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USE OF THE PIGTAIL MONKEY, *MACACA NEMESTRINA*, IN SPACE BIOSCIENCE STUDIES*

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ABSTRACT

Project Biosatellite was established to study effects of space flight on a variety of living organisms. Part of the study will include placing a Macaca nemestrina in orbit for a month. Physiological changes due to a 30-day period of weightlessness will be used to estimate the hazards to man of extended space flights planned for the near future. Colony management is designed to yield animals free of disease or other stress. Approximately 500 pigtail monkeys will be used in preliminary studies to establish a basis for evaluation of flight data. Early baseline data reveal the Macaca nemestrina is very similar to man in blood chemistry and serum enzyme levels. Hematological values, rate of growth, and responses to stress are comparable to those of humans of equivalent age.

INTRODUCTION

Project Biosatellite was established to study the effects of space flight on a variety of living organisms. Six flights were scheduled, 2 each for 3, 21, and 30 days.

Invitations were extended by NASA to the scientific community for proposed experiments to be included on each flight group. For each accepted experiment a contract defining each principal investigator's efforts was negotiated. Ames Research Center personnel serve as contract monitors, advising, coordinating, and supporting the experimenters individually and collectively.

The 3-day flight was successfully completed September 9, 1967. It included 13 experiments involving amoeba, frog eggs, plant seedlings, and insects for studying effects of weightlessness with and without radiation exposure. Radiation exposure was provided by an on-board strontium-85 source.

The 21-day flight includes tissue cultures, rats, and rapidly maturing plants. Possible alteration of biorhythms and physiological changes caused by prolonged weightlessness will be studied.

The 30-day flight will utilize the pigtail monkey, Macaca nemestrina. Areas of interest include central nervous system activity, cardiovascular activity, and certain metabolic changes.

MATERIALS AND METHODS

The Macaca nemestrina was chosen by the experimenters because it is tractable, psychologically stable, amenable to training, and of a convenient size. It adapts well to changes in environment and has a chronology of maturation which compares well to that of man.

Only males are used because capsule size requires confinement of the monkey in a closely fitting couch. Females have extensive swelling during estrus which occurs at approximately monthly intervals. Removal of the gonads may cause physiological changes obscuring those caused by weightlessness.

COLONY MANAGEMENT

The monkeys are caught in Thailand and Malaya and shipped to the dealer in the United States. The dealer de-worms, tuberculin tests, and selects suitable monkeys for shipment to our facility. Colony management is designed to yield animals free of disease and of proper size and weight for use in the Biosatellite Program.

During our 6-week quarantine period the monkeys must pass two complete physical examinations, be negative on two consecutive tuberculin tests, and have a chest x-ray and complete blood examination within acceptable limits. Stool samples are cultured for enteric pathogens, especially Salmonella and Shigella, and positive cases are identified as to strain and then are treated. After treatment and before release to experimenters, each animal must have at least two consecutive negative fecal cultures. Most animals have at least one stool sample examined for ova of enteric parasites and infected animals are treated. At least two thick smears of blood are examined for malaria, microfilaria, and other blood parasites. Positive cases are treated, and each animal must have at least two consecutive negative samples before it is released to experimenters. Also during quarantine each monkey is tattooed with a 3 digit number and has its tail and canine teeth removed.

After quarantine the monkeys are weighed and measured monthly. The tuberculin test, stool examinations, malaria tests, and blood counts are

repeated every six months. The multiple monkey pens are cleaned daily and the individually caged monkeys are transferred to a clean cage with a clean water and feed cup daily.

All the monkeys are observed daily and any change in a monkey's behavior pattern is recorded. Those few monkeys with undesirable behavior, such as aggressiveness or resistance to being handled, are removed from the colony.

FLIGHT REQUIREMENTS

Approximately 500 pigtail monkeys will be used in preliminary studies to establish a basis for evaluation of flight data.

Each part of the experiment must be developed and tested with the monkey as an indicator of physiological changes due to that part. In flight, the monkey will have nearly full mobility of his head, forearms, hands, and feet. The rest of his body will be restrained to less than 1 centimeter full range of motion in any direction. His couch includes an opening to a feces collector, padding on all pressure points, and access holes for various wires and tubing.

Dr. W. Ross Adey at the University of California, Los Angeles, is principal investigator of experiments on the 30-day flight. For these experiments the monkey will have implanted electrodes for electroencephlographic sensors, cervical and upper thoracic electromyography, a body temperature sensor, an electrooculograph, and sensors of galvanic skin resistance. Dr. Adey's group will have trained the monkey to perform delayed matching and visuo-motor coordination tasks. The monkey's performance will be analyzed in detail and compared with his ground-based performance. Food will be available automatically as a reward for successful psychomotor activity and may be dispensed by ground command.

