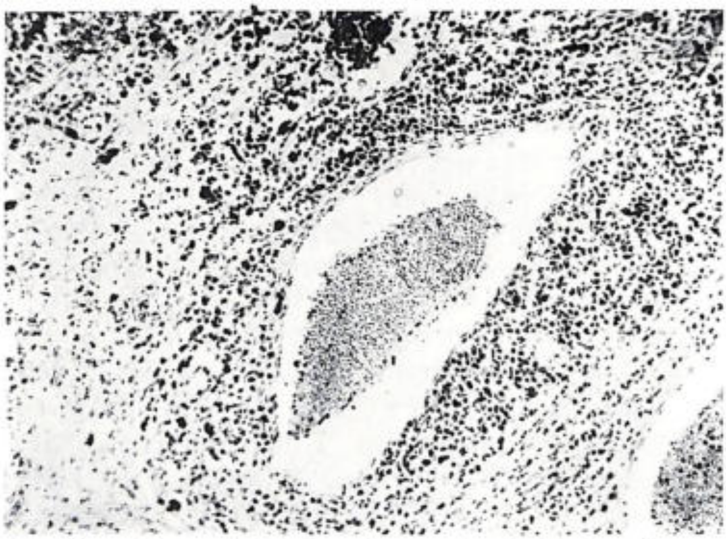


Fig. 90. Photomicrograph. Perivascular growth of cells of ovarian tumor. Anubis baboon Mississippi. Hematoxylin-eosin stain. Obj. 20, oc. 7.

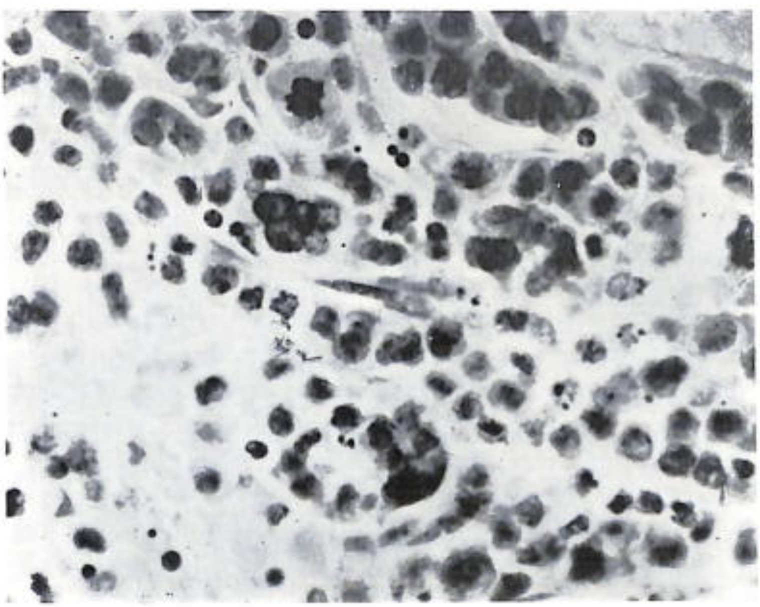


Fig. 91. Photomicrograph. Giant cells and mitoses in tumor cells. Anubis baboon Mississippi. Hematoxylin-eosin stain. Obj. 60, oc. 10.

a more compact fibrous stroma. The tumor tissue was infiltrated throughout by eosinophils. It is noteworthy that the tumor cells — growing principally around the large blood vessels — mainly involved the adventitia and were not found in the inner lining of the vessel. Only now and then was tumor tissue seen to grow through the entire width of the vascular wall.

In the heart, the growth of tumor tissue was observed in the epicardium and myocardium. The tumor tissue—like ovarian tissue—was composed principally of round-cell elements in a fine-fibrous stroma. However, the tumor had a more homogenous character—its cells were almost identical in size; giant cells seldom occurred. The tumor did not extend to the vessels, but permeated the cardiac tissue in a diffuse manner, growing into the myocardium between the muscle fibers. The lumens of the thin-walled veins and sinusoids were often filled with clumps of tumor cells. Unlike the growth in the ovary, the tumor tissue in the myocardium had become necrotic in many areas. There were also extensive necrotized areas in the muscle tissue which where banked by leukocytes, forming a line of demarcation.

The growth of tumor tissue in the axillary, paraaortal lymph nodes and in the soft tissues of the lower jaw was diffuse in character and accompanied by extensive necroses. The internal organs showed signs of dystrophy, irregular admission of blood, and adiposity. Marked hyperplasia of the splenic pulp was observed.

We believe that the monkey "Mississippi" developed sarcoma of the right ovary, which had a peculiar perivascular location. The tumor spread in multiple metastases in different groups of lymph nodes, lower jaw and heart. The metastases revealed a more diffuse character of growth than the original node. Here the tumor was analogous in appearance to reticuloendothelioma. The malignant involvement of the heart, accompanied by the development of extensive necroses, was apparently the direct cause of death.

In the given case the growth of the tumor was accompanied by the development of a large number of metastases. The latter, being typical for human malignant tumors, is not often observed in monkeys. A. V. Vadova and V. I. Gel'shteyn (1956), who followed the development of mammary carcinoma in the M. rhesus

"Undina," noted that the tumor did not metastasize, despite repeated biopsies. In examining archival material collected at the Institute for a period of many years, these authors discovered sarcomas in two animals, which also did not metastasize. Metastases developed in a few cases of experimentally induced osteosarcoma (N. N. Petrov, A. V. Vadova, N. A. Krotkina, Z. A. Postnikova, 1951).

We found no description in the literature of ovarian cancer of monkeys. According to K. P. Ulezko-Stroganova, primary ovarian sarcomas of human beings constitute 2% of the total number of ovarian tumors.

The given observation is of interest from the standpoint of both the localization of neoplasms and the development of a true malignant tumor with multiple metastasis.

The second malignant tumor was observed in the hamadryad baboon "Beluga" that died in 1958 at 19 years of age. Its anamnesis included hypertension of 15 years' duration and multiple abortions. Twenty-four days prior to death, a tumor of the sexual skin was observed in the form of an extensive ulcer with a dirty-gray base and slight discharge.

Dissection of the dead animal revealed considerable wasting and adipose dystrophy of the parenchymal organs. On the sexual skin, left of the anal orifice, was a deep cone-shaped ulcer 5 cm in diameter. The center of the ulcer's surface was covered with dirty-gray necrotic membranaceous deposits. The margins of the ulcer were elevated in an embankment and had a cartilaginous consistency. A section made through the ulcer revealed a very compact, somewhat granular, yellowish-gray tumorous tissue, vaguely delimited from the surrounding tissues. The tissue of the tumor extended close to the walls of the rectum and vagina, but did not infiltrate them, being separated from the latter by a thin interlayer of cellular tissue. The mucous membrane of the rectum and vagina was edematous.

Histological examination of the sexual skin in the area of the ulcer revealed the disappearance of stratified squamous epithelium. The base of the ulcer consisted of granulation tissue. Somewhat below the base of the ulcer, in the thickness of the granulation tissue, were vacuoli of round, somewhat pycnotic oval-shaped cells

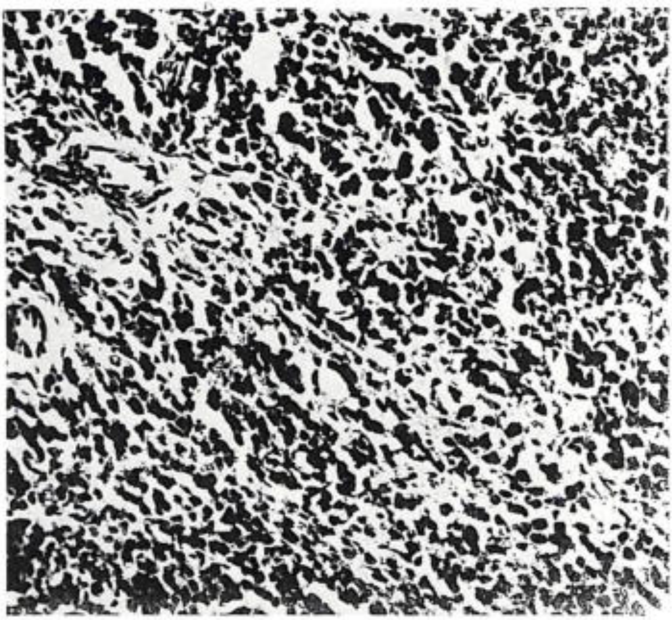


Fig. 92. Photomicrograph. Cancer of genital skin. Hamadryad Beluga. Hematoxylin-eosin stain. Obj. 20, oc. 7.

with a slightly off-center arrangement of the nuclei. The tumor, a squamous-cell carcinoma, was constructed entirely of these vacuoli and solid cellular columns, which were arranged between connective interlayers (Fig. 92). Although the tumor was morphologically characterized by pronounced infiltrative growth and was connected with the extensive ulcerous surface, there were no metastases. In this respect, the present observation differs from the preceding one, and is apparently characteristic for malignant tumors of monkeys.

Benign Tumors

Benign tumors occur in monkeys somewhat more often than malignant tumors. The benign tumors that have been mentioned include ovarian cysts, polyps of the uterine cervix, uterine adenoma, adenoma of the prostate, gastric polyps. The latter, as well as polyps of the uterine cervix, are perhaps more common than the other benign tumors.

Gastric Polyps

Single cases of benign tumors of the stomach were mentioned in the researches of Ratcliffe and Fox. In 1939, C. Bonne and J. H. Sandground contributed a report on adenomatous polyps of the stomach which were connected with the parasitism of the stomach with Nochita nochti nematodes. The article by A. V. Vadova and V. I. Gel'shteyn in 1956 contains a description of four cases of gastric polyps. The authors found on malignant neoplasms of the stomach.

Between 1952 and 1959, we observed four cases of adenomatous polyps of the stomach in M. rhesus monkeys, two of which had lived for a long time at the breeding farm. One of the monkeys had been brought to the farm at the age of two years, and remained there for 17 years; the second monkey was born at the farm and killed in a harsh experiment at the age of six years. Two monkeys had been brought from India to the Institute's breeding farm not long before they were killed at the age of approximately two years.

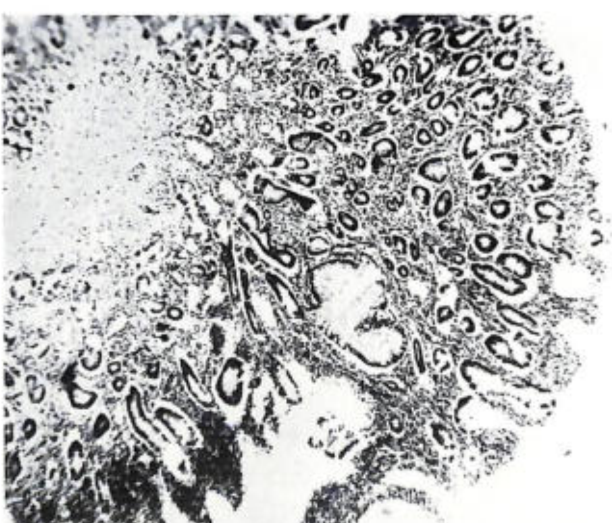


Fig. 93. Photomicrograph. Tubular polyp of stomach. M. rhesus Ruta. Hematoxylin-eosin stain. Obj. 2, oc. 5.

The first two monkeys (Nos. 752 and 777) had small, single polyps on a short pedicle. The polyps were formed from incorrectly constructed mucous membrane with disorderly arranged glandular lumens. Some of them were distended, some were stretched out in cystlike formations (Fig. 93). Here and there, the juicy, high epithelium formed small papillose protuberances. The mucosa of the polyps was diffusely infiltrated by round cells. Considerable aggregations of lymphatic cells were seen occasionally, erasing the picture of the tissue of the polyp. In two cases (protocol of dissections Nos. 1420, 1459), in young monkeys that had just been brought to the breeding farm, papillomatous growths in the stomach were quite extensive. The mucous membrane of the base and body of the stomach was rough, with many small—the size of a large pea, or smaller—polyps projecting into the lumen (Fig. 94).

Under microscopical examination, the polypous outgrowths

Fig. 94. Polyp of base of stomach. M. rhesus Garuk.

Fig. 95. Polyp of uterine cervix. Javanese macaque Krasnushka.

had the structure of a tubular polyp, with incorrectly formed glandular cavities lined with juicy, columnar epithelium. The lumens of individual glandules were very small and vaguely defined. In certain glandular tubes the epithelium was stratified. In connection with the proliferation of epithelium, the tube was transformed into a solid cellular vacuole. In two cases, individual areas revealed the inclusion in the glandular epithelium of islets of stratified squamous epithelium with initial signs of cornification (in connection with the proximity of the areas removed for study to the esophagus).

Polyps of the Uterine Cervix

Among benign tumors of the female reproductive organs, we observed six cases of polyps of the uterine cervix (Fig. 95). In four cases, polyps were discovered in adult simians 8, 10 and 12 years of age; in two cases, in old simians 19 and 22 years of age. The anamneses of four of these animals showed diverse obstetrical pathology (stillbirth, adherent placenta, endometritis, etc.). In five cases the structure of the polyp was approximately the same. The polyps consisted of dense, collagenic tissue with a slight impregnation of fibers of smooth muscle. The surface of the polyp was lined with columnar epithelium forming a considerable number of deep ducts (in the form of a crypt) leading into the body of the polyp. Occasionally, these ducts were distended, forming cystic cavities containing mucus. Gelatinization of the epithelial lining took place in individual cavities. Some cavities contained no mucus. The mucous membrane of the polyp from the aspect of the cervical canal was transformed into glandular cervical epithelium. The glands of the latter, close to the polyp itself, were distended and filled with mucus. From the aspect of the external os of the uterine cervix, the epithelial lining of the polyp was transformed into stratified squamous epithelium. In one of the five cases, the epithelial lining of the polyp consisted of stratified squamous epithelium. Only for an insignificant extent—changing into cervical mucosa—did the epithelial lining of the polyp acquire the character of the cervical. We must assume that, in the given case, metaplasia of the glandular cervical epithelium into stratified squamous occurred because the very high location of the polyp (its base was in the internal os of the uterine cervix) precluded the participation of vaginal epithelium in the polyp's formation.

The sixth case differed morphologically from those described above. In this case, the polyp was discovered in a Javanese macaque that died at the age of 12 years during a harsh experiment. Its anamnesis included numerous pregnancies, all terminating in stillbirth.

In examining this animal's reproductive system, attention was immediately drawn to the large polyp projecting from the external os of the uterine cervix. Opening of the cervix permitted us to establish that the polyp was attached by a narrow pedicle to the cervical mucosa of the internal cervical os. Slightly above the place where this growth was attached was another polyp which was the size of a cherry pit and looked like a cauliflower. Histological examination revealed that leading from the original polyp which had dense connective-tissue structure were numerous xyloid branching outgrowths lined with columnar epithelium. Near the surface of the polyp, columnar epithelium was replaced here and there by stratified squamous epithelium (Fig. 96). The polyp, composed mostly of branching, narrow trabeculae covered with col-

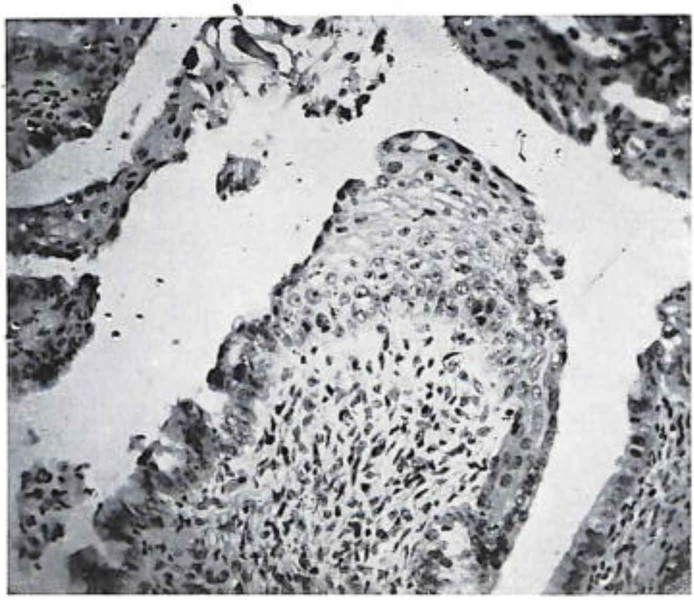


Fig. 96. Photomicrograph. Metaplasia of columnar epithelium of uterine cervix into stratified squamous epithelium. Javanese macaque Krasnushka. Hematoxylin-eosin stain. Obj. 20, oc. 10.

umnar epithelium, was covered on the exterior with a strong layer of stratified squamous epithelium. Minute cavities formed under this external epithelial layer, and they, in turn, developed small papillary outgrowths of epithelial tissue, which were generally columnar, but occasionally replaced by stratified squamous (Fig. 97). In individual cavities the proliferation of their epithelial-tissue lining lead to the formation of solid cellular vacuoli.

Glandular Polyp of the Uterine Body

The anamnesis of the hamadryad baboon "Ipatiya," killed in a harsh experiment at the age of 10 years, indicated that the second delivery was followed by uterine hemorrhages which led to a rather persistent anemia. Opening of the uterus revealed an insignificant increase in its size. Leading from the posterior wall into the uterine cavity was a node the size of a hazelnut, which was lined with mucous membrane (Fig. 98). Histological examination revealed that the node possessed the structure of endometrium

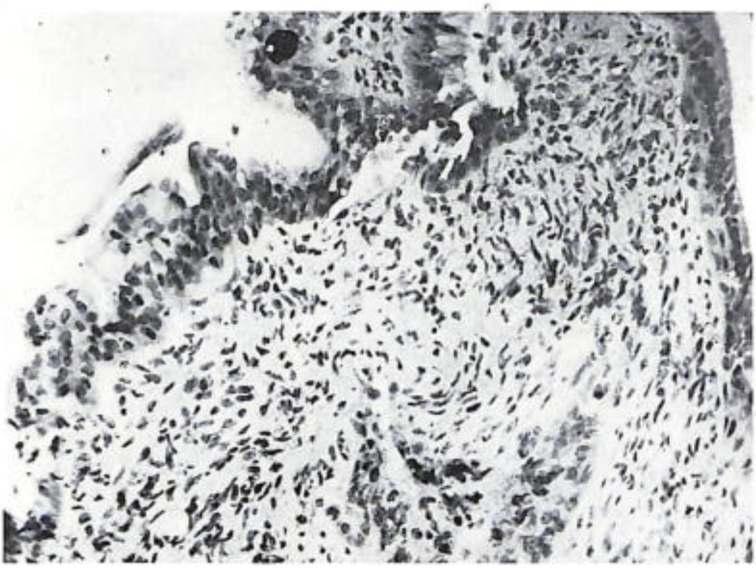


Fig. 97. Photomicrograph. Proliferation of metaplastic epithelium of polyp; metastases with formation of solid cellular columns. Javanese macaque Krasnushka. Hematoxylin-eosin stain. Obj. 20, oc. 10.

Fig. 98. Polyp of uterine body. M. rhesus Ipatiya.

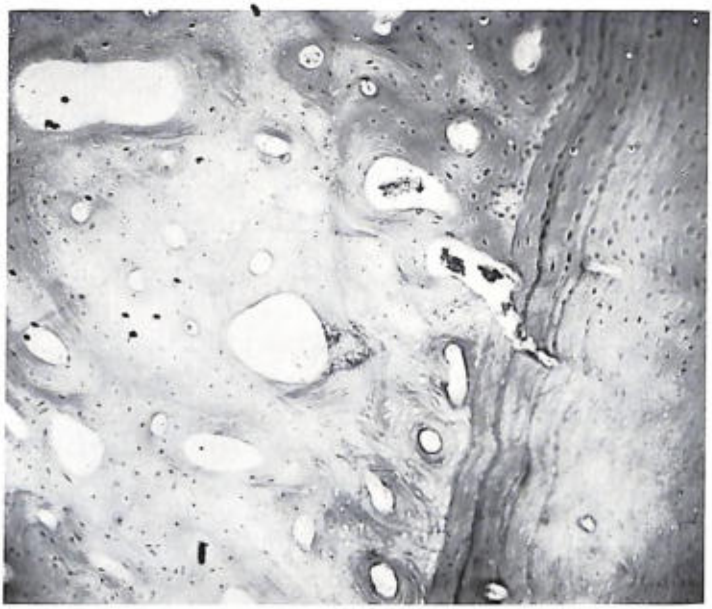


Fig. 99. Photomicrograph. Osteoma. Hamadryad Cheleken. Hematoxylin-eosin stain. Obj. 10, oc. 7.

with certain features of atypical structure. The stroma contained numerous glandular cavities of various sizes.

