

LABORATORY PRIMATE NEWSLETTER

Volume 2, Number 2

April, 1963

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POLICY STATEMENT  
(Revised April, 1963)

The primary purpose of the Newsletter is to provide information on maintenance and procurement of non-human primates for laboratory studies. A secondary purpose is dissemination of general information about the world of primate research. Examples of the kind of practical information that would be useful are as follows: new drugs; novel aspects of cage design; new products; evaluations of various products; references to or short summaries of articles of general interest; experiences in connection with the procurement of monkeys. The Newsletter will also publish offers to exchange monkeys (for example, older monkeys for young or infant monkeys) and requests for monkeys with special characteristics (for example, good breeders or pregnant females). If someone has a special problem, he might want to request help through the Newsletter.

As a rule, only research articles or summaries which have some practical implications or which provide general information likely to be of interest to investigators in a variety of areas of primate research will be accepted for inclusion in the Newsletter. Descriptions of current research projects will also be welcome. It should be kept in mind that the Newsletter is not a formal publication and that it is not likely to be obtainable in libraries. Therefore, citation of Newsletter notes or articles in publications is not recommended.

Information for the Newsletter will be welcome from anyone in any research area who is using monkeys. The Newsletter will appear quarterly and will continue so long as people are interested enough to contribute items of information. The mailing list is open to anyone expressing an interest. There is no subscription charge. However, only new issues and back issues for the current year will be mailed to new subscribers free of charge. Volume 1 of the Newsletter may be purchased for \$1.00. (Please make checks payable to Brown University.)

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Acknowledgements

The Newsletter is supported in part by a Grant (MH-07136) from the National Institute of Mental Health, U. S. Public Health Service.

Fred Stollnitz of the Psychology Department at Brown University has been of considerable help in the preparation of this, as well as previous, issues of the Newsletter.

#### EDITORS' NOTES

Dr. Donald E. Pickering has resigned as Director of the Oregon Regional Primate Research Center. Dr. William Montagna has been appointed, effective August 1, 1963, the new Director of the Center and Professor of Experimental Biology at the University of Oregon Medical School. Dr. Montagna is presently a member of the Biology Department at Brown University and is L. Herbert Ballou University Professor.

As indicated in the present Newspaper Clippings section, Dr. Leon Schmidt has been appointed Director of the National Primate Conditioning Center, which will be constructed on the Davis campus of the University of California.

We might point out that the present issue was delayed primarily because of a lack of contributions. At the moment there is no material for the July issue. We can, of course, use articles, but we have also had almost no contributions for such sections as Recent Articles and Books. It should not be too much trouble to scribble a reference along with, perhaps, a descriptive sentence or two (if the title is uninformative) on a postal card.

CONTENTS

Editors' Notes.....iii

Disease of Unknown Etiology in Monkeys..... 1

A Rapid-Acting Tranquilizer and Pre-Anesthetic Agent..... 3

Information on Congenital Anomalies Sought..... 4

Experimental Primate Breeding Colony at San Diego Zoo..... 4

Recent Articles and Books..... 5

Newspaper Clippings..... 6

Additions to Mailing List..... 8

Address Changes..... 10

Corrections..... 10

## DISEASE OF UNKNOWN ETIOLOGY IN MONKEYS

L. M. van Putten, M. J. de Vries, and D. W. van Bekkum

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A disease of unknown etiology occurs in the monkeys in our Institute. The first symptoms appear from two to six months after arrival and the disease runs a progressive course. So far the disease has occurred in Macaca mulatta, Macaca nemestrina, Macaca irus and in Cercopithecus aethiops. The colony consists mainly of Macaca mulatta monkeys so that the description of the disease is based on the findings in this species. Early symptoms are blepharitis and lacrimation, followed by disappearance of the normal gloss of the hair and patchy hair loss. Later loss of weight may occur with skin changes which differ locally. The skin may be considerably thickened, with formation of coarse folds especially of the skin of the back and the base of the tail (elephantiasis cutis). In addition to an erythema surrounding the orbits, nose and mouth, follicular papules develop in the skin of the face. The margins and interior surface of the eyelids characteristically develop pinhead-sized white nodules. On the skin of the trunk, fine dry scaling is apparent. The nails may show onychogryposis. In the later stages of the disease there is anorexia and severe weight loss. The disease has a high rate of mortality and the severity varies widely among individual animals kept under seemingly identical conditions.