Dr. Patrick Meehan at the University of Southern California will have the monkey equipped with sensors for electrocardiography and respiration, and surgically implanted blood pressure manometers.

Dr. Abraham Cockett of Harbor Genral Hospital devised the procedure for implanting a urinary catheter and will study urinary steroid levels before and after flight.

Dr. Nello Pace at the University of California, Berkeley, and Dr. Joon Rho at The Jet Propulsion Laboratory, will be studying metabolic alterations before, during, and after flight. Urinary creatine, creatinine, and calcium will be analyzed during weightlessness.

Dr. Pauline Mack at Texas Woman's University is responsible for investigating changes in bone density resulting from the flight.

RESULTS AND DISCUSSION

Implanting the sensors and electrodes and training the animals to operate the psychomotor test panel requires a period of 30 weeks. Since the capsule restrictions limit the size of the monkeys to 15 pounds (6.8 kg), the proper selection of candidates depends on their growth rate. A study was therefore initiated and final data are yet to be obtained.

Macaca nemestrina weighing 4 to 9 pounds (1.9 to 4.1 kg) gain approximately 1 pound (0.5 kg) in 6 months. As the monkeys enter late adolescence their growth rate accelerates gradually. At 9 to 11 pounds (4.1 to 5.0 kg) they gain approximately 1 pound (0.5 kg) every 4 months. When they weigh above 11 pounds (5.0 kg), a divergence in growth occurs, related to the onset of puberty. Those maturing early gain as much as a pound (0.5 kg) a month until they reach 16 to 18 pounds (7.2 to 8.2 kg); then their growth slows rapidly until they reach a mature weight of 20 to 25 pounds (9.0 to 11.4 kg).

Those maturing later continue gaining about a pound (0.5 kg) in 3 months until the onset of puberty, when the rapid growth phase occurs.

To aid in anticipating the onset of puberty a study of epiphyseal closure has been started. Those monkeys in the rapid growth phase show slightly wider epiphyses in the humerus, radius, ulna, femur, tibia, and fibula and nearly complete closure of the epiphyses of the metacarpals, carpals, metatarsals, and tarsals. A few 10-pound (4.5 kg) monkeys with noticeably wide or narrow epiphyses in comparison to the other 10-pound monkeys are being weighed frequently. The theory that epiphyseal changes may precede rapid growth by several weeks is being investigated.

Hematology studies have shown values similar to those of humans of equivalent age. The average adolescent monkey has approximately 45% packed cell volume, 12 to 14 grams of hemoglobin and 9 to 13 thousand white blood cells per cubic millimeter of blood. The differential count shows a ratio of 40% segmented neutrophiles to 60% lymphocytes. Trauma, such as surgery, will cause a 7 to 10 day elevation of white blood cell count to 15 to 18 thousand and a shift in the differential to 50% segmented neutrophiles, 10% band form neutrophiles, and 40% lymphocytes. Part of the change may result from barbiturate anesthesia.

Trauma or infection in mature monkeys results in a less dramatic elevation of leukocytes and less severe alteration of proportions in the differential count.

Blood chemistry studies suggest most electrolytes, enzymes, and other constituents are within the ranges established for man. Some differences exist, however. For example, alpha 2 globulin and gamma globulin are higher in the monkey than in man, whereas albumin, beta globulin, and glucose averages are lower in the monkey than in man, and the observed range is somewhat narrower.

In early tests when a monkey was placed in a couch conforming to the restrictions of the capsule, certain physiological changes occurred. Over the first two or three days there was a lowering of blood glucose, and in most monkeys serum enzymes associated with muscular activity reached very high levels. Over the next two weeks the monkeys demonstrated slow but progressive return to pre-confinement levels.

In a recent test a period of education was instituted. Prior to continuous confinement the monkeys were placed in restraint for a few hours daily and the confinement was gradually increased as the start of the test approached. Because of limitations of time and manpower the length of pre-test training varied. Analysis demonstrated an inverse relationship between hours of training and severity of response to confinement. One monkey which had participated in an earlier couch test showed little change due to confinement.

SUMMARY

Investigation of weightlessness utilizing all forms of living organisms from amoeba to man contributes invaluable information in the study of basic physiological processes. Extrapolation of findings from flights of subhuman primates will aid in reducing uncertainties of projected long term space flight by man. The Macaca nemestrina appears to be an excellent choice for this task.

FOOTNOTE

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