Osteoma

Opening of the left thigh of the hamadryad "Chelekena" that died at the age of 10 years disclosed a tumorous growth of bony tissue with rounded margins, approximately 5 cm long, 1.5 cm in width and height. Histological examination revealed that the compact layer of the femur in the area of the tumor had been transformed into tumor tissue without any boundary. The tumor tissue had the structure of compact bony tissue with no atypical features (Fig. 99).

Cortical Adenoma

We observed cortical adenoma in one monkey – a Javanese macaque called "Tsikada." The adrenal gland was enlarged to approximately the size of a large hazelnut. Adenomatous proliferation of the cortical cells was noted in the medullary layer.

A transverse section of the adrenal gland revealed a narrow strip of the cortical layer along the surface of the section, which was rich in lipids of pale yellow color, followed by a narrow grayish-brown layer of medullary cells, and then—occupying a large portion of the central region of the adrenal gland—the tissue of the cortical layer, in the form of a rounded, pale-yellow node.

Microscopical examination established that the described formation was constructed of cells containing a large amount of lipids and similar to the cells of the cortical layer.

Table 8 shows that tumors rarely occur in monkeys. Between 1952 and 1959, we discovered 15 tumors (Table 10) in a total of 1,179 dead animals.

One monkey had two tumors of different localizations—polyp of the stomach and polyp of the uterine cervix. The number of tumors constituted 1.27% of the total of dead animals. Twelve tumors were discovered in the original herd; two tumors in newly-arrived animals (Table 10).

Thus, the percentage of tumors was incomparably higher in the original herd of monkeys (417) than in the imported animals (762); 3.1% in the former, 0.25% in the latter.

A comparison of Tables 8 and 9 with analogous Tables in the

TABLE 10

TUMORS OBSERVED IN MONKEYS AT BREEDING FARM FROM 1952 TO 1959

No.	*Species*	*Age (years)*	*Kind of tumor*
1	Macaca rhesus	6	Polyp of stomach
2	Macaca rhesus	8	Polyp of uterine cervix
3	Macaca lapunder	10	Polyp of mucosa of uterine body
4	Macaca rhesus	10	Polyp of uterine cervix
5	Javanese macaque	12	Polyp of uterine cervix
6	Macaca rhesus	12	Polyp of uterine cervix
7	Javanese macaque	18	Cortical adenoma
8	Macaca rhesus	19	Polyp of uterine cervix
9	Macaca rhesus	19	Polyp of stomach
10	Macaca lapunder	22	Polyp of uterine cervix
11	Hamadryad baboon	11	Osteoma of tibia
12	Hamadryad baboon	19	Cancer of sexual skin
13	Anubis baboon	20	Ovarian sarcoma

article of A. V. Vadova and V. I. Gel'shteyn shows that the occurrence of primary tumors coincides with the periods of prepuberty and puberty in monkeys. Also, the first tumors to develop were polyps of the stomach. In our material, both tumors in the imported animals were polyps of the stomach and occurred in M. rhesus monkeys that died at the age of two years. Polyps of the stomach were also discovered in two adult macaques of the original herd, constituting 0.94% of all the dead macaques of the original herd.

The most common benign tumor among our experimental animals was polyps of the uterine cervix, which occurred only in the M. rhesus monkeys. Polyps were discovered in six out of 51 adult M. rhesus females that died at the age of more than four years; this constituted 11.76% of the simians of the given group. The remaining tumors that occurred in the original herd were solitary.

Two neoplasms were found to be malignant. The latter comprised 0.48% of the total number of dead monkeys of the original herd. Considering that in the original herd tumors were discovered only in adult animals, we calculated the rate of malignant tumors in relation to all the deaths among the adult animals of the original herd, i.e., those over four years of age. In this case, the percentage of malignant tumors was 1.16.

However, if you consider the fact that malignant tumors were seen only in adult baboons (56 animals over four years of age), the malignant tumors that were found comprised 3.5%. Although we found malignant tumors only in adult animals, Vadova and Gel'shteyn discovered them also in relatively young monkeys (3, 6, 9 years of age). The situation was analogous with respect to benign tumors.

If we exclude from the materials of Vadova and Gel'shteyn the cases which, in our opinion, were not tumors, the rate of monkey tumors would be significantly lower. We believe that vaginal papillomatosis and ovarian cysts cannot be classified as tumors.

In addition to this, it would seem that the tumors described by the given authors should not include the case of gastric polyps in the monkey "Ganimed." In the dissections of hamadryad

Fig. 100. Normal stomach of adult baboon.

baboons, we directed our attention to the pyloric region of the stomach, which contained areas of hyperplastic mucous membrane surrounding the pylorus in the form of ridges. Coming across these phenomena regularly, we arrived at the conclusion that this structure of the gastric mucosa of baboons was their specific norm (Fig. 100). Vadova and Gel'shteyn apparently encountered the same situation. Thus, the total number of tumors, both in our material and in that of the above-mentioned authors, attests to the insignificance of tumors in the nosologic aspect of monkeys.

Regarding the localization of benign monkey tumors, it may be said that they constitute, for the most part, adenomatous polyps of the stomach and tumors of the female reproductive organs (mainly polyps of the uterine cervix). The latter usually occur in middle-aged and old monkeys, while polyps of the stomach generally occur in young animals.

In connection with the fact that the monkeys lived for a more or less long period of time under conditions that were not entirely adequate at the breeding farm, we have basis to assume that tumors occur considerably less often in monkeys in their natural habitat than in captivity. We were unable to make a scientific conclusion as to the rate of tumors among monkeys of the original herd which were peculiar to them in general. The supposition stated above was indirectly confirmed by the results of research in monkeys that had just been brought to the breeding farm from India and China. The tumors that were discovered in two young animals that had just arrived should unquestionably be considered as having developed while the animals were still in their natural habitat, comprising 0.26% of all the imported macaques (761) that died under 13 years of age; only one animal was older (16 years old), and was not included in the calculation.

A comparison of the obtained results with the data concerning tumors of macaques in the same age group from the original herd at the breeding farm (189 animals) indicates that tumors occurred more often in the latter, constituting 3.17%.

It should be mentioned that growths on the mucous membrane of the stomach, connected with the infestation of the submucous layer with helminths, were seldom observed (only once, in distinction to the data of Bonne and Sandground) in our material, and were not included under true tumors. It can also be pointed out that tumors (gastric polyps) were rarely found in the materials of the Moscow institutes of poliomyelitis, at the present time numbering more than 20,000 dissections of newly-imported monkeys.

Despite the absence of information on the age make-up of the animals used—the latter being obtained from one source—we have basis to believe that the number of adult and old animals exceeded 15% of the total number of 20,000.

All the presented facts indicate that monkey tumors—both benign and malignant—are extremely rare in breeding farms and zoos. Even more rare are tumors in monkeys that have just been imported from their natural habitat. Apart from the fact that monkey tumors occur less often than human tumors, unlike the latter, even the long-lasting and malignant tumors seldom metastasize.

DISEASES OF THE FEMALE REPRODUCTIVE ORGANS

Among the diseases of the female genital organs of monkeys, we observed endometriosis, follicular cysts of the ovaries and hyperkeratosis of the vagina. These diseases, with the exception of hyperkeratosis and papillomatosis of the vagina, are fairly common in human beings. Ovarian cysts are often found in cattle, pigs and horses. Endometriosis occurs in cattle, dogs, cats, and rabbits.

In monkeys these diseases were reported as solitary cases by individual authors. In 1951, Klüver and Bartelmetz described endometriosis with intergrowths of endometrium in the serosa of the lesser pelvis. The authors believed that the endometriosis was caused by "hormonal dyscrasia" connected with injury of the hypothalamus. In 1953, Scott, Te Linde and Wharton described spontaneous endometriosis in a monkey, and carried out experimental implantation of endometrium in the abdomen, disrupting the flow of menstrual blood. In 1933, Hamerton described a cystic tumor of the "internal genitalia." The description of this tumor led us to believe that the given case concerned endometriosis. Regarding ovarian cysts, we found only one reference made to them in the work of A. V. Vadova and V. I. Gel'shteyn (1956). Thus, the literature contains only solitary references to the pathology of the female genital organs that we observed in monkeys at the breeding farm.

Endometriosis

In the material of more than 493 dissections of female monkeys of various ages we observed phenomena of endometriosis, accompanied by macroscopical changes, in five animals. The study of their anamneses and the observation of living animals permitted us to establish the defects in the genital sphere.

The first of these monkeys, a hybrid macaque called "Zlatka," was born at the breeding farm and, after reaching puberty, mated repeatedly. Pregnancy did not occur. On several occasions, however, pregnancy was suspected because of enlargement of the uterus to the size of a small egg. The monkey was experimentally killed at the age of seven years and we found that the uterus was greatly enlarged. Dissection revealed a bloody content with an admixture of mucus in the uterine cavity. The wall of the uterus was markedly thickened; section of the uterine wall revealed a fibrous structure. A microscopical study of the uterus showed that the endometrium in a number of areas had invaginated into the thickness of the myometrium, with the transformation, prior to this, of the normal mucosa into an incorrect structure, with papillary outgrowths of the glands. In the thickness of the uterine musculature were numerous cavities varying in size and shape and lined with glandular epithelium. In some cavities the epithelium was arranged in a single layer. The walls of the cavities were smooth. In the greatest part of the cavities it was clearly seen that the epithelium was uterine. In some cases there were numerous branching papillary growths. The ovaries were unchanged.

The second monkey, a 15-year-old Macaca lapunder called "Nal'ma," was experimentally killed. Its anamnesis indicated prolonged persistent swelling of the sexual skin. In the last one and one-half years, tenderness and abdominal distention were noted. Surgical opening revealed that the uterus was slightly enlarged and had very thick walls. In the thickness of the wall, near the vagina, a nodule about the size of a cherry stone could be discerned. Microscopical examination revealed numerous areas of mucous membrane (possessing structure identical to endometrium) in the thickness of the myometrium, varying in size from very small islets to rather large fields. Apart from this, columns of mucous membrane branched out from the endometrium to the muscle wall, delaminating it. The ovaries were normal.

The third monkey was a 20-year-old M. lapunder called "Lovkaya." Her anamnesis included seven pregnancies—one pregnancy ended in abortion, two ended in stillbirth—and instances of uterine bleeding beginning in 1956. The uterus was removed because of fibromyoma of the uterus, which was diagnosed by clinicians. The excised uterus was enlarged, its mucosa was considerably thickened. Microscopical examination revealed in the thickness of the uterus

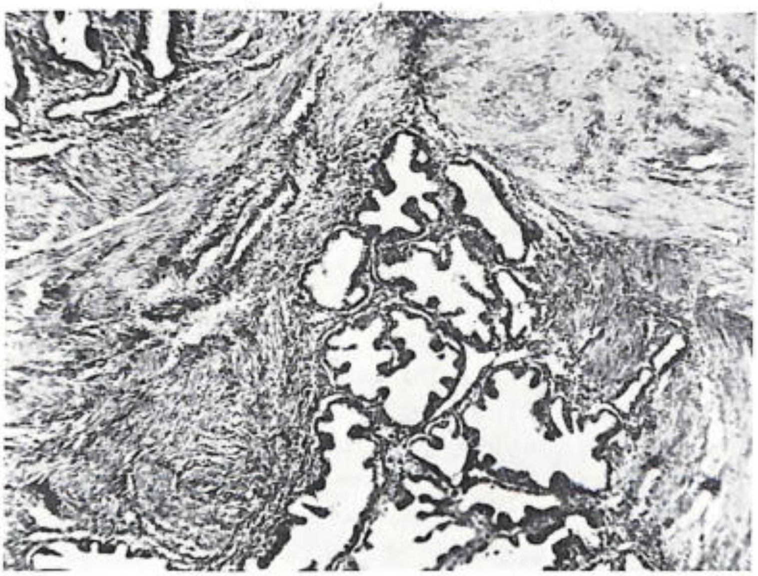


Fig. 101. Photomicrograph. Endometriosis. Macaca lapunder Lovkaya, 20 years of age. Hematoxylin-eosin stain. Obj. 8, oc. 7.

thick columns of connective tissue and many cavities, some of which looked like ordinary glandular tubes—sometimes branching incorrectly — forming conglomerates of glandular formations which varied in shape and size. Here and there the myometrium contained large cavities lined with glandular epithelium, ramifying and forming papillose growths and interlacings (Fig. 101). The ovaries were unaltered.

The fourth monkey was a hamadryad baboon called "Keto" that died of intestinal obstruction at 12 years of age. The animal's anamnesis showed three normal deliveries. There were no pregnancies during the last six years prior to death. On dissection, the uterus was enlarged, asymmetric because of protrusion of the right half of the body. The surface of the uterus at its base was bumpy due to whitish-gray nodules located in the surface layers under the serous lining and ranging in size from a pinhead to a matchhead. The peritoneum above these nodules was dull, rough, with a few adhesions to the serous lining of the intestinal loops. On incision, the nodules appeared to be formations with thick, grayish walls and a small cavity filled with a gelatinous mass. Analogous formations were also found in the deeper layers of the uterine wall, mainly in the right half of the body of the uterus. In the thickness of the right broad ligament and in the peritoneal adhesions were cysts filled with viscous masses of a tenacious secretion. Microscopical examination revealed cystic growths of endometrium filled with homogenous masses of glandular secretion located in the surface and deeper layers of the myometrium. The cysts in the broad ligament and in peritoneal adhesions also proved to be endometrial glandular cavities filled with homogenous masses of secretion with a slight admixture of mucus.

Examination of the ovaries established no noticeable deviations from the norm. In the given observations the endometrial growths projected beyond the uterus, became implanted in the peritoneum and, evoking the process of adhesion, brought about intestinal obstruction.

The anamnesis of the fifth monkey—a Javanese macaque called "Krasnushka" that died at the age of 12 years—included five pregnancies ending in stillbirth. Dissection of the animal, after it was killed in a harsh experiment, revealed a uterine polyp; microscopical examination disclosed endometriosis. Without attempting to determine the causes of the stillbirths, we will note that the five pregnancies and births, not having been followed by the nursing of the infant animal, could have led to a disturbance in the balance of the sex hormones, which had significance in the development of endometriosis.

The next five cases of endometriosis in the monkeys "Sena," "Keta," "Vesta," "Fauna," and "Espa" were discovered in a study of histological preparations obtained in dissections on choice of 25 uteri. Three of these five cases are interesting.

One of them concerns the hamadryad "Vesta" that died from tetany at the age of 25 years. Examination of the uterus revealed no essential defects. However, examination of the left ovary (the right ovary contained a cyst) revealed, in addition to its involutional changes, papillary glandular endometrial growths.

Two cases (the Chinese macaque Espa, seven years of age, and Fauna, seven and one-half years of age) had a very similar morphological manifestation: the glandular cysts located in the thickness of the myometrium revealed considerable proliferation of epithelial cells, transforming the cavity in individual areas into a solid aggregation of cells. The proliferating cells were large and juicy. In individual areas the epithelium in certain cavities had undergone metaplasia and was transformed into stratified squamous epithelium. Stretching out lengthwise, the epithelial cells adjacent to the lumen acquired an elongated polygonal form.

Analysis of the material permitted the conclusion that, in the majority of cases, endometriosis develops in monkeys of mature and middle age. A detailed study of the case history and the pictures of the development of disease revealed that the majority of monkeys with endometriosis had been affected by some disturbances connected with the hormonal regulation of sexual functions. The question concerned sterility, stillbirth, disturbances in the sexual cycles, etc. The case histories of the two monkeys Espa and Fauna, in which no pronounced endocrine disturbances were found, indicated that the animals had been subjected to general roentgen irradiation; this could have produced injury of the ovaries, which are sensitive to radiation.

This data agrees with the observations of Vadova and Gel'shteyn (1956) and Vadova and Smoylovskaya (1959), who induced endometriosis in monkeys by the prolonged introduction of estrogenic hormones.

Follicular Cysts of the Ovaries

Ovarian cysts were discovered in six monkeys of various species. In two cases they were small—slightly larger than a matchhead; in four cases they attained the size of a large hazelnut. In four animals the cysts protruded from the ovarian tissue, forming thin-walled protuberances filled with clear, yellowish fluid; in two animals the cysts were thin-walled, globular formations filled with clear fluid, and it was difficult to define the remnants of ovarian tissue at the base of the cysts where they were attached to the fallopian tube.

Microscopical examination established the classification of these cystic formations as follicular cysts of the ovaries. Their inner surface was lined with characteristic follicular epithelium—

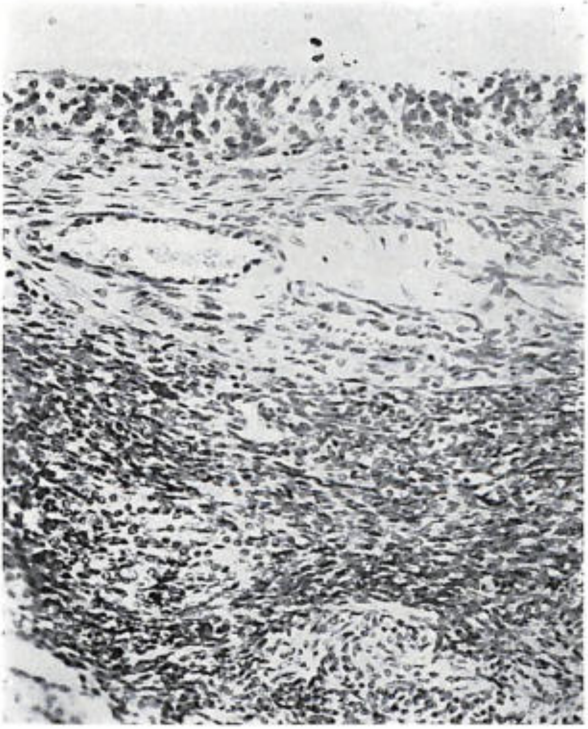


Fig. 102. Photomicrograph. Wall of follicular cyst of ovary. Green marmoset Kashtanka. Obj. 20, oc. 7.

polystichous, consisting of small polygonal cells (Fig. 102). It is necessary to note the relative rarity of follicular cysts of the ovaries and the fact that they occur mainly in old monkeys. Only one of the six monkeys was young (four years of age); the remaining five animals were 15-25 years old, which corresponds to middle and old age in man.

Polyps of the Cervix and Body of the Uterus

Polyps of the uterine cervix and glandular polyps of the uterine body may occur in adult monkeys. A description of these growths is given in the section on tumors.

Hyperkeratosis and Papillomatosis of the Vagina

A study of the structure of the vaginal wall in monkeys of various species did not enable us to establish any essential difference from the structure of the human vagina. The vaginal wall in monkeys, as in human beings, may be subdivided into three layers: mucous, muscle, and fibrous. The mucous layer consists of stratified squamous epithelium and underlying areolar connective tissue which is very rich in blood vessels. Located underneath the mucous layer is a thin muscle layer consisting of an internal longitudinal and an external circular layer, alternating with an external fairly areolar connective-tissue layer containing large, thick-walled vessels. The thick layer of stratified squamous epithelium often produces outgrowths into the tunica propria. The papillae of connective tissue that projected between the outgrowths of epithelium were usually infiltrated with lymphoid cells with an admixture of a small number of plasma cells and solitary segmented-nuclear neutrophils. The thickness of the mucous membrane varied within a considerable range, being small in infancy and acquiring considerable width in the period of puberty. In approximately 10% of the cases, beginning at the age of four years, there were signs of cornification with an accumulation on the surface of the epithelial coat of varying thickness of a layer of cornified structureless masses. The degree of cornification of the vaginal epithelium varied from incipient to very pronounced.

Our attempt to correlate the degree of cornification with the monkey's age was not successful since a slight cornification of the vaginal epithelium was noted in old monkeys and, at the same time, a considerable degree of keratosis was observed in young animals. Monkeys in which the epithelial lining of the vagina showed no traces of cornification belonged to different age groups, including very old animals. In five monkeys the symptoms of hyperkeratosis were accompanied by the formation of papillomatose outgrowths of epithelium. The stroma, penetrating into the epithelial outgrowths, consisted of very areolar connective tissue, parts of which were richly infiltrated with lymphoid elements. In one case there was considerable sclerosis of the stroma, and the connective tissue growing into the papillary processes was constructed of dense collagenous fibers.