Usually the number of reticulocytes increases early in the development of the disease, sometimes followed by severe anemia, thrombopenia and leukopenia. The bone marrow in these animals usually is of normal cellularity, but with relative increase of the number of erythroid precursors. In one animal, areas of hypocellular marrow were found next to areas of normal cell content.

At autopsy a diversity of lesions of the gastro-intestinal system is found. Yellowish papules are seen on the tongue, often with induration of the viscus. In a number of cases great thickening of the wall of the stomach is present. Similarly affected areas may be found in the duodenum and colon.

The extra- and intrahepatic bile ducts are often severely dilated. The gall bladder also may be distended but it is empty and shrunken in other cases. The wall is often thickened and the mucosa shows hyperemia.

The entire bile tract is filled with a highly viscid bile. In the liver, multiple abscesses are found in a few monkeys. The pancreas may be slightly to considerably indurated. On cross section, cystic spaces filled with mucous fluid are seen in these cases. Lymph glands throughout the body are enlarged. In a few cases petechial hemorrhages in the skin and in mucosal and serosal membranes were present.

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Microscopically the affected parts of the skin show acanthosis with excessive cystic distension of hair follicles by plugs of keratin.

The other changes are:

- 1) Cystic dilation of mucosal glands, associated with an apparent over-production of mucus.
- 2) Proliferation of mucosal epithelium and glandular elements, characteristically breaking through the normal anatomical limits of the mucosa, i.e., infiltrating the submucosa, which contributes to the great increase of thickness of the affected organs.
- 3) Squamous metaplasia of surface and glandular epithelium.
- 4) In some cases, atrophy of glands and necrosis (necrosis of liver and pancreas), probably as a result of retention caused by obstruction by viscid mucous secretion on the one hand and gland proliferation on the other hand.
- 5) A chronic inflammatory infiltrate and fibrosis, probably caused by secondary bacterial infection. In the skin follicular abscesses and in the liver cholangiogenic abscesses may be found.

The changes mentioned above are seen in mucous membranes of the eyelids, tongue, esophagus, stomach, duodenum, colon, bile ducts, pancreatic ducts, bronchi, and urinary bladder. Parasitic organisms or viral inclusion bodies have not been found to be associated with any of these lesions. In two cases a generalized arteriolar disease was present, resembling periarteritis nodosa in morphology and localization.

The pathological features of this disease in many ways seem to be identical to those of so-called X-disease or hyperkeratosis in cattle (Smith & Jones, 1961). The disease in cattle has been shown to be caused by poisoning with chlorinated naphthalenes and allied compounds. An extensive search has not revealed the presence of such compounds in the food and environment of our monkeys. A more detailed description of the disease has been published in the Proceedings of a symposium on bone marrow therapy and chemical protection in irradiated primates (de Vries, 1962).

The staff of the Radiobiological Institute is extremely interested in receiving information of anybody who has experience with a similar disease in the monkey. Photographs of the diseased animals and of the histological preparations are available and will be sent on request.

#### References

- Smith, H. A., & Jones, T. N. In Veterinary Pathology. Philadelphia: Lea & Febiger, 1961, p. 650.
- de Vries, M. J. In "Bone marrow therapy and protection in irradiated primates." Radiobiological Institute T.N.O., Rijswijk, 1962, p. 273.

## A RAPID-ACTING TRANQUILIZER AND PRE-ANESTHETIC AGENT

Phenylcyclidine has proved useful as a safe, rapid-acting tranquilizer and pre-anesthetic agent in work with primates. Phenylcyclidine was developed by Parke-Davis & Co. and was known as experimental compound C-1-395. It was called "Sernyl" during its developmental stage, and will probably be released for general use shortly under a somewhat different trade name. Chemically, it is: 1- (1-phenylcyclidine) piperidine, monohydrochloride.

We have administered more than 100 doses of this drug over a period of two years to cynomolgus (Macaca philippinensis) and rhesus monkeys and anubis baboons. Typically, the dosage was at the rate of 5 mg/kg (I.M.). Effects were observed in less than 5 min. and full tranquilization and flaccid prostration resulted within 10-15 min. The animals returned to what appeared to be normal in approximately 4 hr. In one instance, the drug was given intramuscularly once weekly for a period of five weeks with no local reaction observed.