It should be noted that the anamneses of all the monkeys with symptoms of vaginal hyperkeratosis included either prolonged or recurring infectious diseases and prolonged detention under experimentation. The anamneses of some animals included roentgen-ray irradiation. The direct causes of cornification of the vaginal mucosa remain unclear to us; we may assume, however, that it is connected with a deficiency of vitamin A.

PATHOLOGY OF PREGNANCY AND BIRTH

Despite the fact that we can now speak of the fairly complete acclimatization of the monkeys at Sukhumi, the rate of stillbirths and abortions among them is still high. Essentially, only in the last few years has there been a slight decrease in the number of stillbirths, abortions and other pathology of pregnancy and birth. To some extent, this decrease was brought about by a decrease in the number of convulsive seizures in pregnant monkeys—these phenomena are nonspecific for pregnancy, but quite often complicate early pregnancy in hamadryad baboons.

The examples presented in this section on the pathology of pregnancy and birth in monkeys are rare. However, comparing the obstetrical pathology of man with that of monkeys, we may conclude that pathological symptoms of pregnancy and birth occur more frequently in monkeys than in human beings. A possible exception is extrauterine pregnancy, occurring very rarely in domestic animals (Nieberle and Kohrs, 1954) and monkeys, but very often in man.

A description is given below of displacement of a gravid uterus (this pathological phenomenon is very rare in the human female and occurs more often in animals), several cases of rupture of the uterus during labor, occurring quite seldom in man and considerably more often in animals, as well as several cases of extrauterine pregnancy.

Displacement of the Uterine Cervix

Tilting of the uterine cervix is a very rare form of human obstetrical pathology. M. B. Belkin and I. P. Zhornik (1955), describing displacement of a myomatous uterus, pointed out that tilting occurs most often in the pregnant or myomatous uterus. Displacement may also occur after surgical interference in the region of the lesser pelvis, connected with the processes of adhesion. Sometimes displacement may occur seemingly spontaneously, without any outwardly apparent cause. However, in nearly every case this condition is brought about by external exogenous factors. In 1954, Y. G. Paliy described uterine displacement connected with a podalic version performed for the neglected transverse position of the fetus. In 1949, A. P. Studentsov pointed out that torsion of the uterus in domestic animals—in contrast to human beings—occurred relatively often and had been reported in cows, sheep, goats and carnivorous animals. This pathological condition depends on the peculiarities of the ligamentous apparatus of the uterus of animals and on the changes in the position of the uterus during pregnancy. The concrete causes of uterine torsion, according to Studentsov's data, are sudden and rapid movements of the pregnant animal. In particular this pathological condition occurs in cats after climbing up steep steps, in dogs (working, circus, hunting dogs) after leaps. The clinical picture in animals resembles acute gastroenteritis, in carnivorous animals it resembles an acute abdomen. We were unable to find any data in the literature pertaining to this pathology in wild animals and, particularly, in monkeys.

We observed one case of retroflexion of the uterus to 360°. The monkey, a hamadryad called "Shotlandiya," had a normal delivery one year before her death. The last pregnancy ran a normal course. Two days prior to death (several days before labor was expected to occur), the monkey was removed from her cage for purposes of medical examination and the injection of antimeasles serum. On the following day the animal was very lethargic, there was a sharp drop in blood pressure and body temperature. Within one day the monkey died following increasing symptoms of collapse.

Dissection revealed that the uterus was greatly enlarged, reaching the base of the diaphragm. The walls of the uterus were thinned out and cyanotic, with greatly distended veins located on the surface and resembling sinuses. The uterine appendages were bluish and engorged with blood, the lower segment of the uterus and cervix had turned 360°, so that this entire complex had the appearance

Fig. 103. Displacement of cervix of pregnant uterus. Hamadryad Shotlandiya.

of a thick, twisted braid. A massive blood clot had detached itself from the upper pole of the placenta which was situated at the left edge of the uterine body. The fetal sac was intact; the amniotic fluid contained a large full-term fetus in cephalic presentation (Fig. 103).

We are unable to give a cogent explanation of the mechanism of the uterine retroflexion. The latter occurred not in the course of labor but in the last days of pregnancy. Examination of the abdominal cavity and lesser pelvis revealed no adhesions or pathological phenomena which could have explained the cause of retroflexion. It appears most likely that the examination of the monkey led to alteration of the uterine position, and the turning over of the animal during examination resulted in complete retroflexion of the uterus in its most labile portions—in the cervix and lower segment.

The other clinical features of this condition included all the symptoms of collapse, and depended upon compression of the nerve trunks and plexuses which were so abundant in the parametrial cellular tissue. We have already pointed out that displacement of the pregnant uterus occurs very rarely in the human female. Displacement of the myomatous, pathologically altered uterus is mentioned somewhat more often in the literature.

Displacement of the pregnant uterus in monkeys—as in man—occurs very seldom. This is particuarly interesting to us in connection with the fact that the monkey's usual way of life changes very little during pregnancy. However, despite the great activity of the pregnant monkey, its leaping and sharp changes in the condition of the body, displacement of the uterus does not occur.

Ruptures of the Uterus (Metrorrhexis)

Out of 715 cases of birth in the past six years, we observed three instances of metrorrhexis. In two observations the ruptures occurred in baboons (to 352 births), in one— in a macaque (to 286 births). In both the hamadryad baboons—Kameliya and Bukashka—the ruptures took place approximately according to one mechanism and may therefore be described together. The anamneses of both monkeys indicated several pregnancies, stillbirths and abortions.

These ruptures were clinically characterized by the fact that in the course of protracted labor, after the escape of amniotic fluid, fresh, bright-red blood began to flow. Initial symptoms of collapse caused us to assume internal bleeding, and constituted grounds for the performance of a Caesarian section. During this operation we discovered extensive ruptures in the margin of the lower segment of the uterus with the cervix. In Bukashka the rupture extended from the lower segment to the vagina (Fig. 104). The tissue adjacent to the rupture was diffusely impregnated with blood. The margins were gangrenous. In connection with the state of collapse

Fig. 104. Rupture of uterine cervix. Hamadryad Bukashka.

and beginning symptoms of peritonitis, the animals died soon after the operation. Examination established that the ruptures were caused in both cases by a discrepancy between the size of the caput and the mother's pelvis.

Microscopical examination revealed in the margins of the ruptures massive necroses of the tissues, diffuse impregnation of the latter with erythrocytes, and beginning signs of leukocytic infiltration along the periphery of the necrotic area. The uterine walls in the area of the lower segment contained diffuse infiltrates of round cells and histiocytes, as well as small foci of sclerosis. The given findings were analogous to those observed in ruptures of the human uterus. Ye. I. Belyayev (1938), A. Ye. Blinder (1940), A. I. Galaktionov (1940), V. M. Forshtater (1940), R. M. Ospovat (1940) and others observed in metrorrhexis of the human uterus significant sclerotic and cicatricial changes in the uterine wall, which play a decisive role in the occurrence of ruptures. Analogous changes were discovered by L. L. Libenzen in 1958 in a histological study of fragments of human uterine cervix removed from the margins of ruptures during surgical repair of the latter.

In the third cases—a macaque—the anamnesis indicated two pregnancies and a third pregnancy that terminated in labor at term. However, placental separation did not follow expulsion of the fetus. For three days after parturition there was vaginal bleeding and partial detachment of the placenta. The uterus did not contract completely; the cervix admitted two fingers. Abdominal distention was noted; there was no stool. The monkey died in three days. Dissection disclosed a picture of fibropurulent peritonitis. The uterus was enlarged up to 15 cm in length and 7 cm in width.

The base of the uterus contained perforations large enough to admit the fingertips. The margins of the openings were pulpy and bordered by dirty-gray scraps of tissue; the uterine tissue surrounding the openings, for a distance of 2 to 2.5 cm, was dark brown in color, very flaccid, and bordered at the periphery by a corona of hyperemia. Section showed the tissue to be dull, greenish-gray in color and delimited from the adjacent unaltered areas of the uterus by a red line of demarcation along the periphery. Fragments of the placenta and greenish-yellow membranaceous deposits were observed on the inner surface of the uterus. Placental tissue, impregnated with exudate, had emerged through the openings into the abdominal cavity.

Histological examination of the uterus in the area of the perforations revealed a field of necrosed myometrium bordering the perforation. The zone of necrosis was entirely devoid of nuclei, but contained remaining outlines of muscle fibers and blood vessels filled with thrombotic masses. A fusion of the necrotic masses with leukocytes was noted. At the margin of the necrosis, in the portions of myometrium with normal structure, were seen numerous vessels with lumens filled with obstructing thrombi. A faintly defined leukocytic line of demarcation was observed here.

Thus, the third case was principally distinct from those described above. The first distinction was the fact that the perforation of the uterus occurred not in the course of birth but after birth had taken place. The second distinction was the site of rupture.

In the previously described instances the rupture occurred at the margin of the lower segment and the cervix on the lateral surface. In the last case the rupture occurred at the base of the uterus. Finally, the third distinction consisted in the mechanism of the ruptures. In the first two cases trauma, crushing and necrosis of the tissue were primary; in the third case necrosis was primary, resulting in connection with the retention of the placenta, postpartum endometritis and thrombosis of the uterine blood vessels. These ruptures apparently occur very seldom in man.

Ruptures during birth in the lower segment of the uterus are also rare in man. In 1936, S. K. Mironova pointed out that ruptures in the lower segment of the human uterus during parturition occurred at the rate of 0.05%; B. V. Azletskiy (1939) reported the figure 0.05%. R. M. Ospovat (1940) reported that out of 20,000 deliveries at the obstetrical clinic of a Far-Eastern medical institute during a period of five years he observed seven instances of ruptures of the uterus, constituting 0.03%. M. S. Malinovskiy maintained in 1955 that the rate of uterine ruptures ranged between 0.03 and 0.05% and had not changed for a long period of time. Thus, the described form of pathology is rare in man—approximately ten times as rare as in monkeys. The rate of ruptures in baboons was 0.56%, and in macaques 0.34%. However, ruptures of the uterus in monkeys apparently develop by the same mechanism as in man.

Regarding domestic animals, K. G. Bol' reported in 1938 that uterine ruptures occurred in all domestic mammals. The mechanism of uterine rupture during parturition is probably the same as in man and monkeys. Bol' and A. P. Studentsov pointed out in 1949 that ruptures of the pregnant uterus in parturition occurred as the result of great straining with incorrect positions of the uterus, as well as with sclerotic changes in the uterus due to previous inflammatory processes. These ruptures usually occurred near the uterine cervix.

Extrauterine Pregnancy

Extrauterine pregnancy is common in human pathology. A. I. Petchenko (1954), referring to the data of the obstetrical clinics in Leningrad, pointed out that the rate of extrauterine pregnancy had increased in recent years. In 1912-1915, the rate of extrauterine pregnancy constitute 1.2% of the total number of pregnancies. In 1922-1924, this rate increased to 1.95%. In 1941-1951, it increased to 2.95%.

In the author's opinion, the increase in the rate of recorded extrauterine pregnancies was not connected with an increase in their absolute number, but was explained by improvement in the diagnosis of this pathologic condition.

Analogous figures have been reported by other authors. Nieberle and Kohrs reported in 1954 that extrauterine pregnancy was extremely rare in animals.

Regarding this anomaly in monkeys, we know of only one report—contributed by A. N. Sergeyev in 1939—describing this condition in a M. rhesus. One case of extrauterine pregnancy—in a hamadryad called "Mal'va"—was noted at the monkey-breeding farm in 1937. Mal'va was imported as an adult in 1933, and this was her first pregnancy. The third case was recorded by us in 1954 in a green marmoset called Kashtanka that died suddenly at the age of five years as the result of massive hemorrhage in the abdominal cavity from an eroded fallopian tube. Microscopical examination of the affected tube revealed a deep ingrowth of chorionic villi in the wall of the tube, under the serous lining (Fig. 105).

Thus, during the entire period of existence of the monkey-breeding farm, extrauterine pregnancy was recorded three times out of 1,892 cases of pregnancy, which constitutes 0.15%, and occurred in practically every species of animal kept at the breeding farm—green marmosets, baboons, macaques. The rate of extrauterine pregnancy is significantly smaller in monkeys than in man—approximately 20 times; however, if its rate were counted in each species of monkey, it would remain insignificant for baboons and macaques, but would increase to nearly 1% in green marmosets.

We are unable to form a conclusion as to the reasons for the significant difference between the rate of extrauterine pregnancy in man and monkeys. We can only assume that the latter is connected with the fact that animals—including monkeys—are much less often affected by diseases of the genital organs, which in a large percentage of cases, cause the development of extrauterine pregnancy.

Fig. 105. Photomicrograph. Growth of chorionic villi into wall of uterine tube. Green marmoset Kashtanka. Hematoxylin-eosin stain. Obj. 2, oc. 7.

Inversion of the Uterus

Inversions of the uterus are extremely rare in the obstetrical pathology of man. According to M. I. Ryzhkov, postpartum inversions of the uterus occurred once in 300,000 births. K. K. Skrobanskiy reported in 1946 that uterine inversions occurred once in 400,000 births. According to A. P. Studentsov (1949), inversion of the uterus is not very rare in domestic animals, occurring primarily in cows and goats, less often in horses and other animals with a short umbilical cord or with overstretching of the uterus and flaccidity of its musculature.

Among the monkeys at the breeding farm, during 30 years of its existence, only one case of uterine inversion out of 1,693 births (0.05%) was registered.

Convulsive Seizures in Pregnancy

Convulsive seizures in pregnant female hamadryad baboons, although very common, apparently do not represent a toxemia of pregnancy. Convulsions occur relatively often in animals that are not pregnant, occasionally in males. The greater rate of convulsive seizures in pregnant baboons is probably explained by the fact that pregnancy provokes seizures in baboons that have a strong tendency toward them.

Stillbirth

From 1953 to 1958, the prosectorium of the Institute carried out 95 dissections of stillborn animals. This figure includes the total number of stillbirths at the Institute during this period of time and constitutes 13.4% of the total number of births in this period. In relation to the total number of births correspondingly in each species, stillbirths occurred: in 36 macaques, 12.3%; in 48 baboons, 13.6%; in 11 green marmosets, 14.6%. However, despite the fact that the rate of stillbirth is still very high, a certain decrease was noted from 1953 to 1958 (Table 11).

TABLE 11

DYNAMICS OF STILLBIRTH IN MONKEYS AT BREEDING FARM BETWEEN 1953 AND 1958

Year	*No. of births*	*No. of stillbirths*	*% of stillbirths*
1953	73	12	16.4
1954	106	17	16
1955	120	14	11.6
1956	123	17	13.9
1957	143	18	12.5
1958	141	17	12
Total	706	95	

The most frequent cause of stillbirth is traumatic injury of the mature fetus during parturition, resulting in subdural or even subpial hemorrhage which frequently extends to both hemispheres (Fig. 106). In individual cases there is bone displacement in the fornix of the cranium with considerable crushing of brain matter. Stillbirths connected with trauma were observed by us 26 times—in 13 baboons and 13 green marmosets.

Birth injury was not always limited to brain damage. In some cases the internal organs were injured, with subsequent development of hemorrhage in them, and there was one instance of rupture

Fig. 106. Extravasation of blood in area of pia mater at arch of cerebral hemispheres.

of the liver. In two cases—one premature and one mature fetus, born with breech presentation—rupture of one of the suprarenal glands occurred with extensive destruction of the gland's tissue.

A very rare complication of the normal course of birth was the aspiration of amniotic fluid with subsequent asphyxiation of the fetus. In certain cases birth injury was apparently connected with the large size and unusually great weight of the fetus. These factors brought about the development of weakness of uterine contractions in the mother and, consequently, protracted labor.

In certain cases injury of the fetus with diffuse hemorrhage of the soft tissues of the brain, the meninges, and sometimes with mechanical injury of the brain matter was connected with a face or breech presentation of the fetus. Death of the fetus in either of the given presentations was relatively common. We observed 12 such deaths, eight of which occurred in baboons. Usually, face or breech presentation causes considerable prolongation of labor, which leads to asphyxiation of the fetus.

The pathoanatomical changes in the fetus during birth with face presentation were fairly characteristic and included considerable edema and cyanosis of the soft tissues of the face and of the tongue. The edematous tissue often contained numerous petechial hemorrhages. The latter were observed during microscopical examination in the brain tissue, mainly in the cerebral cortex and brain stem.

Regarding breech presentation, dissection of the fetus revealed in some cases considerable edema of the perineum and particularly of the scrotum. The abdominal cavity sometimes contained a large amount of ascitic fluid. In two cases, histological examination of the brain revealed a few small hemorrhages. In one case extensive hemorrhage had taken place following the rupture of the tentorium cerebelli.

Before moving on to the question of fetal death in connection with prematurity, we should discuss the signs of premature fetuses. The mature monkey newborn is almost entirely covered with thick, long (up to 0.7 cm) hair, dark brown—nearly black—in color. The hair is sparse on the abdomen, face, inner surfaces of the thighs and shoulders. The palms of the hands and soles of the feet are completely devoid of hair. The weight of the newborn varies considerably both in monkeys of different species and within one species. According to the material of our prosectorium, the average weight of the mature newborn baboon was 916 g, varying in individual cases from 840 to 1220 g. The average weight of the M. rhesus newborn was 439 g, with individual variations from 342 to 534 g. There were three exceptions, whose weights were 610, 640 and 700 g. The average weight of the Javanese macaque newborn was 255 g, varying from 235 to 300 g. The average weight of the green marmoset newborn was 392 g, ranging between 307 to 500 g.

The nails of the mature newborn were long and extended somewhat beyond the tips of the fingers. Because of the very delicate gingival mucosa, the frontal incisors were usually visible through the gums, particularly in the upper jaw. Some newborns, particularly the heavy baboons, had partly erupted frontal and—less often—lateral incisors in the upper jaw. Dissection revealed a small amount of fat in the cellular tissue, especially in the epicardium and adrenal glands. The stomach usually contained a small amount of mucus. The lumen of the large intestine was filled with mushy masses that were dark greenish-brown in color.

Fairly often—mainly in baboons (15 cases)—stillbirth was connected with prematurity. The stillbirth of a premature fetus was observed six times in macaques, twice in green marmosets. We judged the degree of prematurity of the stillborn by the weight of

Fig. 107. Left, fetus of hamadryad baboon at term. Right, abortive fetus.

the dead fetus and the degree of development of its hairy coat (Fig. 107). It should be noted that the nails of even the considerably premature fetuses reached the fingertips.

A more or less exact judgment of the term of pregnancy can be made only in baboons because of their very pronounced sexual cycle. Because of this, it was possible in certain cases to establish the species and weight of the newborn that corresponded to the period of pregnancy in the baboons. Unfortunately, we were unable to collect material on the early periods of fetal development because early abortions, on the one hand, seldom occur and, on the other hand, the fetus and amniotic membranes are usually eaten by the monkeys. We can only say that when the baboon gives birth three months before term (the general length of pregnancy in baboons is 5½ months), the newborn is completely devoid of a hairy coat. The weight of the fetuses varied greatly in approximately the same periods of pregnancy. In the third month of pregnancy the weight of the fetus varied from 210 to 600 g; at 4½ to 5½ months the weight of the fetus ranged from 436 to 700 g. Pilosis appeared in the third month and increased in proportion to the increase in body weight. It began in the occipital region, then progressed to the shoulders and end of the tail. In fetuses weighing 300-350 g, the back underwent pilosis; fetuses weighing 350-400 g (which corresponds approximately to the period of the fourth to fifth month of pregnancy) were completely covered with short, black fur resembling plush. All the tissues of the premature fetus were distinguished by delicacy and a small amount of cellular tissue which never contained fat. The brain had a very soft, pulpy consistency.

There is very little available data pertaining to the external signs of prematurity in the M. rhesus. We observed in fetuses weighing 170-190 g nearly a complete absence of hair. Only the head—mainly the occipital region—contained sparse, short, light-colored hairs. The fur of the premature fetus weighing 280 g was considerably shorter than usual. The abdomen, chest and lateral surfaces of the torso were completely devoid of hair. The eyelashes were clearly visible.

In fetuses with a large period of prematurity (in M. rhesus monkeys and baboons) attention was drawn to the excessive mobility in all the joints of the upper and lower extremities. The bones of the cranium were also easily displaced in relation to each other, being united only by a thin connective-tissue membrane. This soft union of the cranial bones was unchanged up to the end of the intrauterine period; strong union did not take place in the mature monkey fetus. The fontanels of the cranium were indefinable, in contrast to those of the human newborn.

The brain tissue in premature and mature stillborn offspring revealed—sometimes by macroscopical examination, but principally by histological study—hemorrhages of various size, analogous to the picture observed in the death of newborn human infants

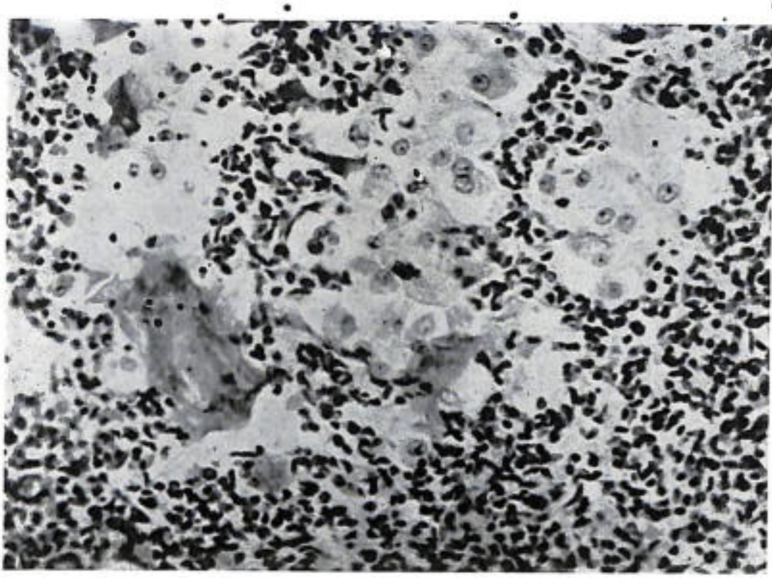


Fig. 108. Photomicrograph. Phagocytes in lumens of alveoli of stillborn fetuses. Resorption of protein masses in alveoli by macrophages. Hematoxylin-eosin stain. Obj. 40, oc. 7.

(S. S. Vayl', 1949, 1950; Gutner, 1945; Grontoft, 1953; Saunders, 1953, etc.).

Since in the majority of cases of the stillbirths investigated by us, the death of the fetus occurred in the process of birth, the lungs in most of the animals were not fused. The oval opening of the heart was always open. Microscopical examination revealed dense proteic masses that had undergone phagocytosis by macrophages (Fig. 108) in the lumens of the alveoli in the lungs of all the stillborn offspring, most frequently in fetuses that had not matured completely. In some areas the lumens of the alveoli were completely filled with macrophages, in others with semi-lunar cells compactly filling up the alveoli. The lumens of the bronchi were free most of the time; however, in individual cases they, also, were filled with rose-colored masses containing an admixture of faintly-stained cellular elements. The described phenomenon of phagocytosis of the proteic masses that filled the alveoli of the nonfused lung was apparently a physiological phenomenon common in man, and proved, in itself, the preparation of pulmonary tissue to the new function of respiration which was absent in the intrauterine existence of the fetus.

Death of the fetus resulting from intrauterine sepsis occurred very rarely in our material; it was observed twice in hamadryad baboons. In both these observations, hemolytic streptococci—pathogenic for white mice—were disseminated from all the internal organs and the blood of the stillborn fetuses. The internal organs revealed small hemorrhages which were more pronounced under the serous membranes. It is necessary to point out that no infectious or septic diseases were observed in the mother during this period. Intrauterine death of the fetus resulting from tetanus, and the subsequent expulsion of a macerated fetus were noted in one baboon. In part of the cases we were unable to determine the cause of stillbirth, and a thorough pathoanatomical examination of the fetus did not enable us to establish any changes which might have been considered causative factors. We also failed to find any diseases in the mother that might have been the cause of stillbirth.

It is a known fact that death of the fetus in the process of birth may result from prolapse of the umbilical cord and its compression during the passage of the head through the bony ring of the pelvis. Since parturition in monkeys usually takes place at night (I. S. Yeligulashvili, 1957), it is natural that obstetrical pathology such as prolapse of the umbilical cord or premature separation of the placenta could easily be missed. In studying the charts of the development of the female monkeys in which stillbirths had been established, we were able to establish the cause of stillbirth as prolapse of the umbilical cord in only one case. In one case the cause of stillbirth was premature separation of the placenta.

On the whole, we have touched upon only the direct causes of stillbirth. A number of factors have been pointed out by other researchers who have studied this problem. I. S. Yeligulashvili (1957), L. G. Voronin and co-authors (1948) and M. A. Grigoliya (1957), after investigating the causes of stillbirths and abortions at the Sukhumi monkey-breeding farm, reported a connection between stillbirth and a regular succession of pregnancies. Voronin and Yeligulashvili pointed out that the rate of unfavorably ending pregnancies was quite high in primiparas, but decreases with subsequent pregnancies. Grigoliya noted that the rate of stillbirths—decreasing after the first pregnancies—increased anew in later pregnancies. These authors pointed out that the number of unfavorable pregnancies was greater in baboons than in rhesus monkeys; the rate of stillbirth was higher in the winter than in the summer; parturition had a more favorable outcome in voleries, or monkey houses, than in cages.

The above information is of interest from the standpoint of practical measures of breeding monkeys at the monkey-breeding farm, but it does not disclose the basic causes and mechanisms of stillbirth.

We failed to note a substantial predominance of stillbirths in baboons over macaques (13.6% in the first, 12.3% in the second). A slightly higher rate of stillbirths was noted in green marmosets (14.6%), however. With the general tendency in recent years of the rate of stillbirths to decrease (Table 11), the number of stillbirths in green marmosets did not decrease and even increased somewhat. The reduction in the stillbirth rate was brought about by the decreased rate of stillbirths in baboons.

The higher stillbirth rate in baboons, compared to macaques, according to Voronin and his co-workers (1948), was not the result of tetanic seizures that occur frequently in baboons. The authors pointed out that most of the females with tetanus had normal pregnancies and gave birth to viable and healthy offspring. Attention was directed to the fact that the principal mass of stillborn were mature fetuses that died in the course of parturition.

It seems to us that the basic cause of the high stillbirth rate is the not fully adequate living conditions of the monkeys—even at the breeding farm. This is confirmed by the fact that in voleries (under conditions corresponding more closely to natural conditions) the incidence of stillbirth is lower than in cages. An important role in disturbance of the mechanism of birth is played by the constant limitation of movement, adiposity and weakness of the musculature of the females, particularly in those that are kept in cages. The latter considerably disturbs the process of parturition and is often the cause of protracted labor in connection with weakening of muscular action, which leads to subsequent asphyxiation of the fetus. Weak muscular activity may also lead to incorrect positions and trauma of the fetus. This hypothesis was also supported by the observations of Grigoliya in 1957, which established the fact that the rate of complications of pregnancy and birth was considerably lower in the monkeys imported to Sukhumi than in those born in Sukhumi.

Abortions

The number of abortions in monkeys up to the present time is still quite large. Out of 775 pregnancies in baboons, macaques and green marmosets between 1953 and 1958, inclusively, there were 69 abortions, which constitutes 8.9% of the total number of pregnancies in this period. However, analysis of the changes in the rate of abortions during the past six years shows a considerable decrease in their number (Table 12).

TABLE 12

DYNAMICS OF ABORTIONS IN MONKEYS AT THE BREEDING FARM FROM 1953 TO 1958

Year	*No. of pregnancies in current year*	*No. of abortions*	*No. of abortions in %*
1953	85	12	14.1
1954	119	13	10.9
1955	132	12	9.1
1956	132	9	6.8
1957	159	16	10
1958	148	7	4.6
Total	775	69	

It was established that the rise in the number of abortions in 1957, connected with the increase in their number in macaques, was explained by the fact that they occurred in female monkeys that had been under harsh experimentation not long before conception: the experiments included roentgenray irradiation in large doses. In two monkeys—Espa and Fauna—that died as the result of the experiments, microscopical examination of the uterus revealed widespread endometriosis with squamous-cell metaplasia of the endometrial growths in the uterine wall. The possibility is not excluded that abortion in these cases was connected with endometriosis.

Thus, abortions and stillbirths are the most common phenomena in the pathology of pregnancy. Other pathology, e.g., ruptures and displacement of the uterus, extrauterine pregnancy, eversion of the uterus, is interesting from the standpoint of the mechanisms of development, as well as similarities with and distinctions from analogous pathologic phenomena in man; however, it has no practical significance in the reproduction of monkeys under the conditions at the breeding farm. There is practical significance only in stillbirths and abortions, which represent the basic mass of the pathology. Extremely interesting from this point of view are the dynamics of abortions and stillbirths in the course of recent years. We have already pointed out that the latter have a slight tendency to decrease, which has been noticeable during the past six years. However, although there was a very significant decrease in the number of abortions, the decrease in the number of stillbirths was much smaller. The latter is easily explained. A decrease in the abortion rate may be realized by observing a number of zootechnical rules— in particular, avoiding the capture of animals in the early periods of pregnancy, providing the animals with an adequate diet, etc. These measures would ensure the normal development of the fetus and a favorable outcome of pregnancy. In the majority of cases, stillbirth occurs during parturition as the result of the incorrect position of the fetus, protracted labor due to weakness of the musculature, especially prelum abdominale, considerable adiposity, etc.

We believe that stillbirth in monkeys occurs much less often in nature, and that the most correct course of action toward reducing the stillbirth rate is to create conditions for the animals that are closest to the natural conditions: first of all, by keeping the animals in sufficiently large compartments—preferably in voleries, providing the animals sufficient freedom of movement.

Twin Birth

We have found only solitary indications in the literature regarding the possibility of twin delivery in monkeys. In 1937, Hamerton described twin birth in a macaque, in which the parturient monkey died. In 1954, Stott described the birth of twins in capuchin monkeys, in which both the mother and offspring felt well after delivery. In 1941, N. P. Tsvetayeva reported a twin birth in a chimpanzee, in which the mother died of postpartum eclampsia.

Twin deliveries also occurred in monkeys at the Sukhumi monkey-breeding farm. Two such deliveries were registered out of a total of 837 deliveries in baboons (this figure includes normal and stillbirths). There were also two cases of twin births registered out of 745 deliveries in macaques. The first twin birth, registered in 1929, occurred in a female baboon called Tamara, a primipara, who gave birth prematurely to two stillborn offspring. In the next four pregnancies this animal gave birth to a single offspring each time. The second instance of twin birth in a baboon was recorded in 1953 in a female called Barabul'ka. The twin birth occurred in the ninth pregnancy. The preceding eight pregnancies terminated in single deliveries. Both offspring in the multiple birth were viable and healthy. Since the mother was unable to nurse both offspring, the latter were taken from her and placed in a crib where they were artificially fed.

In 1947, a twin delivery was registered for a macaque called Onega. It was the animal's third pregnancy; both offspring were viable, healthy, and were nursed by the mother. In the subsequent five pregnancies only single offspring were born. The second instance of twin birth in macaques was registered in February 1959 for a monkey that was brought to the monkey breeding farm two years before at approximately two years of age and had given birth at the farm for the first time. In this case, the fetuses were already dead when labor began; one of the newborn was a monster.

It is necessary to point out that in the baboons and in the first macaque, pregnancy resulted from mating them with different male monkeys.

The birth of twins occurs in macaques in approximately 0.26% of all deliveries; in baboons, in 0.23% of the cases. Premature labor may occur in twin pregnancies; however, delivery at term of both offspring and the delivery of viable offspring is possible. The feeding of both offspring simultaneously is possible; besides the feeding of two offspring by Onega, we observed at M.lapunder feeding two infant monkeys—her own, and one belonging to a dead monkey.

DEVELOPMENTAL DEFECTS AND MONSTROSITY

Various anomalies of development are widespread in man and animals. According to data reported in 1955 by Coffey and Jessop, who observed 12,550 newborn children, congenital anomalies occurred in 1.7% of the cases.

The reported causes of defective development include diseases of the mother's genital organs, infectious diseases contracted during pregnancy, avitaminosis during pregnancy, the effects of radiation, and many other factors. The only information known to us pertaining to developmental defects and monstrosity in monkeys is contained in the work of Schultz (1938) concerning experiments conducted in Siam and Borneo in the study of monkeys in their natural habitats. After studying several hundreds of killed animals, a large part of which consisted of gibbons, the researchers discovered a significant number of monsters. Brachydactylia—particularly of the toes—was discovered in many animals. Frequent discoveries were palmature and an excessive number of fingers. Spina bifida was observed in seven gibbons. Of course, these very valuable observations still cannot provide us a more or less complete conception of the nature and rate of monstrosity in monkeys. In 1955, Coffey and Jessop emphasized that 36% of the defective human offspring are stillborn. This phenomenon is apparently analogous in monkeys. Of course, this does not include a significant number of more serious developmental defects. Part of the viable malformed infants with serious defects die soon after birth.

Among the stillborn and newborn offspring of monkeys at the Sukhumi monkey-breeding farm between 1952 and 1958, the overwhelming majority of congenital malformations were defects of the cardiovascular system. In individual cases cardiovascular defects were combined with other developmental anomalies. Considering the fact that the malformations usually involved the heart or the major blood vessels, we shall describe—with corresponding grouping of defective cardiac development—developmental defects of the major blood vessels and the combined irregularities of development of the heart and major blood vessels, as well as other developmental defects.

Altogether, we observed seven cases of congenital defects of the cardiovascular system. In two cases we discovered aplasia of the interventricular septum. In essence, the singular irregularities of development of the heart were settled by defects of the interventricular septum. In one case, aplasia of the interventricular septum was observed in a M.rhesus that died at the age of three years. The second case of aplasia of the interventricular septum was discovered in a stillborn M.rhesus whose death was caused by extensive hemorrhage in the pia mater. One animal that had already survived for three years was diagnosed as having a cardiac defect as early as several months after birth. Apart from the murmurs in the heart, a pronounced cyanosis was noted. Despite the fact that the offspring survived to three years of age, it is still necessary to point to its lowered vital activity. Death occurred two days after a minor operation in which an attempt was made to introduce a probe into the ulnar vein.

The pathoanatomical picture of the aplasia of the interventricular septum was characterized by marked hypertrophy of the right ventricle of the heart and by congestive hyperemia of the internal organs. The opening in the interventricular septum was located in its upper portion and was no larger than 0.5 cm in diameter. The hypertrophy of the right ventricle of the heart reached considerable proportions; the thickness of its wall exceeded the thickness of the wall of the left ventricle of the heart. Around the opening of the given ventricle, along the upper semicircumference, was a duplicature of endocardium, forming a likeness of a valve (Fig. 109).

There were three instances of defective development of the major blood vessels. The first of them, involving aplasia of the patent ductus arteriosus (Botallo's duct) was observed in a stillborn M.rhesus. Directly above the ostium of the aorta, approximately 0.6 cm higher than the free margin of the similunar valves, a thick vascular trunk branched off from the aorta, connecting the aorta with the pulmonary artery. The width of the patent ductus arteriosus was approximately equal to the width of the trunk of the pulmonary artery. There was considerable hypertrophy of the muscle of the right ventricle of the heart, equal in thickness to the left ventricle, as well as a moderate hypertrophy of the right atrium cordis.

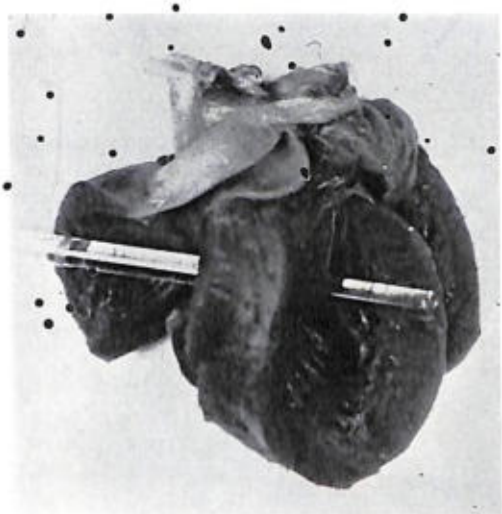


Fig. 109. Aplasia of interventricular septum. M. rhesus Mops.

The second case—a stillborn hamadryad baboon—was also, in essence, an aplasia of the patent ductus arteriosus, although it possessed certain peculiarities and distinctions from the preceding one. The considerable thickness of the patent ductus arteriosus created the impression that the pulmonary artery, branching off into two trunks to the lungs, then merged with the aorta as one common trunk. This impression was also contributed to by the fact that the aorta, proceeding from the arch into the thoracic region, also thinned out somewhat, becoming a patent ductus arteriosus. There was defective development also of the valves of the aorta and pulmonary artery. The latter had four incorrectly formed valves that represented not pockets but bright translucent buttons. The aorta, in turn, had only two valves, instead of three. Both coronary vessels lead from under one of these valves.

The third case concerned stenosis of the pulmonary artery in an imported M.rhesus monkey approximately one and one-half years of age. The animal died in connection with chronic colitis and a phlegmonous haunch resulting from the injection of medicinal substances; apparently, the latter only contribute toward the development of cardiac insufficiency which was the direct cause of

Fig. 110. Projection of aorta and pulmonary artery from right ventricle. Stillborn hamadryad baboon.

death. Dissection revealed a marked hypertrophy and dilatation of the right atrium cordis and ventricle of the heart, congestive hyperemia of the internal organs, ascites and hydropericarditis. Examination of the heart and major blood vessels showed that the cause of the hypertrophy of the right side of the heart was contraction of the pulmonary artery directly above the free margin of the valves.

In two cases there was a combination of defective cardiac development with defective development of the major blood vessels. In both of these instances there was communication through the opening in the interventricular septum of the cavities of the right and left ventricles. In one of these observations, in a stillborn hamadryad baboon, the defect of the interventricular septum was combined with the aorta issuing from the right ventricle of the heart. The ostium of the aorta was located next to the ostium of the pulmonary artery and was separated from the latter by a low fold of endocardium (Fig. 110). The aorta was in communication with the cavity of the left ventricle only through the opening in the interventricular septum. The valves of the aorta and pulmonary artery were markedly contracted, thickened, and had a cartilaginous consistency. The patent ductus arteriosus was preserved. The wall of the right ventricle represented a thickened roof of the heart, and was rounded. It must be assumed that this considerable degree of defectiveness in the development of the cardiovascular system renders the fetus nonviable.

In this case, besides the above-mentioned defects of the heart and blood vessels, there were other anomalies in the form of clearly pronounced lobulation of the kidneys, as well as the presence of a sixth finger on both upper extremities. There was palmature of the second and third toes of both lower extremities.

Still another instance of combined malformation of the interventricular septum and the major blood vessels was observed in a hamadryad that died of pneumonia at the age of seven days. The mitral valve in the left ventricle lacked an anterior cusp, the ostium of the aorta was considerably constricted. The cavities of both ventricles maintained contact with each other through an opening in the interventricular septum. In the right ventricle there was complete adherence of the middle cusp of the tricuspid valve to the wall of the ventricle. The heart was considerably enlarged due to marked hypertrophy of the right ventricle (the wall was 1.5 cm thick) and a certain dilatation of the ventricle. The pulmonary artery was greatly dilated. The left ventricle was very small, resembling an appendage of the very large right ventricle.

In addition to the congenital defects of the heart and major blood vessels, we also observed other defects that occurred in solitary cases. They included defects that were fully compatible with viability, e.g., palmature of the hands and feet. In the lungs of an adult baboon we observed multiple hemorrhagic cysts which we defined as developmental defects of the pulmonary cardiovascular system. In one monkey we discovered multiple cysts in the white matter of the brain, which were also presumed to be developmental defects.