Phenylcyclidine in combination with pentobarbital sodium was frequently used to produce anesthesia. The former was administered as indicated above followed by the latter, which was administered intravenously and to effect. Anesthesia was maintained satisfactorily for 3-4 hr. by further appropriate intramuscular doses of pentobarbital sodium.

Recently, it was found necessary to remove a 2-day-old infant rhesus from its mother for some 5 hr. A dose of 5 mg/kg (I.M.) phenylcyclidine was administered to the mother and the infant was removed without a struggle in about 4 min. When the infant was returned, the mother was still somewhat unsteady but accepted the infant instantly. No untoward aftereffects were noted in either mother or infant.

The only precaution found necessary was to keep the animals warm after the administration of phenylcyclidine alone, or with an anesthetic. Within 1 hr. after administration, a marked body-temperature drop was noted when the animals were kept in a room which was at approximately 75 degrees F. Body temperature fell as much as 10 degrees F. in the animals receiving anesthetics and several deaths resulted. By supplying heat from heating pads during recovery from the drug, all mortality has since been avoided.

Overdosage will produce convulsive tremors. Occasionally, these tremors were observed for short periods with the dosage level described above.

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## INFORMATION ON CONGENITAL ANOMALIES SOUGHT

I am interested in gathering data on the incidence of congenital anomalies (gross or observed post-mortem) in the rhesus monkey. I would therefore appreciate hearing from any individuals who have such data. I plan to pool the data in order to get a rough estimate of the incidence in breeding colonies. I will send copies of the data obtained to any other workers interested in this problem.

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## EXPERIMENTAL PRIMATE BREEDING COLONY AT SAN DIEGO ZOO

The San Diego Zoo has been awarded a contract by the National Cancer Institute of the National Institutes of Health to study the feasibility of establishing breeding colonies of several species of monkeys. Current cancer research is handicapped by the lack of a suitable supply of small easily-handled primates. The Zoo will study and attempt to develop caging and nutritional requirements for pilot breeding units. Precautions will also be taken to insure that the breeding colony stock will be reasonably free of pathogens.

The research colony comprises 40 "family" cages, a well-equipped trailer-laboratory, 3 full-time Keepers, a Project Director and his Technical Assistant. Presently the colony is acclimating Naviasha vervets, Cercopithecus aethiops callidus; yellow-thighed galagos, Galago senegalensis braccatus; thick-tailed galagos, Galago crassicaudatus; pigmy marmosets, Callithrix pygmaea; and tamarins, Mystax sp. In the process of being collected and delivered are squirrel monkeys, Saimiri sciurea; owl monkeys, Aotus trivirgatus; and cottop-top marmosets, Oedipomidas oedipus. Other species may later be included in the program.

Clyde A. Hill



## RECENT ARTICLES AND BOOKS

### Books

A stereotaxic atlas of the squirrel monkey's brain (Saimiri sciureus). Gergen, J. A., & MacLean, P. D. U. S. Public Health Service Publication No. 933. For sale by the Supt. of Documents, U. S. Government Printing Office, Washington 25, D. C.

A new atlas consisting of 79 plates. Whole hemispheres are shown on each plate. Also included is a section on variability in position of cerebral hemispheres.

### Disease

Tuberculin test in monkeys. Bywater, J. E. C. et al. (Vaccine Testing Unit, Pfizer Ltd., Sandwich, Kent, England) Vet. Rec., 1962, 74, 1414-1416.

Approximately two weeks after arrival, rhesus monkeys were tuberculin-tested with 0.1 ml. purified protein derivative of mammalian tuberculin (containing 2.0 mg/ml). Each animal was examined 24, 48, and 72 hours after inoculation. Reactions were scored as follows: 0--no redness or edema, 1--redness without edema, 2--slight edema, 3--edema, 4--marked edema. A score of 3 or 4 at any time after the first 24 hours was considered a positive reaction. A score of 2 for more than two days was considered a doubtful reaction. Positive reactors were autopsied within one week and negative reactors within 7-9 weeks. Of 2,301 animals tested, 25 showed positive reactions, 21 showed doubtful reactions, and the remainder negative reactions. Autopsy revealed gross lesions of tuberculosis in 13 of the 25 positive reactors, in 2 of the 21 doubtful reactors, and in 22 of the negative reactors. The conclusion is that, while the tuberculin test gives some indication of the incidence of tuberculosis within a colony, it is not reliable enough to be recommended as a means of eradicating the disease.