Finally, we observed a very pronounced multiple monstrosity in a prematurely born twin M.rhesus. One of the twins had no defects at all and weighed 130 g; the other twin was a nonviable monster weeighing 215 g. Instead of a head, it had a cutaneous sac with a funnel-shaped retraction on the anterior surface, corresponding to the oral cavity. On the lateral surfaces were two cutaneous folds resembling the external ears. The cephalic sac extended into a shapeless, saclike torso, separated from the head only by a cutaneous fold. The umbilical cord issued from the anterior surface of the torso; below the cord, along the median line, was a cleft in the skin 1.5 cm long and 1 cm wide, through which the peritoneum with its blood vessels were visible. Situated on the anterior surface of the lower portion of the torso was the scrotum, markedly edematous, with the glans penis issuing from its center. The tail of the monster was short and thick; under it was the anal orifice. The extremities were short, thick, shapeless, and markedly edematous. There were no hands on the upper extremities, the latter terminating with boneless processes. The lower extremities contained creases at the knee joints, and feet with clearly defined soles. The left foot contained four deformed toes—one with a nail; the right foot contained two toes, one of which also had a nail. The subcutaneous cellular tissue was considerably thickened because of edema, and appeared gelatinous.

Removal of the skin in the region of the cephalic sac revealed a small cranium—approximately three times smaller than usual at that age. The vault of the skull was formed by a fibrous lamina, thin and very pliable. In the area of the facial skeleton were orbital cavities and a small rudiment of the mouth lined with mucous membrane. The pharynx was blind-ended, the esophagus could not be found. On opening the thorax, it was found empty: fine films were defined at the usual site of the lungs. There was no heart; at the level where the cervical vertebrae join the thoracic vertebrae was a small thin-walled muscular sac approximately 3 mm in diameter and attached to a large blood vessel which, in turn, branched out into subclavian blood vessels, blood vessels at the upper extremities and head, etc. In the abdominal cavity this blood vessel continued to the lower extremities, branching out along the way into small vessels leading to the kidneys and intestines. The liver was not found in the abdominal cavity. The kidneys were situated in the proper place; above them were located large adrenal glands that were triangular in shape. In the upper left half of the abdomen was a small stomach—a sac—changing into the small intestine. The latter changed into the cecum, becoming the beginning of the large intestine. The large and small intestines were situated in one mesentery. The spinal canal was not dissected; we were therefore unable to determine the presence or degree of development of the spinal cord. However, we discovered large nerve trunks in the extremities (at the usual sites). The cerebrum was very small, comprised almost entirely of the parietal lobes, sharply delimited from rudiments of the frontal lobes. The cerebellum was also very small, from *vermis cerebellum*, more normally developed, the "cerebellar hemispheres" led in the form of two symmetrical leaflets of brain tissue. The brain did not occupy the greater part of the cranium; the space between them contained fluid.

Many suppositions may be mentioned regarding the cause of monstrosity in the given case. We believe it highly probable that a connection exists between the development of monstrosity and prolonged, almost incessantly recurring dysentery in the pregnant monkey, as well as the repeated administration of massive doses of various antibiotics.

It should be emphasized that M. Grigoliya's suggestion that the highest rate of monstrosity occurred among offspring of hypertensive female monkeys was not confirmed by our material: out of eight monsters, only in one case did the mother have hypertension.

We will not presume in this chapter to discuss the causes of monstrosity in monkeys in general, and in our observations in particular. We do not have sufficient material for this purpose. At the same time, we will permit ourselves to express the supposition that the development of monstrosity in monkeys at the breeding farm was to some degree connected with avitaminoses, and in particular, with a deficiency of vitamin A. An interrelation between the latter and monstrosity was mentioned by Wilson, Roth and Warkany (1953), who obtained convincing experimental confirmation of their hypothesis. As regards vitamin-A deficiency, we mentioned our supposition of its influence in the discussion of hyperkeratosis of the vaginal mucosa.

We observed monstrosity in animals that were born at the breeding farm and in those that had been imported. Monsters occurred in all the species of animals that comprised—to all practical purposes—the herd at the breeding farm.

The birth rate of anomalous offspring among monkeys, according to our data, constituted 0.48%. We were unable to compare the birth rate of monsters at the breeding farm with the birth rate of monsters in nature. Nevertheless, the brief report by Schultz in 1938 permits the assumption that monstrosity occurred no more often at the monkey-breeding farm than in nature.

BILIARY CALCULI, CHOLECYSTITIS

Biliary calculi occur in horses, cattle (largely in old animals) and fairly seldom in other animals and birds (K. G. Bol' and B. K. Bol'). Cholelithiasis in monkeys was described by Hamerton in 1931; the disease was discovered in a green marmoset that was affected by cholecystitis and died of obstruction of the common bile duct by calculi. Gallstones in farm animals are usually calcic or are composed of pigment.

Biliary calculi containing cholesterol are extremely rare in animals (K. G. and B. K. Bol').

In the dissections of monkeys that died of various causes at the Sukhumi monkey-breeding farm, an investigation was made of the content of the gallbladder and its mucosa. It was established that the bile was not homogenous in all cases. Occasionally—in 14 cases—the bile revealed very fine (the size of semolina or finer) inclusions of semi-soft consistency. These grains varied in appearance: in nine cases they were dark-green—almost black—clumps; in five cases, light-yellow, slightly glossy particles were suspended in the bile.

The above-mentioned monkeys included 11 macaques, two baboons and one gelada. Eight of the macaques were young animals (1½ to 2 years) that were brought to the breeding farm in 1955-1958. The remaining monkeys were born at the breeding farm and died at the age of 5 to 20 years. The gelada was imported in 1948 and died at approximately nine years of age. The animals died of various causes, i.e., during labor, dysentery, malignant neoplasms; two monkeys died of radiation disease.

The mucosa of the gallbladder was unaltered in all 14 cases. In four adult monkeys of this group, that died at the ages of 8, 9, and 20 years, changes that were characteristic for one or another disease were accompanied by atherosclerotic patches in the aorta.

In addition to the above-mentioned findings, large calculi up to 0.7 cm in diameter were discovered in the opened gallbladders of five animals: Livan, a green marmoset 8½ years of age;

Fig. 111. Faceted calculi in gallbladder. Green marmoset Livan.

Ona, a green marmoset 12 years of age; Vasilek, Anis and Kuznechik, three hamadryad baboons 20, 8, and 7 years of age, respectively. The calculi differed in external appearance. In the marmosets the lumen of the gallbladder was entirely filled with large, solid, faceted calculi which were greenish-yellow in color. Section of the stones (Fig. 111) showed them to have a crystalline radial structure. Chemical analysis established a 77% cholesterol and 0.28% calcium content of the calculi. The gallbladder also contained a small amount of bile which was light yellow in color. The calculi in the baboons were rounded, some had the appearance of mulberries.

The stones varied in size from 0.1 to 0.5 cm in diameter and were light gray—almost white—in color. The gallbladders of the different animals contained two to eight stones. Chemical analysis established a 65% cholesterol and 0.35% calcium content of the calculi.

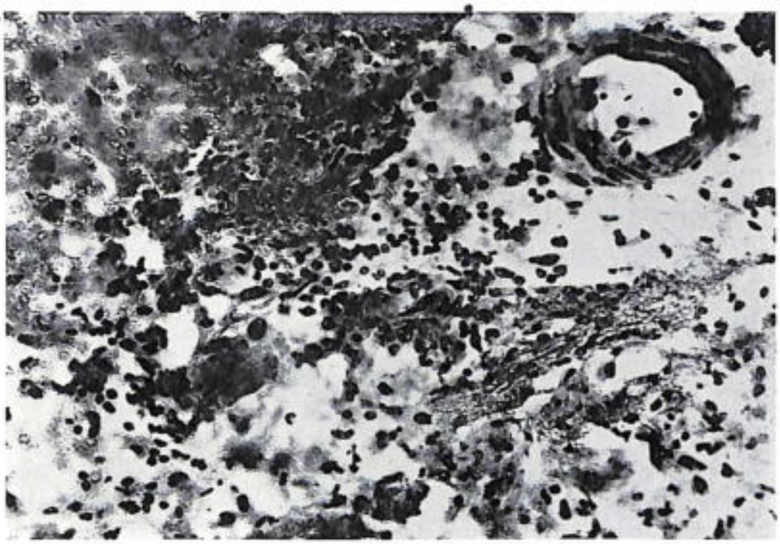


Fig. 112. Photomicrograph. Edema, round-cell infiltration and extravasation of blood into wall of gallbladder in calculous cholecystitis. Hematoxylin-eosin stain. Obj. 20, oc. 10.

In two monkeys—Ona and Kuznechik—neither macroscopical nor microscopical examination of the gallbladder revealed any changes. In the other three animals, however, the gallbladder was greatly distended, and its wall—particularly in the monkey Vasilek—revealed hemorrhages of different sizes. Histological examination revealed thickening of the wall of the gallbladder in connection with the development in it of collagenic tissue and marked edema. Here and there the wall was pierced with fresh hemorrhages (Fig. 112). There was moderate infiltration of the tissue of the gallbladder wall, mainly with lymphocytic and histiocytic elements. Leukocytes and plasmatic cells were seen on rare occasions.

In addition to the changes in the gallbladder, atherosclerotic patches of different sizes were discovered in the aortas of three of the five monkeys.

Most of the animals in which calculi were discovered in the gallbladder were killed in acute experiments. One monkey died of dysentery and only one monkey's (Vasilek) death was directly caused by cholelithiasis. In this case, a calculus from the common bile duct penetrated into the pancreatic duct and, having caused its obstruction, led to the autolytic liquefaction of the glandular tissue. In addition to necroses and extensive hemorrhages in the pancreas, multiple necroses were observed in the omentum and in the cellular tissue of the left kidney. The liver contained round-celled perivascular infiltrates.

As mentioned above, all five animals were full-grown. They had lived at the breeding farm for a long time (7-20 years), during which period they had been kept in cages.

The given data indicates that cholelithiasis in monkeys is not a frequent phenomenon. Apparently, calculi may form only after prolonged captivity at the breeding farm. It must be assumed that the confinement of the animals in cages also contributed toward the development of the given process. The formation of calculi in the gallbladder was sometimes accompanied by an inflammatory process in its wall. Disturbance of the cholesterol metabolism in the majority of the above-mentioned animals was manifested not only in the formation of biliary calculi, but also in the development of atherosclerosis—a relatively rare phenomenon in monkeys at the breeding farm. The fine granules of cholesterol and the concentration of bile in the form of deeply stained fine clumps were seen somewhat more often than calculi. In distinction from the latter, they were often found in newly-imported young monkeys.

Thus, the formation of calculi in the gallbladders of monkeys was distinguished from this process in farm animals by the composition of the concretions formed. In distinction from them, the calculi in monkeys were composed mainly of cholesterol. We did not observe the development of cholecystitis without the formation of concretions; it was manifested to an insignificant degree and, apparently, was secondary.

RICKETS

Rickets is widely known in man and animals. A comparative study of the pathomorphological manifestation of rickets shows that the morphogenesis of this disease and the pathological pictures of its developed forms are essentially the same in man and animals. They consist in disturbance of endochondral ossification, copious formation of osteoid substance, disappearance of the zone of preliminary calcification of the cartilage. Closely interlocking with this disease are fibrous osteodystrophy and osteomalacia, which rarely occur in man, but are comparatively common in animals. As I. V. Davydovskiy pointed out in 1958, these diseases have a pathogenic kinship.

Rickets occurs in every species of domestic mammal and bird, but especially frequently affects chicks, puppies and young pigs (K. G. and B. K. Bol', 1954). Among wild animals, N. P. Tsvetayeva described this disease in the llama, tiger cubs, the Central-Asiatic sheep Ovis ammon, common goats, squirrels and many other animals. She also described rickets in young Australian ostriches, which caused the death of a large number of these animals at the Moscow Zoo in 1937. The disease ran a severe course in young ostriches, and was characterized by curvature of the bones and polyarthritis.

Rickets, osteomalacia and fibrous osteitis occurring in monkeys are widely known from numerous reports by various authors: Todd, 1913; Corson-White, 1922; Khel'ner, 1927; Hamerton, 1930, 1932, 1933, 1935, 1937, 1939, 1942; Stadie, 1930; Doberstein, 1936; Hill, 1951, and others. In recent years the mass occurrence of rickets in the monkeys at the London Zoological Park was not looked upon in distinction from that of previous years, when a very severe form of rickets affected large groups of animals at the same time (Hamerton, 1937, 1939). The most recent description of rickets in a monkey was written by Hill in 1951.

In our dissections of young monkeys that had been raised for a long period of time in the cribs of the breeding farm, we repeatedly noted skeletal changes which could have been considered sequela of rickets. We found no analogous changes in the animals that had been fed by the mother. We will describe two cases of rickets in young baboons–the anubis Misa and the hamadryad Venta–that were placed in cribs on artificial feeding, and remained there until they died. The first animal died at the age of six months, the second died at the age of one year. Both animals were

Fig. 113. Curvature of shin bones. Hamadryad Misa.

ill during the entire period of their confinement in the cribs: one monkey was ill for a long period of time with pneumonia; the other with pneumonia and dysentery. From the age of six months, Venta was observed by the physicians of the monkey clinic to have seizures of the spasmophilic type.

Misa died of penumonia and Venta of traumatic hemorrhage in the meninges during the period of spasmophilic seizure. Dissection of the monkeys revealed monotypic changes in the skeletal system: gonycampsis (Fig. 113), thickening of the carpus, moniliform thickening of the ribs in the region of the anterior epiphyses. Misa also had a thoracic deformity—"chicken breast"—and a considerable spinal kyphosis.

Microscopical examination revealed a rather characteristic and monotypic picture. There was marked disturbance of the endochondral ossification in the anterior epiphyses of the ribs, low-

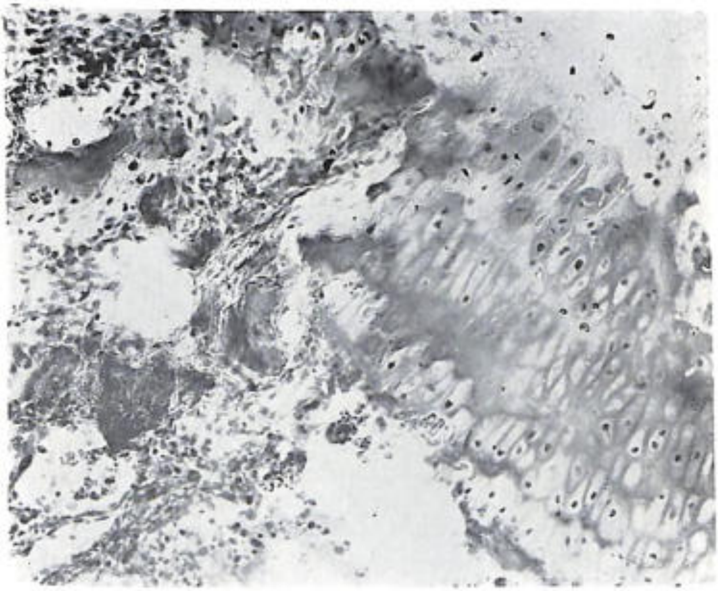


Fig. 114. Photomicrograph. Protuberance of cartilaginous tissue, penetrating far into bone-marrow tissue. Hamadryad Misa. Obj. 8, oc. 7.

er epiphyses of the haunch, epiphyses of the tibia and in the anterior epiphyses of the radial bones. The line of endochondral ossification was irregular, serrated, seemingly corroded.

Growth of the cartilage was noted, with the formation of cartilaginous processes that penetrated far into the osteoid or into the bony tissue. The areas of cartilage directly adjoining the line of endochondral ossification revealed rather extensive vascularization of the cartilage, with engorgement of the newly-formed vessels with erythrocytes. Intensive formation of osteoid tissue was noted in the epiphyseal cartilage; there was no preliminary calcification of the cartilage (Fig. 114). Only individual, small areas of cartilaginous tissue bordered with the bony tissue, and it was in these areas that islets of bony tissue were seen to penetrate into the cartilaginous. An analogous observation was the penetration of cartilagious tissue into the adjacent osteoid or bony tissue and a moderate endosteal formation of osteoid tissue.

In the region of the metaphyses there was evidence of osteosclerosis, as well as the transformation of active bone marrow into fibroreticular tissues. Progressive anemia was observed in the first animal; prior to its death, the erythrocyte count was 2,200,000 per 1 mm^3 blood. Evidences of anemia, though not as pronounced, were also discovered in the second animal. Thus, the picture we observed was very similar to that observed in human rickets, from the standpoint of both the causes of development and morphological manifestation. It should be emphasized again that the development of rickets in young monkeys occurs correlatively in the same age groups as in man, and is connected, as it frequently is in man, with alimentary factor—in the given case, with artificial feeding.

Venta's spasmophilic seizures were apparently connected with a disturbance in calcium metabolism, which, as we know, is sometimes observed in rickets in connection with hypocalcemia.

CONCLUSION

According to the materials of the Sukhumi monkey-breeding farm, the most common diseases of monkeys were infectious diseases. However, as it was pointed out, the nosologic aspect of the diseases of the newly-imported animals and the animals that had been at the breeding farm for a long period of time was essentially different. In the former (except for mild parasitic diseases), three forms of illness figured on the whole: dysentery, pneumonia, tuberculosis. In the latter, there was a considerably larger number of disease forms, some of which were characteristic for man. The general impression was created that most of the diseases that we observed in the monkeys resulted from the close contact of the animals with human beings. The latter was connected not only with the exposure of the monkeys to a number of infectious agents but also with the fact that the conditions imposed on the animals were inadequate for their existence. The exception, apparently, were the parasitic diseases, particularly tick disease of the lungs, the pathomorphological manifestations of which attested to the significant remoteness of the process, occurring also among the newly-imported animals. The complete compensation by the organism in the given diseases, despite the extensive involvement of the lungs that sometimes occurred, attested to the fact that the monkey organism was quite adapted to tick parasitism.

The literature contains no data whatever concerning the fact that the infectious diseases observed by us also occur in monkeys in their natural habitats. Also, we cannot overlook the possibility of animals contracting infections through close contact with human beings. Apparently, conditions exist in India where monkeys, being "sacred" animals, are not destroyed, and come in contact with man on a rather wide scale. Infections, in turn, creates conditions for the spread of the infectious agents in an area where animals do not come in contact with man. However, we by no means consider that diarrhea which is caused by an infectious agent in the monkey's natural habitat leads to the development of diseases such as tuberculosis or dysentery. We believe, and we have attempted to demonstrate, that the resistance of monkeys to "human" infections is quite high under living conditions that have maximal similarity to their living conditions in nature.

Our analysis, as well as material in the literature, indicate that the invasion of the monkey's organism by a pathogenic agent is not in itself sufficient to produce the corresponding infectious disease in the animals. Actually, various dysentery agents are widespread among the monkeys at the monkey-breeding farm. However, despite the wide distribution of dysentery carriers, clinically manifested cases of dysentery occurred incomparably less often. This fact was indicated in all the researches in dysentery conducted at the Sukhumi monkey-breeding farm. The study of the incidences of this disease indicated that among the basic herd at the breeding farm (in animals that had undergone a period of adaptation and acclimatization), clinically manifested cases of dysentery were very rare, occurring most often in the animals that had just recently been brought to the breeding farm. In a number of cases, even intensive antibiotic therapy did not improve the animal's condition. Also, it often seemed that the therapy—more so, the catching of the animal and the restraint applied in order to administer treatment—produced a negative rather than positive result. Apparently, the "psychological traumatization" incurred by this handling had a very noxious effect on the animal's general condition. In some cases the discontinuation of treatment and release of the animals to the volery produced a more positive effect than the continuation of treatment under confinement in a cage.

The opinion established in the literature that monkeys are extremely susceptible to dysentery was based on the fact that the researchers who investigated this disease in monkeys usually worked with animals that were living under extremely adverse conditions. These were usually animals from the zoo, often recently brought from their natural habitat. At the Sukhumi monkey-breeding farm, as well, the more or less serious outbreaks of dysentery with a high death rate usually occurred among the newly-imported animals. It is characteristic that the death rate, being often high in the first two or three months after the monkeys arrived at the breeding farm, subsequently dropped sharply to solitary cases. It may be assumed that in the course of two to three months death occurred among the most weakened animals, whereas the monkeys that survived this period underwent their own kind of adaptation and became more resistant to infection.

The rather high resistance of monkeys to dysentery was also indicated in numerous experiments with attempts to induce this disease in monkeys (M. A. Tumanyan, 1956; E. K. Dzhikidze, 1958, and others). Despite the administration of huge doses of bacteria (up to 30-90 billion microbe bodies), the disease did not always develop in clinically manifested form, very often terminating in temporary bacillary secretion.

We shall not attempt to examine the different aspects of the susceptibility of monkeys to dysentery. Their resistance to this disease is quite high, and only "extraordinary" circumstances lead to the breakdown of this natural immunity and to the development of the disease. Equally, successfully induced dysentery was apparently connected in each case with certain factors that weakened the animal's natural resistance to the disease, which are usually difficult to establish. It should be emphasized that the question concerns natural nonspecific immunity which is not connected with the indexes of immunological reactivity (with the titer of specific antibodies, indexes of phagocytic activity), often not determining the possibility of infection. Experimentally induced disease may occur right after previous dysentery or against the background of dysentery carriage (E. K. Dzhikidze, 1957) with a sufficiently high content in the blood of specific immune bodies and considerable phagocytic activity of the leukocytes.

Usually, when they speak of the characteristic, most prevalent and serious diseases of monkeys, tuberculosis is mentioned along with dysentery. In K. L. Kovalevskiy's manual published in 1958 on animal breeding in the laboratory, only dysentery and tuberculosis were mentioned, in essence, among the infectious diseases of monkeys. In the section describing tuberculosis in the monkeys at the Sukhumi monkey-breeding farm, we discussed this problem in detail. The recent experience of the monkey-breeding farm, as well as many zoos, seems to indicate that the incidence of tuberculosis among monkeys has dropped sharply. This disease has become rare even among the newly-imported monkeys. Solitary cases of disseminated tuberculous infections were observed only with especially unfavorable cartages, when a considerable part of the animals arrived with acute symptoms of dystrophy. Of definite interest is the fact that, out of a large group of animals that were kept in one house or volery in close contact with each other, only solitary instances of tuberculous infection occurred. A mass outbreak of tuberculosis—as could have been expected on the basis of the peculiar sensitivity of monkeys to this disease—did not occur. We believe that only extremely unfavorable conditions of confinement, leading to a sharp weakening of the organism's resistance to infection, renders the monkey sensitive to tuberculous infection. According to our material and data in the literature, there has been a significant decrease in the morbidity and death rates of tuberculosis in monkeys in recent years. This is connected not so much with the decrease in the circulation of the pathogenic agent in the surrounding environment as with the rational conditions of confinement that have been established for animals at the breeding farm and zoos.

The considerable resistance of monkeys to tuberculosis is indicated by the following facts: the capacity of tuberculous monkeys for self-healing in individual cases, which is demonstrated by the presence of petrifactions in the lungs and nodes at the bifurcation of the trachea; the transition of the infectious process from acute to chronic form in some animals, sometimes with the development of the organic forms of tuberculosis; and finally, the capacity of the animals in some cases for developing immunity when coming into contact with the agent, without the development of an acute form of tuberculosis. The latter was indicated by the animals' positive allergic reaction to tuberculin. Also attesting to the high resistance of monkeys to tuberculosis under suitable living conditions was the prolonged positive allergic reactions of the monkeys to tuberculin—often lasting for many years, and the fact that no manifestations of this disease were found in dissected monkeys that had died of other causes or were killed in experiments.

The possibility of the experimental reproduction of tuberculosis in monkeys cannot attest to an increased sensitivity of these animals to the disease. The method of experimental infection (parenteral introduction of mass doses of bacteria) differs greatly from any possible means of natural infection.

We touched upon the two most common infections in monkeys, which are customarily called the "scourge" of monkeys. We can agree with this thesis in that the pronounced weakening of the animal's resistance in connection with various noxious factors—most often, the abrupt alteration of living conditions after capture, aggravating the rigors of transit—created a premise for the greater or lesser prevalence of these infections, the more common and important outbreaks of disease being caused by the pathogenic agents of dysentery. This was possibly connected with the wider distribution of the given agents in the areas where the animals were captured, but more probably with the fact that there was a sharp disruption of their feeding habits in transit, with consequent digestive disturbances which apparently had great significance for the development of dysentery.

One of the common diseases of monkeys is pneumonia, occupying second place after dysentery in rate of occurrence. As we pointed out previously in the corresponding section, pneumonia (bronchopneumonia, in the overwhelming majority of cases) was extremely rare as a primary disease. Ordinarily, these rare cases concerned bronchopneumonia in young monkeys. As a rule, bronchopneumonia in monkeys was a complication of some other disease, although it was often the direct cause of death. Microbiological examination showed that pneumonia could be caused by different cocci, but the diplococcus was discovered most often. As in human pneumonias, bronchopneumonia of monkeys is a typical autoinfection that develops in connection with noxious factors (most often with chilling) on the base of the animal's own microflora of the lungs. Primary pneumonia of young monkeys is not an exception in this respect.

Lobar pneumonia of monkeys is not common. As a rule, it occurred in the imported monkeys and was connected with extremely adverse conditions of transportation in wintertime, accompanied by severe chilling of the animals. Morphological examination of a number of animals affected by lobar pneumonia revealed many morphological indications that established a similarity between lobar fibrinous pneumonias of monkeys and man.

Among other infections, it is necessary to mention—as a rarity—Morgan's toxinfection and poliomyelitis. The causative agent of the first disease is Proteus morganii which was found in the monkey's intestinal tract comparatively often (far more often than toxic infection occurs). Despite the fact that the pathogenic agent of Morgan's toxinfection does not belong to the Salmonella group, the pathological changes produced by this disease were at first glance extraordinarily similar to the changes occurring in typhoid fever and the abdominal form of paratyphoid. The pronounced from of Morgan's toxinfection was manifested by an enlargement of the spleen and mesenteric lymph nodes, and Peyer's patches in the small intestine at the ileocecal junction. However, microscopical examination revealed essential differences in these cases. In the diseases caused by the paratyphoid agent, the question concerned hyperplasia of the reticular cells in the Peyer's patch; while, in Morgan's toxinfection the enlargement of the latter was caused by hyperplasia of the lymphoid tissue.

At the same time, if the disease nevertheless occurred, it ran a very acute course and was largely fatal. In essence, all the cases of Morgan's toxinfection that were known to us were fatal. A most curious problem is the contagiousness of this disease. The three cases of toxinfection contained in our material developed almost simultaneously in animals that were kept in the same place of confinement. The latter circumstances does not yet indicate the contagiousness of this disease nor a particular virulence of the causative agent. The simultaneous illness of several animals that were confined in the same place may be explained by the general conditions under which the monkeys were confined, which could have led to the development of disease.

In this connection, mention should be made of the only outbreak of poliomyelitis known to have taken place among the lower apes and registered at the monkey-breeding farm in 1957. The expert virological study that was made at our request by M. K.

Voroshilova of the Institute for the Study of Poliomyelitis established that Morgan's infection was a form of poliomyelitis. A most remarkable fact is that the rhesus monkeys that did not contract disease after coming in contact with animals affected by poliomyelitis (although the disease can be induced by special laboratory methods of infection) succumbed in a patent, spontaneous outbreak of poliomyelitis. Also of interest is the fact that the most careful epidemiological analysis produced no indications of the source of the viral attack.

The monkeys possessed considerable resistance to coccal wound infections, possibly in connection with the frequent injuries continuously incurred in nature in view of the great mobility and general activity of these animals. Coccal infection (both wound and other origin) may occur in the form of sepsis in individual, apparently very rare, instances.

Endocarditis of monkeys should be mentioned as a very rare pathological condition. We observed three cases of endocarditis, only one of which was macroscopically manifested. In the other two animals, the endocarditis was revealed only by microscopical examination, and was a complication of sepsis in one instance and tuberculosis in the other. However, in no way did any of these cases resemble rheumatic damage of the valvular apparatus in man. The defects of the cardiac valves that we observed in two other cases were very similar to the same defects that develop after the rheumatic process in man; however, the absence of morphological indications of the aggravation of the process and the corresponding changes in the myocardium did not permit us to form a more definite opinion on their possible rheumatic origin.

Thus, not once did we find in the monkeys evidences of the allergic complications of coccal infection in the form of glomerulonephritis, rheumatism, etc. We may assume that the given manifestations of infection are peculiar only to man. Regarding the problem of the susceptibility of monkeys to different infections and whether or not certain infectious diseases are peculiar to monkeys in their natural environment, we may say that there are a number of infectious diseases which are not peculiar to monkeys in their natural habitat. The question concerns diseases such as hypertension, coronary insufficiency and certain other purely "human" (as far as we know) diseases that are connected with mental and emotional stress. Atherosclerosis, relatively often occurring in captive monkeys, apparently is not peculiar to monkeys in nature; pathological obesity or other metabolic disorders connected with it are probably very rare or nonexistent in monkeys living in their natural habitat.

In this connection, it behooves us to consider the peculiarities of the confinement of animals at the breeding farm, which may cause the development of pathological phenomena that are not peculiar to monkeys. Their development is apparently easier to understand and explain by the results of the experimental reproduction of these pathological conditions, just as this experimental data is being used to clarify the pathogenesis of hypertension and coronary insufficiency in man—human diseases that have long been known and are being investigated in detail by many researchers.

The experimental researchers conducted by D. I. Miminoshvili and co-workers demonstrated that experimental neurosis was the underlying factor in the development of experimental hypertension in monkeys. This research is extremely valuable for an understanding of hypertension in man, and at the same time makes it possible to explain the causes and mechanisms of the development of hypertension in monkeys under the conditions of the breeding farm. The cause of the rise in arterial pressure in monkeys was neurosis resulting from certain factors that stemmed from captivity. As a rule, this was connected with the prolonged retention of the animal under experimentation, evoking considerable disturbance of higher nervous activity as the result of frequent subjection to experiments, as well as the development of other conflicting situations. Hypertension developed much sooner when the animal was confined in a cage and its normal interrelations with the other monkeys was disrupted. Disruptions of the normal diurnal rhythm of the physiological functions, connected with the animal's subjection to experimentation and its confinement in a cage, as the researches of G. M. Cherkovich demonstrated, had great importance in the development of neurotic conditions. Diseases such as hypertension and coronary insufficiency in monkeys apparently possess single mechanisms. The underlying factor in the development of the latter disease—as in hypertension—was neurosis.

The neurogenic and atherosclerotic factors are considered to play the leading role in the development of coronary insufficiency in man, whereas the neurogenic mechanism is considered the most important in the development of coronary insufficiency in monkeys.

The discovery of atherosclerosis in monkeys, including also atherosclerosis of the coronary vessels of the heart, still does not permit connecting the disturbance in the coronary blood flow with atherosclerosis of the vessels since some cases of coronary insufficiency revealed no evidence of atherosclerosis of the coronary vessels; whereas in those cases where it did occur, it was evident that the solitary flat patches, barely projecting into the lumen of the coronary vessels, could not create an obstacle for the coronary circulation.

In our observations a connection between coronary insufficiency and atherosclerosis of the coronary arteries may be assumed only in the scheme of the effect of the atherosclerotic changes in the vascular wall on the capacity of the coronary vessels to produce spasmatic reactions. A supposition may be expressed regarding the existence of reverse interrelations, i.e., the property of the vascular wall to store a surplus of cholesterol in the intima when there are vasomotor disturbances.

We may therefore consider two diseases of monkeys which are connected with neurotic disturbances: hypertension and coronary insufficiency. There is no doubt that they are not the only manifestations of neurosis. D. I. Miminoshvili described certain other pathological manifestations of experimental neurosis—behavioral disturbances, digestive disorders, loss of hair, etc. However, under nonexperimental conditions, with a greater complication of the systematic daily observation of the animal's condition, it is possible to study first-hand the changes in blood pressure and electrocardiograms which are regularly carried out in a large number of the animals.

A number of the diseases of monkeys that are connected with metabolic disturbance depend to a considerable degree on the peculiarities of the confinement of the animals at the breeding farm. The physiologists' observations of the behavior of the monkeys revealed a cessation of locomotor activity—particularly pronounced under conditions of confinement in a cage. In the volery the daily run comprised hundreds of meters, while in the cage it comprised one-tenth the amount. Even in the volery, the monkeys, deprived of the necessity to seek their food, moved about much less than animals living in nature. And already, the conditions of freedom and confinement in a cage are completely incomparable in this respect. In the metabolic disturbances a role is also played by a sufficiently abundant, high-fat diet which has been properly processed and therefore more easily assimilated by the animals. It must be assumed that the development of atherosclerosis in the monkeys at the breeding farm was connected, on the whole, with these two factors.

The organic pathology of atherosclerosis of monkeys is essentially different from that of man; the greatest changes occurred in the aorta. We found no significant vascular damage of the heart or brain, which is so often observed in man.

The same factors that caused atherosclerosis also produced excessive adiposity, often observed in old animals, sometimes to a considerable degree. Apparently, the limitation of the animals' mobility and their adiposity were closely connected with the significant number of stillbirths which are still frequent at the breeding farm. Stillbirths predominated over abortions, birth in a large number of cases of viable offspring; but the nonviable offspring indicated that stillbirths were connected not with the incapacity of the monkeys to carry the fetus to full term but with disturbance in labor. Apparently, an important role in this was played by the inhibition and protraction of labor due to weakness of the musculature in prelum abdominale, and the monkey's adiposity.

Tumorous processes are extremely rare in monkeys. Benign adenomatous growths in the gastric mucosa are more common. In some cases these hyperplastic processes are connected with the presence of specific parasites in the stomach. However, they cannot be considered true tumors.

It must be assumed that the gastric mucosa of monkeys (M.

rhesus) is highly reactive and is capable of responding to different irritants with hyperplasia, without acquiring a malignant character. Polypous growths of the mucosa of the uterine cervix occurred relatively often in adult monkeys. The principal pathology occurring in old monkeys was that of the sexual apparatus, verging on neoplasms, such as endometrioses. The latter, as the anamnesis showed, were often connected with endocrine disturbances relating to the sexual sphere.

Summing up the description of the monkey diseases observed at the Sukhumi monkey-breeding farm, we permit the conclusion that there is a great similarity between the diseases we observed in the monkeys and analogous diseases in man. At the same time, it is necessary to mention that the nosological aspect of diseases of monkeys is quite monotonous, distinguishing it significantly from that of human diseases. In essence, even the common infectious diseases of monkeys included only dysentery, tuberculosis and pneumonia. Morgan's toxinfection, poliomyelitis and certain other infectious diseases rarely occurred in monkeys and cannot be taken into account. As regards the diseases that are more common in man, i.e., malignant neoplasms, rheumatism, cardiovascular diseases, they either occurred seldom or not at all in monkeys. At the same time, we consider it necessary to emphasize again that we are describing diseases in monkeys that survived at the breeding farm for one or another period of time. The material from mass dissections which were performed in connection with the production of poliomyelitis vaccine showed that the animals that were killed soon after arrival usually harbored helminths, tick disease of the lungs, colitis (most often of dysenteric etiology) and tuberculosis. The latter two infections undoubtedly developed during a period of pronounced disturbance in general condition connected with the transportation and uprooting of the monkeys from their natural habitat to a foreign environment.

It is extremely important to emphasize that monkeys, being very similar to man with respect to anatomical-physiological peculiarities, are capable under certain conditions of contracting in similar form various diseases that are characteristic for man. However, many of the above-described diseases are apparently not peculiar to monkeys in their natural environment, and occur under conditions of captivity at the breeding farm through contact with certain irritants intruded by man.

The enumeration of diseases presented above demonstrates not so much the rate of their occurrence in monkeys as the potential possibility of their development in these animals under suitable conditions. The difference between the nosological aspects of monkeys and human diseases depends not so much on their biological distinction (the biological similarity between man and monkey, in particular, is confirmed by the possibility of the development in monkeys of a number of diseases peculiar to man) as on the extremely different conditions of existence.

REFERENCES

Abramova, Ye. V.: *Spontaneous Dysentery in Monkeys.* Works of the Sukhumi Biological Station AMS USSR, p. 244, 1949.

Idem: Spontaneous Dysentery in Monkeys. Dissertation, Sukhumi, 1952.

Azletskiy, B. V.: Clinical Picture of Uterine Ruptures With Respect to Etiology. *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 12, 1933.

Aksenova, A. S. and Khutsishvili, L. M.: *Paratyphoid Infection of Breslau Type in Monkeys.* Works of Sukhumi Biol. Station AMS USSR, p. 270, Moscow, 1949.

Anan'in, V. V. and Karaseva, Ye. V.: Leptospirosis in Monkeys. *Voprosy parazitologii* (Problems of Parasitology), No. 7, p. 96, 1953.

Anichkov, N. N.: *Arterial Changes in Old Age and With Atherosclerosis.* Works of Military-Medical Academy i/m S. M. Kirova, Vol. 33, p. 20, 1941.

Idem: Atherosclerosis. In the book (by Abrikosov, A. I.): *Particular Pathological Anatomy*, Issue 11, p. 350, Moscow-Leningrad, 1947.

Antonov, A. M.: Spontaneous Tumors of the Kidneys in Monkeys (M. rhesus). *Voprosy onkologii* (Problems of Oncology), Vol. 2, No. 2, p. 198, 1956.

Ariyel', M. B.: Comparative Pathological Morphology of Tuberculosis. *Problemy tyberkuleza* (Problems of Tuberculosis), No. 6, p. 14, 1949.

Bam, L. A.: Chronic Ultraparadoxial Phase in the Macaca Lapunder. Materials for the Study of Neuroses in Monkeys. Preliminary Report 4. *Byulleten' VIEM* (Bulletin of MIEM), No. 3/4, pp. 95-98, 1936.

Idem: Disturbance in Conditioned-Reflex Action of Castrated Monkey, Evoked by Large Doses of Bromine. Materials for the Study of Experimental Neuroses in Monkeys. *Fiziologicheskiy zhurnal SSSR* (Physiological Journal USSR), Vol. 27, No. 1, p. 31, 1939.

Bam, L. A. and Kaminskiy, S. D.: Stereotype Alteration of Positive and Negative Conditioned Reflexes in Two M. Lapunder Monkeys. Materials for the Study of Experimental Neuroses in Monkeys. Report 3. *Byulleten' VIEM* (Bulletin of MIEM), No. 11-12, p. 7, 1953.

Baron, M. A.: *Reflex Structures of the Inner Membranes.* Moscow, 1949.

Belkin, M. B. and Zhornik, I. P.: Displacement of Myomatous Uterus Diagnosed Prior to Operation. *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 1, p. 71, 1955.

Belyayev, Ye. I.: The Etiology of Uterine Ruptures During Parturition. *Akush. i ginekol.* (Obstetrics and Gynecology), No. 6, 1938.

Bibinova, L. S.: The Morphologic Characteristics of Dysentery in Children, in its Different Stages and Forms. Dissertation, Leningrad, 1954.

Blinder, A. Ya.: Asymptomatic Uterine Ruptures. *Akush. i ginekol.* (Obstetrics and Gynecology), No. 11, p. 50, 1940.

Blinnikov, K. S.: Materials on the Experimental Study of Virus B. First Scientific-Reports Conference (Moscow Scientific-Research Institute of Preparations Against Poliomyelitis). Theses and Summary Reports, p. 10, Moscow, 1958.

Blokhin, N. N., Vasil'ev, Yu. M. and Pogosyants, Ye. Ye.: New Incidence of Spontaneous Malignant Tumor in M. Rhesus. *Voprosy onkologii* (Problems of Oncology), Vol. 1, No. 2, p. 91, 1955.

Bol', K. G. and Bol', B. K.: *Principles of the Pathologic Anatomy of Farm Animals.* Moscow, 1954.

Bol', K. G.: *Principles of the Pathologic Anatomy of Domestic Mammals and Birds.* Publishing House of Agricultural Literature, 1938.

Vadova, A. V. and Gel'shteyn, V. I.: Spontaneous Tumors in the Catarrhinians, According to Materials of the Monkey-Breeding Farm at the Sukhumi Medical-Biological Station. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments With Monkeys.* p. 107, Moscow, 1956.

Idem: Prolonged Use of Synestrol in Spontaneous Mammary Carcinoma of Monkeys. *Voprosy onkologii* (Problems of Oncology), Vol. 2, No. 4, p. 391, 1956.

Vadova, A. V., Smoylovskaya E. Ya.: Dyshormonal Proliferation in the Uterus and Mammary Glands of Monkeys Following the Introduction of Synestrol. *Voprosy onkol.* (Problems of Oncology), No. 5, p. 515, 1959.

Vayl', S. S.: *Multiple Minor Circulatory Disturbances and Micro-traumas of the Cerebrum of the Newborn.* Works of the Military-Medical Academy, 12, 1949.

Idem: Circulatory Disturbances in the Brain of Abortive Newborn. *Arch. Path.* 2, 1950.