Secondary hyperparathyroidism in monkeys. Krook, L., & Barrett, R. B. (N.Y. State Veterinary College, Cornell Univer., Ithaca, N. Y.) Cornell Vet., 1962, 52, 459-492.

Perivascular fibrosis of splenic vessels in monkeys. Hopwood, R. R. Amer. J. Vet. Res., 1962, 23, 1303-1306.

### Drugs

Sedation and anesthesia in gorillas and chimpanzees. Marsboom, R. et al. (Research Laboratorium Dr. C. Janssen, Beerse, Belgium) Nord. Vet.-Med., 1962, 14, 95-101.

Dehydrobenzperidol combined with Pentanyl is reported to be very effective as a surgical anesthetic for apes without requiring the use of hypnotic agents.

## Physiology

A surgical preparation for chronic intravenous infusion in rhesus monkeys. Niemann, W. H., Schuster, C. R., and Thompson, T. I. Technical Report No. 62-30, 1962. Laboratory of Psychopharmacology, Dept. of Psychology, University of Maryland, College Park, Maryland.

This report describes surgical and restraining procedures that have been successfully utilized for implantation and maintenance of a chronic indwelling jugular catheter.

## General

On the use of the squirrel monkey in behavioral and pharmacological experiments. Kelleher, R. T. et al. (Smith, Kline, and French Laboratories) J. exp. Anal. Behav., 1963, 6, 249-252. For reprints write to R. T. Kelleher, Dept. of Pharmacology, Harvard Medical School, Boston 15, Mass.

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## NEWSPAPER CLIPPINGS

### DIRECTOR NAMED FOR PRIMATE CENTER; 10,000 SIMIANS TO BE HOUSED ON DAVIS CAMPUS FOR MEDICAL RESEARCH

Dr. Leon H. Schmidt, Director of the Christ Hospital Institute of Medical Research in Cincinnati, Ohio, and Research Professor of Biological Chemistry at the University of Cincinnati, has been named director of the primate center on the Davis campus of the University of California.

Announcement of Dr. Schmidt's appointment as Director of the National Primate Conditioning Center was made by UC President Clark Kerr and Davis campus Chancellor Emil M. Mrak. Dr. Schmidt, a pharmacologist with 24 years of research experience with subhuman primates, will head the 300-acre center, set up under a grant from the National Institute of Health.

As Schmidt sees it, the center has a number of immediate objectives. The first of these is to develop simple and effective methods of collecting, importing, housing, feeding, breeding, handling and observing a large variety of species of monkeys and lower apes.

When such procedures are available, it will be possible to pursue studies with representative species in large numbers and to define their utility for various biomedical investigations.

Although there is considerable current work with subhuman primates, most is being carried out with the rhesus monkey, largely because of the ready availability of this subject and its adaptability to conventional laboratory environments.

Despite this wide use, comparatively little is known about the best methods of obtaining healthy specimens and maintaining and rearing them in captivity. Nor is there any certainty that the rhesus monkey is the most suitable subject for the studies where it is being used. Through emphasis on comparative primatology the center will develop a body of information which should resolve these issues.

The long-range objectives of the center encompass the availability and use of the most suitable species of subhuman primates for illuminating and solving some of the complex social and medical problems of the human primate. Behavioral studies, reproductive problems including those of teratology (such as were associated with the use of thalidomide), investigations of aging processes, as well as work on infectious, cardiovascular, and neoplastic diseases will be accommodated.

These investigations will be pursued by a permanent staff of investigators as well as by guest scientists who will come to the Center to learn of its methods and utilize its unique facilities. Hopefully the center will become a truly national laboratory, the primate biology counterpart of the Marine Biological Laboratory at Woods Hole, Massachusetts.

Schmidt anticipates that within five years the center will have a resident population of some 10,000 lower relatives of man. In view of his past experiences, this estimate may not be unreasonable.

His activities at Cincinnati currently embrace work with some 1,200 rhesus monkeys utilized for research on malaria, tuberculosis, formation of bladder and pulmonary tumors, bone transplantation and the pharmacology of anticancer drugs. Many of today's simple techniques of maintaining and working with the rhesus monkey have been developed in this Cincinnati laboratory.

Work in the center will begin in May, 1963, when the first group of investigators and their simian helpers will arrive on the Davis campus.

Davis Enterprise, Davis, California, Jan. 24, 1963

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