Val'ter, A. V.: *Chronic Defects of the Aortal Valves.* Leningrad, 1948.

Verevkina, T. S. and Zubova, N. N.: Materials and Statistics of Tumors of Dogs and Cats. *Voprosy onkol.* (Problems of Oncology), *Trudy AMN SSSR* (Works of AMS USSR), Vol. 21, No. 5, p. 193, 1952.

Viktorova, O. N. and Aksenova, A. S.: Bacillary Dysentery of Macaques. Works of the Sukhumi Biological Station AMS USSR, p. 258, 1949.

Viktorova, O. N., Kaktin, S. G., Kas'yanenko, I. I. and Naletov, N. A.: Experience of Tuberculin-Diagnosis in Monkeys. In the book: *Papers on Scientific-Research Work for 1947* (Med.-Biol. Science), No. 7, p. 55, Moscow, 1955.

Vishnevetskaya, L. O.: Vascular Development According to Age. In the book: *Anatomic-Physiologic Peculiarities of Childhood*, Moscow, 1935.

Idem: Pathologic Anatomy of the Kidneys and Heart in Dysentery of Children. *Pediatriya* (Pediatrics), No. 9, p. 12, 1938.

Vlados, Kh. Kh. and Krayevskiy, N. A.: Classification of the Leukoses. *Sovetskaya meditsiya* (Soviet Medicine), No. 3, p. 33, 1953.

Volkova, K. G.: Arterial Changes with Age in Animals. *(Uber Altersveranderungen der Arterien bei Tieren), Arch. pathol. Anat. u. Physiol., Virchow's,* Bd. 252, S. 208, 1924.

Idem: Changes with Age in the Arteries of Animals. Works of the 1st All-RSFSR Congress of Pathologic-anatomists, p. 333, 1923.

Idem: Atherosclerosis of the Cerebral Arteries. *Arkhiv biologicheskikh nauk* (Archives of Biological Scinces), Vol. 33, No. 3-4, p. 581, 1933.

Voronin, L. G., Kanfor, I. S., Lakin, G. F. and Tikh, N. A.: *Experience of Keeping and Breeding Monkeys at Sukhumi.* Moscow, 1948.

Voroshilova, M. K.: Experimental Poliomyelitis of Monkeys. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments with Monkeys.* p. 165, Moscow, 1956.

Voroshilova, M. K., Golubeva, N. N., Tolgskaya, Ye. A., Lavrova, I. K. and Gol'drin, N. Ye.: *Virological Study of an Outbreak of Poliomyelitis Among Monkeys at Sukhumi; Poliomyelitis and Like Diseases Evoked by Intestinal Viruses.* Theses and Reviews of Reports, 2nd Scientific Session of the Institute for the Study of Poliomyelitis AMS USSR 19-21 June 1958, p. 24, Moscow, 1958.

Galaktionov, A. I.: Three Instances of Uterine Rupture in Pregnancy. *Akusherstvo i ginekologii* (Obstetrics and Gynecology), No. 11, p. 57, 1940.

Garnitskaya, E. A., Shul'ts, F. V. and Gavrilov, S. A.: The Clinical Characteristics and Etiology of Colitis in Children. *Soviet Medical News,* No. 19, 1934.

Gvazava, I. S.: Clinical Peculiarities of Dysentery in Monkeys. *Problems of Infectious Pathology in Experiments with Monkeys.* p. 31, Sukhumi, 1958.

Gekkel', O.: Structure and Developmental Changes of the Cerebral Vessels. *(Uber den Bau und Altersveranderungen der Gehirnarterien). Arch. pathol. Anat. u. Physiol., Virchow's,* Bd. 241, S. 42, 1923.

Grigoliya, M. A.: *The Interrelation Between Hypertension and Pregnancy in Monkeys.* Collected Works of the Medical Society of Abkhaziya, Vol. 1, p. 311, Sukhumi, 1957.

Idem: Stillbirths and Abortions in Monkeys, According to Data of the Sukhumi Monkey-Breeding Farm, Medical-Biol. Station, AMS, USSR. Collected Works of Med. Society of Abkhaziya, Vol. 1, p. 305, Sukhumi, 1957.

Grigorova, O. I. and Nesturkh, M. F.: *Filariasis of Young Chimpanzee.* Works on Dynamics of Development, Vol. 6, p. 197, Moscow, 1931.

Davydovskiy, I. V.: *Pathologic Anatomy and Pathogenesis of the Most Important Diseases of Man.* Vol. 1, Moscow, 1956.

Idem: Pathologic Anatomy and Pathogenesis of Human Diseases. Vol. 11, Moscow, 1958.

Dvizhkov, P. P. and Tsvetayeva, N. P.: *Comparative Pathology of Animal Tumors.* Works of the Moscow Zoological Park, Vol. 3, p. 166, Moscow, 1946.

Devitskiy, V. S.: Structure and Origin of Different Forms of Chronic Changes in the Cardiac Valves. Dissertation, Moscow, 1908.

Dzhikidze, E. K.: Dysentery Carriers Among Monkeys. Dissertation, Sukhumi, 1954.

Idem: Experimental Research into Immunity to Infection in Dysentery. *Zhurnal mikrobiologii, epidemiologii i immunologii* (Journal of Microbiology, Epidemiology and Immunology), No. 4, p. 58, 1957.

Idem: Experimental Model of Flexner's Dysentery. *Problems of Infectious Pathology in Experiments with Monkeys.* p. 55, Sukhumi, 1958.

Yelikulashvili, I. S.: *Pregnancy and Birth in Monkeys.* Moscow, 1957.

Yesipova, I. K.: *The Pathology of Chronic Nonspecific Pneumonias.* Moscow, 1956.

Zdrodovskiy, P. F.: *Problems of Reactivity in the Study of Infection and Immunity.* Moscow, 1950.

Kavtaradze, K. N.: Icteric Leptospirosis of Monkeys. In the book: *Problems of Infectious Pathology in Experiments with Monkeys.* p. 179, Sukhumi, 1958.

Kaktin, S. G.: Spina Ventosa in Monkeys. In the book: *Problems of Infectious Pathology in Experiments with Monkeys.* p. 189, Sukhumi, 1958.

Kaminskiy, S. D.: Pathologic Anomalies in the Higher Nervous Activity of Monkeys Under Experimental Conditions. Report 1, *Byulleten' VIEM* (Bulletin of MIEM), 9/10, p. 12, 1935.

Kovalevskiy, K. L.: *Laboratory Animal Breeding.* Moscow, 1958.

Kokaya, G. Ya.: Electrocardiogram of Lower Apes, Both Normal and with Pathologic Conditions. *Byulleten' eksperimental'noy biologii i meditsiny* (Bulletin of Experimental Biology and Medicine), Vol. 38, No. 12, p. 23-26, 1954.

Idem: Electrocardiogram of Healthy Monkeys of Different Species and Ages. Dissertation, Sukhumi, 1958.

Krinitskiy, Sh. I.: *Inflammation and Sclerosis of the Valves of the Heart.* Rostov-on-Don, 1940.

Lapin, B. A.: Tick Bronchites in Monkeys. *Arkhiv patologii* (Archives of Pathology), No. 4, p. 57, 1956.

Idem: Lymphogranulomatosis in Green Marmosets. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments with Monkeys.* p. 123, Moscow, 1956.

Idem: Chronic Aneurysm of the Anterior and Posterior Walls of the Left Ventricle of the Heart of the Macaca Lapunder. *Arkhiv patologii* (Archives of Pathology), No. 8, p. 92, 1956.

Lapin, B. A., Yakovleva, L. A. and Pekerman, S. M.: Reproduction of Paratyphoid B in Monkeys. *Byull. Eksptl. Biol. Med.* (Bull. Exper. Biol. & Med.), p. 33, 1956.

Lapin, B. A. and Yakovleva, L. A.: *Materials on the Spontaneous Diseases of Monkeys.* Summary reports of General Assembly of the Division of

Medical-Biological Sciences AMS USSR in honor of the 40th anniversary of the Great October Revolution and the 30th anniversary of the Sukhumi Medical-Biological Station AMS USSR, Sukhumi, p. 55, 1957.

Levin, I. Ye.: Zur Kenntnis der individuellen Strukturabweichung der Aorten Intima. *Arch. pathol. Anat. u. Physiol., Virchow's,* Bd. 295, S. 33, 1935.

Libenzon, L. L.: Clinical-Histologic Study of Ruptures of Uterine Cervix During Labor, Dissertation, Moscow, 1958.

Linnikova, M. A.: The Vaccination of Monkeys with BCG, in the collection: Antituberculosis Vaccine, p. 151, Moscow, 1958.

Magakyan, G. O.: *Arterial Pressure in Monkeys.* Works of the 2nd General Scientific Session (Institute of Clinical and Experimental Cardiology AS GSSR) on Hypertension, p. 107, Tbilisi, 1953.

Idem: Hypertension of Monkeys. *Byull. Eksptl. Biol. Med.* (Bull. Exper. Biol. & Med.), Vol. 35, No. 2, p. 44, 1953.

Idem: Hypertension of Monkeys as an Experimental Model of Hypertension of Man. Summary report of General Assembly of Division of Med.-Biological Sciences AMS USSR, in honor of 25th anniversary of the Medical-Biological Station, p. 13-14, Moscow, 1953.

Malinovskiy, M. S.: *Obstetrical Surgery.* Moscow, 1955.

Medvedeva, N. B.: *Experimental Endocrinology.* Kiev, 1946.

Miminoshvili, D. I.: Experimental Neuroses of Monkeys. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments with Monkeys.* p. 46, Moscow, 1956.

Idem: The Role of Conflicting Situations in the Development of Pathologic Conditions. Summary reports of General Assembly of Division of Med.-Biol. Sci. AMS USSR on 40th anniversary of October Revolution and 30th anniversary of Sukhumi Med.-Biol. Station, p. 36, Sukhumi, 1957.

Miminoshvili, D. I., Magakyan, G. O. and Kokaya, G. Ya.: The Obtaining of an Experimental Model of Hypertension and Coronary Insufficiency in Monkeys. In the collection: *Theoretical and Practical Problems of Med. Biol. in Experiments with Monkeys,* pp. 85-97, Moscow, 1957.

Mironova, S. K.: Uterine Rupture Following Cervical Caesarian Section. *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 4, 1936.

Naletov, N. A. and Kas'yanenko, I. I.: Restorative Processes in Tuberculosis of the Lungs in Monkeys. Problems of Tuberculosis, No. 2, p. 46, 1955.

Naumova, N. A.: Alloxan Diabetes. *Uspekhi sovremennoy biologii* (Progress of Modern Biology), Vol. 27, No. 1, p. 111-119, 1949.

Nechayevskaya, M. P., Goncharova, K. V. and Kishenevskaya, M. Ye.: Outbreak of Food Poisoning Caused by Morgan's Bacillus. *Vrachebnoye delo* (Medical Matters), No. 10, p. 745, 1946.

Naletov, N. A., Kas'yanenko, I. I., Viktorova, O. N., Kaktin, S. G. and Gruzdev, G. P.: The Use of Tuberculin for Diagnostic Purposes in Monkeys. *Bulletin of the Institute of Tuberculosis AMS USSR,* No. 2, p. 28, 1950.

Ospovat, R. M.: Uterine Ruptures. *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 11, p. 62, 1940.

Pavlovskiy, Ye. N.: *Course in Human Parasitology*. p. 201, Moscow, 1934.

Paliy, Ye. T.: Displacement of Uterus Didelphys in Pregnancy at Term, *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 3, p. 81, 1954.

Pekerman, S. M. and Dzhikidze, E. K.: Investigation of Outbreak of Pasteurellosis in Capuchin Monkeys, *Problems of Pathology of Infectious Diseases in Experiments with Monkeys*. p. 191, Sukhumi, 1958.

Petchenko, A. I.: *Akusherstvo* (Obstetrics). Kiev, 1954.

Popov, A. I.: *Leukemias of Pigs*. Works of the Kiev Veterinary Institute, No. 12, p. 225, 1955.

Porubel', L. A., Prokhorova, I. A., Sergeyev, A. N. and Slavin, Yu. M.: Pathologic-Anatomic Analysis of Longevity in Monkeys, first scientific conference for the hearing of reports (Moscow Scientific-Research Institute of Poliomyelitis Preparations). Theses and summary reports, p. 41, Moscow, 1958.

Idem: The Pathologic-Anatomic Criteria for the Selection of Monkey Kidneys for the Obtaining of Tissue Cultures, first scientific conference for the hearing of reports (Moscow Scientific-Research Institute of Polioymyelitis Preparations). Theses and summary reports, p. 39, Moscow, 1958.

Robinzon, I. A. and Voroshilova, M. K.: *Poliomyelitis*. Report No. 2, The Histopathology of Experimental Diseases of Monkeys, Reproduced by Moscow, Riga and Berlin Strains, 1949.

Rozenbaum, G. I.: Phytoncide Therapy of Acute Dysentery. Dissertation, Moscow, 1953.

Rozina, N. E.: Histopathologic Study of Experimental Infection Produced by Virus B, first scientific conference for the hearing of reports (Mosc. Sci.-Research Inst. of Polio. Prep.). Theses and summary reports, p. 47, Moscow, 1958.

Ryzhkov, M. I.: The Etiology of Post-Partum Uterine Rupture. Collected articles dedicated to L. L. Okinchits, p. 293, 1924.

Ryazantseva, N. Ye.: Outbreak of Measles Among Monkeys. *Zhurnal microbiologii, epidemiologii i immunobiologii* (Journal of Microbiology, Epidemiology and Immunobiology), No. 4, p. 88, 1956.

Savinov, A. P. and Tyufanov, A. V.: *Experience of the Mass Pathologic-Anatomic Study of Monkeys Killed for the Purpose of Preparing Poliomyelitis Vaccine*. 1st Scientific Session of the Institute for the Study of Poliomyelitis, theses of the reports, p. 36, Moscow, 1957.

Sergeyev, A. N.: *Tick Invasion of the Lungs of M.Rhesus Monkeys*. Works of the Sukhumi Biological Station AMS USSR, p. 295, 1949.

Idem: Extrauterine Pregnancy in Hamadryad Baboons. *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 2/3, p. 120, 1939.

Sinitsyna, T. A.: *The Method of Reproducing Experimental Atherosclerosis in Dogs*. Theses of reports of the session on atherosclerosis and myocardial infarct, p. 31, Moscow, 1958.

Skvortsov, M. A.: *Pathologic Anatomy of the Most Important Diseases of Children*. Moscow-Leningrad, 1946.

Skrobanskiy, K. K.: *Textbook on Obstetrics*. Leningrad, 1946.

Skryabin, K. I. and Shikhobalova, N. P.: *Filariae of Animals and Man*. Moscow, 1948.

Sokoloverova, I. M.: Spontaneous Diabetes Mellitus in Monkeys. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments with Monkeys*. p. 130, Moscow, 1956.

Stepanov, P. N.: *Chronic Dysentery*. Moscow, 1946.

Studentsov, A. P.: *Veterinary Obstetrics and Gynecology*. Moscow, 1949.

Tymanyan, M. A.: Experimental Reproduction of Sonne Dysentery in Monkeys. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments with Monkeys*, p. 154, Moscow, 1956.

Tyumyakova, Yu. A.: *Report on the Fourth Leningrad Conference on Nutritional Hygiene*. Leningrad, 1939.

Ulezko-Stroganova, K. T.: *Normal and Pathologic Anatomy and Histology of the Female Reproductive Organs*. Moscow, 1939.

Fadeyeva, V. N.: *Morphologic Changes in the Lungs in Lobar Pneumonia That Has Not Been Treated by Sulfanilamides or Antibiotics*. Works of the Leningrad Sanitary-Hygienic Medical Institute, Vol. 41. Pneumonia (Etiology, Pathogenesis, Pathologic Anatomy), p. 30, Leningrad, 1958.

Feringer, Ye. P.: Developmental Changes in the Walls of Human Coronary Arteries. Dissertation, Leningrad, 1952.

Forshtater, V. M.: Spontaneous Uterine Rupture During Labor. *Akusherstvo i ginekologiya* (Obstetrics and Gynecology), No. 11, p. 62, 1940.

Friauf, V. A.: Bact. Morgani, its Biology, Role in Human Pathology and Place in the System of Microbes. Dissertation, Ashkhabad, 1949.

Tsvetayeva, N. P.: *Diseases of Animals at the Moscow Zoological Park*. Moscow, 1941.

Tsinzerling, V. D.: Pathologic Changes in the Aorta of Horses in Connection with the Study of Atherosclerosis in Man. (German), *Arch. pathol. Anat. u. Physiol., Virchow's*, Vol. 213, p. 23, 1913.

Tsinzerling, V. D. and Krinitskiy, Sh. I.: *Comparative Pathology of Arteries*. Pathologic Changes in the Aortas of Cows. *Arch. pathol. Anat. u. Physiol., Virchow's*, Vol. 252, p. 117, 1925.

Tsinzerling, V. D.: *Controversial Problems in the Study of Pneumonie*. Works of the Leningrad Sanitary-Hygienic Medical Institute, Vol. 41. Penumonia (Etiology, Pathogenesis, Pathologic Anatomy), p. 9, Leningrad, 1958.

Chekareva, G. A.: Sclerosis of the Aortal Valves Under Different Pathologic Conditions of the Blood Circulation. Dissertation, Moscow, 1950.

Chumakov, M. P., Prisman, I. M. and Zatsepin, T. S.: *Poliomyelitis. Spinal Paralysis of Children*. p. 18, Moscow, 1953.

Shtefko, V. G.: Changes in the Adrenal Glands of Man and Monkeys Produced by Starvation. (German), *Krankheitsforsch.*, Bd. 6, p. 442, 1928.

Idem: Comparative Pathology of Tuberculosis of Monkeys and Reptiles. Works of the Moscow Zoological Park, Vol. 2, No. 1 1940.

Idem: Materials on the Comparative Pathology of Bone Tuberculosis of Monkeys. Works of the Moscow Zoological Park, Vol. 1, p. 223, 1940.

Shtefko, V. G. and Khar'kov, A. A.: *Comparative Pathomorphology of the Primary Tuberculous Focus in Monkeys.* Works of the Moscow Zoological Park, Vol. 1, p. 285, 1940.

Yakovleva, L. A.: Atherosclerosis of Macaca Rhesus Monkeys. In the book: *Theoretical and Practical Problems of Medicine and Biology in Experiments with Monkeys,* p. 126, Moscow, 1956.

Idem: Atherosclerosis of Lower Monkeys. Theses of the Broadened Session of the Division of Medical-Biological Sciences AMS USSR with the participation of the Sukhumi Medical-Biological Station and Institutes of the Academy. In the book: *The Physiology and Pathology of the Cardiovascular System,* p. 60, Moscow, 1954.

Idem: Pathologic-Anatomic Characteristics of Spontaneous Dysentery in Monkeys. *Arkhiv patologii* (Archives of Pathology), No. 7, p. 61, 1958.

Idem: The Pathologic-Anatomic Manifestations of Dysentery in Monkeys. In the book: *Problems of Infectious Pathology in Experiments with Monkeys.* p. 65, Sukhumi, 1958.

Atanasiu, P., Vallee A. and Martinet J.: Diagonostic de la lucose limphoide chez le porc. *Rec. méd. vét.,* 1955, v. 131, N. 4, p. 246.

Bach, F. W., Fulschner, I. and Harnack, S.: Uber eine durch Affen Verursachte Ruhrepidemie. *Veröffentl. aus dem Geb. der Med.,* 1931, Bd. 34, s. 2.

Baumann, F. B.: A note of the spontaneous occurrence of bacillary dysentery in Monkey. *Philippine J. Sci.,* 1910, v. 5, p. 481.

Benson, R. E., Fremming, B. D. and Jung, R. I.: A Tuberculosis Outbreak in a Macaca Mulatta Colony. *Am. Rev. Tuberc.,* 1955, v. 72, N. 2, p. 204.

Blackek, F. G. and Cecil, R. L.: Studies on experimental pneumonia. III Spontaneous pneumonia in monkeys. *J. Exptl. Med.,* 1920, v. 31, p. 499.

Blacklock, B. and Adler, S.: The pathological effects produced by strongyloides in a Chimpanzee. *Ann. Trop. Parasitol.,* 1922, v. 16, p. 283.

Bonne, C. and Sandground, J. H.: On the production of gastric Tumors bordering malignancy, in Iavanen monkeys through the agency of Nochtia Nochti, a parasitic Nematode. *Am. J. Cancer,* 1939, v. 37, N. 2.

Carter and D'Abrera: *Trans. Roy. Soc. Trop. Med. Hyg.,* 1946, v. 39, p. 373.

Coffey, V. P. and Jessop, W. I. E.: Congenital abnormalities. *Irish J. Med. Sci.,* 1955, N. 349, p. 30.

Corson-White, E. P.: Osteomalacia. *Arch. Internal Med.,* 1922, v. 30, p. 620.

Corson-White, E. P.: Ostitis deformans in Monkeys. *Arch. Internal Med.,* 1922, v. 6, p. 790.

Cotchin, E.: Neoplasia in the dog. *Vet. Record,* 1954, v. 66, N. 52, p. 879.

Dobberstein, I.: Uber die häufigsten Todesursachen der in Zoologischen Garten gehaltenen Tiere. *Med. Klin., Munich,* 1936, N. 10, s. 311.

Dobberstein, I.: Der Krebs der Tiere in Vergleich zum des Menschen. *Stralen therapie*, 1955, Bd. 96, H. 2, s. 259.

Dormanns, E.: Zwei Acarinenarten als Endoparasiten bei Affen. *Virch. Arch., pathol. Anat. u. Physiol.*, 1930, v. 20, s. 276.

Engle, M. T. and Stout, A. P.: Spontaneous primary carcinoma of the prostate in a Monkey. *Am. J. Cancer*, 1940, v. 39, p. 334.

Fairbrother, R. W. and Hurst, E. W.: Spontaneous diseases observed in 600 monkeys. *J. Pathol. Bacteriol.*, 1932, v. 35, N. 6, p. 2.

Fortner, I.: La lucose des bovins. *Bull. Office internat. epizooties*, 1953, v. 40, p. 181.

Fox, H.: *Repts. Lab. Comp. Pathol. Zool. Soc. Philadelphie*, 1926.

Fox, H.: Some observations on comparative constitution in man and lower animals. *Proc. Am. Phil. Soc.*, 1929, v. 68, p. 27.

Fox, H.: Special subject of pathological interest. *Repts. Lab. Comp. Pathol. Philadelphia*, 1932.

Fox, H.: Atherosclerosis in lower Mammals and Birds. (B kh.: Cowdry, E. V., *Atherosclerosis*), New York, 1933.

Fox, H.: *Repts. Lab. Comp. Pathol. Philadelphia*, 1934.

Fox, H.: Mortality and matters of pathological interest. *Repts. Penrose Research Lab. Zool. Soc. Philadelphia*, 1936.

Fox, H.: *Repts. Lab. Comp. Pathol. Philadelphia*, 1937.

Gay, D. M. and Branch, A.: Pulmonary acariasis in monkeys. *Am. J. Trop. Med.*, 1927, p. 40.

Gibson, E. A. and de Cruchy, P. H.: Aortic rupture in Turkeys Subsequent to dissecting aneurysm. *Vet. Record*, 1955, v. 67, p. 650.

Gildmeister, E. *u.* Baerthlein K. *Deut. med. Wochschr.*, 1913, Bd. 21, S. 982.

Gotlieb, H. and Lalich, J.: The occurrence of arteriosclerosis in the aorta of Swine. *Am. J. Pathol.*, 1954, v. 30, N. 4, p. 851.

Gröntoft, O.: Intracerebral and meningeal hemorrhages in perinatally diseased infants. *Acta Obstetr. Gynecol. Scand.*, 1953, v. 32, N. 3, p. 308.

Cross, L. and Kugel, M. A.: *Topographie Anatomy and Hystology of the Valves in the Human Heart.* 1931.

Grzimek, B.: Tod durch Lungenmilben bei einem Schimpansen. *Zool. Gart., Lpz.*, 1951, B. 18, S. 249.

Grzimek, B.: Kurze Mitteilung über die Behandlung von Schimpansen, Strauszen und Geparden im Frankfurter Zoo. *Zool. Gart., Lpz.*, 1953, Bd. 20, S. 191.

De Haan und Griyns: Eine neue endoparasitäre Acaride. *Zentr. Bakteriol. Parasitenk.*, 1901, Bd. 30, 1, S. 57-59.

Habel, K.: Tuberculosis in a Laboratory Monkey Colony. *Am. Rev. Tuberc.*, 1947, v. 55, N. 1, p. 77.

Halloran, P.: Bibliography of References to Diseases in Wild Mammals and Birds. *Am. J. Vet. Research*, 1955, v. 16.

Hamerton, A. E. Demonstration on the morbid anatomy of monkeys. *Proc. Roy. Soc. Med.*, 1929, p. 22.

Hamerton, A. E.: Report on the Societys Prosector for the year 1928. *Proc. Zool. Soc., London*, 1929, v. 1, p. 49-59.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1929. *Proc. Zool. Soc., London*, 1930, v. 11, p. 357-380.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1930. *Proc. Zool. Soc., London*, 1931, v. 101, p. II, p. 527-555.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1931. *Proc. Zool. Soc., London*, 1932, v. 102, p. III, p. 613-638.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1932. *Proc. Zool. Soc., London*, 1933, v. 103, p. II, p. 451-481.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1933. *Proc. Zool. Soc., London*, 1934, v. 104, p. II, p. 389-422.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1934. *Proc. Zool. Soc., London*, 1935, v. 105, p. II, p. 443-474.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1935. *Proc. Zool. Soc., London*, 1936, v. 106, p. III, p. 659-686.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1936. *Proc. Zool. Soc., London*, 1937, v. 107, p. II.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1937. *Proc. Zool. Soc., London*, 1938, v. 109, p. III.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1940. *Proc. Zool. Soc., London*, 1941, v. III, p. III.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1941. *Proc. Zool. Soc., London*, 1942, v. 112, p. III.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1942. *Proc. Zool. Soc., London*, 1943, v. 113, p. III.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1943. *Proc. Zool. Soc., London*, 1944, v. 114, p. 307.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1944. *Proc. Zool. Soc., London*, 1946, v. 115, p. III, IV.

Hamerton, A. E.: Report on the Deaths occurring in the Society's Gardens during the year 1945. *Proc. Zool. Soc., London*, 1947, v. 116, p. III, IV.

Helner, H.: Zur vergleichen den Pathologie der Osteodistrophia Fibrosa der Affen. *Virch. Arch. pathol. Anat. u. Physiol.*, 1927, Bd. 264, H. I. S. 238.

Hill, O.: Report of the Society's Prosector for the year 1950. *Proc. Zool. Soc., London*, 1951, p. III.

Hill, O.: Report of the Society's Prosector for the year 1951. *Proc. Zool. Soc., London*, 1952, p. II.

Hill, O.: Report of the Society's Prosector for the year 1952. *Proc. Zool. Soc., London*, 1953, p. II.

Hill, O.: Report of the Society's Prosector for the year 1953: *Proc. Zool. Soc., London*, 1953, p. II.

Hill, O.: Report of the Society's Prosector for the year 1954. *Proc. Zool. Soc., London*, 1955, p. III-IV.

Hill, O.: Report of the Society's Prosecutor for the year 1955 and 1956. *Proc. Zool. Soc., London*, 1957, p. III.

Hindle, E.: Filterable viruses. *Proc. Roy. Soc. Med.*, 1929, v. 22, p. 822.

Horstman, D. M.: Poliomyelitis virus in blood of orally infected monkeys and chimpanzees. *Proc. Soc. Exptl. Biol. Med.*, 1952, v. 79, p. 417.

Howe, H. A. and Bodian, D.: Poliomyelitis by accidental contagion in the chimpanzee. *J. Exptl. Med.*, 1944, v. 80, p. 383.

Hueper, W. C.: Experimental Studies in cardiovascular pathology. XIV. Experimental atheromatosis in macacus rhesus monkey. *Am. J. Pathol.*, 1946, 22, 6, p. 1287.

Innes, I. R. M., Colton, M. N., Jevick, P. P. and Smith, C. L.: Lung Mites: Pulmonary Acariasis as an Enzootic Diseases Caused by Pneumonissus Si micola in Imported Monkeys. *Am. J. Pathol.*, 1954, 30, p. 813.

Johsoni, I.: Uber Ruhrerkrankungen bei Menschenaffen. *Zentr. Bakteriol. Parasitenk.*, 1939, I. S. 144.

Kalmett, A.: Preventive vaccination against tuberculosis. L. 1929. [Russian.]

Kameron, W. M.: Helminth Parasites. *Proc. Roy. Soc. Med.*, 1929, v. 22.

Kawamura, R.: Neue Beiträge zur Morfologie der Cholesterrinsteatose. Jena, 1927.

Kennard, M.: Cutaneous Test for Tuberculosis in Primates. *Science*, 1939, v. 84, N. 2314, p. 442.

Kennard, M.: Abnormal findings in 246 consecutive autopsies on monkeys. *Yale J. Biol. & Med.*, 1941, v. 13, N. 5, p. 701.

Kirsch, E: Pathologischen Lungenverenderungen beim rhesus Affen hervorgerufen durch pneumonyssus Symicola (acarina). *Z. Parasitenk.*, 1950, 13-14, S. 626.

Klüver, H. A. and Brunschwig, A.: Oral Carzinoma in a monkey colony. *Cancer Research*, 1947, 7, p. 627.

Klüver, H. A. and Bartelmez, G.: Endometriosis in a rhesus monkey. *Surg. Gynec. & Obst.*, 1951, 92, 6, p. 650.

Koch, W. and Deimel, B.: *Uber Krankheiten der Menschen Affen.* Jena, 1952.

Kotchin, E.: Neoplasia in the dog. *Am. J. Vet. Research*, 1954, N. 52, 66.

Krause, C.: Krankheiten der wilden Tiere. *Ergeb. allg. Pathol. u. pathol. Anat.*, 1939, Bd. 34.

Krischman, K. V.: Spontaneous tuberculosis in laboratory monkeys. *Indian J. Med. Res.,* 1936, 23, p. 721.

Krook, L.: A statistical investigation of carcinoma in the dog. *Acta Pathol. Microbiol. Scand.,* 1954, 35, N. 5, p. 407.

Lambl: Primäre Excreczenzen und semilunar Klappen der Aorta. *Wiener med. Wochschr.,* 1856, Bd. 6.

Lindau, H.: Uber einem Fall von Poliomyelitis bei einem Schimpansen. *Tierärztl. Rdsch.,* 1938, Bd. 49, 134.

Lovell, R.: The Bacteriological Findings in certain Fatal cases of Enteritis occurring in the Gardens during the year 1928. *Proc. Zool. Soc., London,* 1929 p. IV, p. 623-632.

Lovell, R.: Bacterial diseases. *Proc. Roy. Soc. Med.,* 1929, v. 22, p. 821.

Lovell, R.: Isolation of Bacterium Morgani from mammals, birds and reptiles at zoological gardens. *J. Pathol. Bacteriol.,* 1929, v. 32, p. 79.

Lovell, R.: Bacteriological Report. *Proc. Zool. Soc., London,* 1930, p. I.

Lubarsch, O. R.: *Ergebnisse der allgemeinen Pathologie und patologischen Anatomie des Menschen und der Tiere.* Wiesbaden, 1917, S. 200.

Mann, G. V., Andrus, S. B., McNelly, A. and Stare, F. J.: Atherosclerosis. *J. Exptl. Med.,* 1953, v. 98, N. 3, p. 195.

Masserman, G. H. and Pachtel, C.: Neurosis in Monkey. *Ann. New York Acad. Sci.,* 1953, v. 56, p. 253.

McCoy, O. R.: Filarial parasitic of Monkeys of Panama. *Am. J. Trop. Med.,* 1936, v. 16, p. 383.

Melnik, J. K. and Ledinko, N.: Immuniti following oral administration of poliomyelitis virus to monkeys. *J. Immunol.,* 1951, 67, p. 213.

Morgan, H.: Upon the bacteriology of the summer diarrhoae of infants. *Brit. Med. J.,* 1907, v. 11, p. 16.

Müller, W.: Spontane Poliomyelitis beim Schimpansen. *Monatsschr. Kinderheilk.,* 1935, Bd. 63, 2.

Mulligan, R. M.: Statistical and histological study of one hundred twenty canine neoplasmus. *Arch. Path.,* 1948, v. 45, p. 216.

Nieberle, K. and Cohrs, P.: *Lehrbuch der speziellen patholo Anatomie der Haustiere.* Jena, 1954, Bd. 3.

Palaske, G.: *Pathologische Histologia.* Jena, 1955.

Platt, B. C. and Nagchaudhuri, I.: Malnutrition and Hair Pigmentation. *Proc. Nutrition Soc. Engl. and Scot.,* 1954, v. 13, p. 2.

Plimmer, H. G.: Report on the cases of deaths in the society's gardens during 1912. *Proc. Zool. Soc. London,* 1913, p. 141.

Plimmer, H. G.: Report on the cases of deaths in the society's gardens during 1914. *Proc. Zool. Soc., London,* 1915.

Pocock, R. I.: An albino Monkey at the Zoological Gardens. *Field,* 1926, v. 148, p. 1154.

Porter, A.: Report of the Honorary Parasitologist for the year 1943. *Proc. Zool. Soc., London,* 1944, v. 114, p. III.

Porter, A.: Report of the Honorary Parasitologist for the year 1953. *Proc. Zool. Soc., London*, 1954, v. 124, p. II.

Porter, A.: Summary of the Report of the Honorary Parasitologist for the year 1954. *Proc. Zool. Soc., London*, 1955, p. III, IV.

Preston, W. S. and Clark, F. F.: Bacillary disentery in rhesus monkey. *J. Infectious Diseases*, 1938, v. 63, p. 238.

Ratcliffe, H. L.: Incidence and natura of tumors in captive Wild Mammals and Birds. *Am. J. Cancer*, 1933, v. 17, N. 1, p. 116.

Rewell, R. E.: Report of the patologist for the year 1947. *Proc. Zool. Soc., London*, 1948, p. II.

Rewell, R. E. and Bridges, R. F.: On outbreak of Shigella Flexneri in seccion among rhesus monkeys. *Monthly Bull. Minist. Health*, 1948, v. 7, p. 25.

Rigdon, R. H. and Stratman, W. K.: A study of the pathological lesions in p. knowles infection in m. rhesus monkeys. *Am. J. Trop. Med.*, 1942, v. 22, N. 4, p. 329.

Rinechart, J. F. and Greenberg, L. D.: Arteriosclerotic Lesions in pyridoxine-deficient monkeys. *Am. J. Pathol.*, 1949, v. 25, N. 3, p. 481.

Rivers, T.: *Viral and rickettsial infection of men.* 1952.

Ross, M. A., Gainer, J. H. and Inner, J. R. M.: Distrophie Calcification in the Adrenal Glands of Monkeys, Cats and Dogs. *A.M.A. Arch. Pathol.*, 1955, v. 60, N. 5, p. 655.

Rudolphi, C.: *Entzoorum sive vermium intestinalium, historia naturalis.* Amsterdame. 1857, v. 2, p. I.

Ruch, T.: *Diseases of Laboratory Primates.* Philadelphia, Saunders, 1959.

Salomon: Ein Beitrag zur Leucose beim Schwein. *Monatsh. Veterinärmed.*, 1955, Bd. 10, N. 5, S. 109.

Saunders, C.: Intracranial haemorrhage in the newborn. *J. Irish Med. Assoc.*, 1953, v. 33, N. 193, p. 10.

Schlotauer, C. F. and Essex, H. E.: Pulmonary acariasis in the monkey. *J. Am. Vet. Med. Assoc.*, 1929, v. 76.

Schlumberger, H. G.: Tumors in parakeets. *All Pets Mag.*, 1953, v. 24, N. 9, p. 120.

Schmey, M.: Das Magencarcinom bei Säugetieren. *Deut. tierärztl. Wochschr.*, 1914, Bd. 1.

Schmitt, M.: *Die Krankheiten der Affen.* Berlin, 1870.

Schoen, R.: Um cas de poliomyelite par cantamination de cage. *Compt. rend. soc. biol.*, 1936, v. 121.

Schreader, G. A.: Diagnostic Test for the Recognition of Tuberculosis in Primates. *J. Am. Tuberc. Assoc.*, 1938, v. 23, p. 397.

Schultz, A.: To Asia after Apes. *Am. J. Phys. Anthropol.*, 1938, v. 23, p. 499.

Scott, H. H.: Report on the Deaths occurring in the Society's Gardens during the year 1926. *Proc. Zool. Soc., London*, 1927, p. I, p. 173.

Scott, H. H.: Report on the Deaths occurring in the Society's Gardens during the year 1927. *Proc. Zool. Soc., London*, 1928, p. 1, 81-119.

Scott, R. B., Te Linde, R. W. and Wharton, L. R.: Further studies on experimentall endometriosis. *Am J. Obstet. Gynecol.*, 1953, N: 5, p. 66.

Smith, H. C.: Pasteurellesis in Monkeys. *J. Am. Vet. Med. Assoc.*, 1954, v. 92, p. 124.

Stadie, R.: Etwas über Erkrankungen von Affen. *Zool. Garten*, 1930, 3.

Stefanopoulo, B. kh., W. Kolle, R. Krause, P. Uhlenhuth: *Handbuch den pathogenen Microorganismen.* 1929, Bd. 7, S. 383-486-752; Bd. 8, S. 487.

Steiner, P. E. *et al.*: Three carcinomas of the tongue in two Monkeys. *Cancer Research*, 1942, v. 2, p. 704-709.

Stott, K.: Twinning in hooded capuchin. *J. Mammology*, 1953, v. 34, N. 3, p. 385.

Tamaschke, C.: Die spontanen Tumoren der kleinen Laboratoriums-säuger in ihrer Bedeutung für die experimentelle Onkologie. *Strahlentherapie*, 1955, Bd. 96, N. 1, S. 150.

Tanaca, T.: Uber spontane Poliomyelitisinfektion bei Affen. *Nagasaki Igakkai Zassi*, 1939, Bd. 17, S. 1802.

Thompson, I. G.: Protosoal parasites. *Proc. Roy. Soc. Med.*, 1929, v. 22, p. 822.

Todd, T. W.: Observations on osteomalacia in the Zoological Collections of Manchester and Cleweland. *Proc. Zool. Soc., London*, 1913, p. 888.

Urban, A.: L'infection tuberculose spontane chez les mammiferes sauvages on captive. Museum national d'Hisore naturelle. *Ann. inst. Pasteur*, 1938, T. 61.

Weidholz, A.: Tuberculose-keine typische Affenerkrankung. *Zool. Gart. Lpz.*, 1928, Bd. 1, H. 3/4.

Wiegert, W.: Todesursachen frischimportierten Oranges. *Zool. Gart. Lpz.*, 1928, Bd. 1, H. 5-6.

Wielbert u. Delorme, B kh.: W. Kolle, R. Krause, P. Uhlenhuth: *Handbuch der pathogenen Microorganismen.* 1929, Bd. 7, S. 383, Bd. 8, S. 487.

Wilson, I. G., Roth, C. B. and Warkany, I.: An analysis of the syndrome of malformations induced by material vitamin A deficiency, effects of vitamin A at various times during destation. *Am. J. Anat.*, 1953, N. 2, p. 189.

Wisner, B.: Epidemie de pneumococcia chez les singers inferieurs, arretée par la vaccination preventive. *Compt. rend. soc. biol.*, 1928, T. 98, p. 458.

Work, T. H. and Trapido, H.: Summary of Preliminary Report of investigations of the Virus Research Centre on an Epidemic Disease Affecting Forest Villagers and Wild Monkeys of Shimosa District Mysore. *Indian J. Med. Sci.*, 1955, v. 11.

Work, T. H., Trapido, H., Murthy, D., Rao, R. L., Bhatt, P. N. and Külkarmi, K. G.: Kuasanur forest disease. III. *Indian J. Med. Sci.*, 1957, v. 11, N. 8, p. 619.

Wurm, H.: Uber eine Milbenerkrankungen der Lunge bei Macacus rhesus. *Zentr. Bakteriol. Parasiten., Abt. I*, 1926, Bd. 98, S. 514.

Zuckerman, S.: A rhesus monkey (macaca mulatta) with carcinoma of the mouth. *Proc. Zool. Soc., London*, 1930, v. 59.

INDEX

...GICAL GARDEN ...CUTTA