Reports

Biosatellite III: Preliminary Findings

Abstract. *Physiological deterioration in the male macaque monkey flown in Biosatellite III necessitated its recall after 8.5 days of a planned 30-day flight. For the first 7 days the only telemetered signs of a progressive general decline were falling brain temperature and lowered central venous pressure, which occurred in the last 3 days of flight. Fluid loss in flight was high, caused initially by sweating and later by diuresis, and appeared to arise in redistribution of blood in visceral pools as a consequence of weightlessness. Death occurred suddenly 12 hours after the flight and was caused by ventricular fibrillation.*

The recent flight of Biosatellite III, with a male macaque monkey (*Macaca nemestrina*) as test subject, was the culmination of more than 5 years of intense collaborative scientific effort by participating academic institutions and the NASA Ames Research Center. As the experiment grew in complexity from its initial formulation, its final goals included a comprehensive evaluation of the effects of prolonged weightlessness on the central nervous, cardiovascular, and metabolic systems of the primate. The experiment was regularly reviewed by a committee of the American Institute of Biological Sciences which offered valuable advice at all stages of the flight preparations. The flight lasted only 8.5 of a planned 30 days. The following is a preliminary account of major findings, including factors leading to premature termination of the study.

The physiological deterioration of the monkey flown in Biosatellite III is mainly attributed to the effects of weightlessness. These effects may be of considerable significance in prolonged manned flight and in determining safe limits of physical effort by astronauts. However, in view of the surprising termination to the flight, further tests are planned to determine whether certain factors, such as diet and the environmental parameters of temperature, airflow, and humidity, may have sensitized the animal to weightlessness. The monkey was in excellent physical condition at the time of launch on 28 June 1969, and had been fully adapted to restraint in the flight couch and to long periods of isolation.

All physiological sensors functioned perfectly throughout the flight and after recovery. There were 33 channels of physiological information. Telemetry data and data from the on-board flight recorder and camera jointly formed a uniquely complete record of the animal's condition and behavioral responses in weightlessness. The range of these measurements in different body systems and their detailed character are without parallel in any single previous experiment on earth or in space.

Preliminary examination of these data indicate that the monkey remained alert in his waking periods until day 8. Much new information has been gathered on cycles of sleep and wakefulness in weightlessness. From brain wave records, heart rate and respiration, and brain and body temperatures, and from spacecraft data on carbon dioxide excretion, it is clear that the animal lost his normal circadian or 24-hour rhythm and was no longer synchronized to the capsule day-night cycle. This longer period gave a progressive phase displacement of 8 hours in the daily peak of his metabolic and brain wave activities so that by day 8 he slept late into the morning period. No such changes were seen prior to launch in the flight monkey or in numerous control animals.

For the first time in any space flight of man or animals, the occurrence of rapid-eye-movement (REM) sleep was confirmed. This sleep constitutes about 20 percent of normal sleep on earth and, in man, is associated with dreaming. It is essential in full amounts for continued behavioral well-being. Further analysis of the data will indicate approximate proportions of REM and other sleep states. Sleep throughout the flight was characterized by rapid changes in state quite different from base-line studies. Transitions from the waking state to light sleep then to deep or REM sleep and reversion to wakefulness occurred at 20- to 30-second intervals. The first and second nights showed very little deep sleep, but deep sleep occurred in increasing amounts later in the flight. The day periods were also characterized by sudden shifts to brief episodes of drowsiness or actual sleep followed by sudden waking. These rapid shifts in the awake state also characterized brain wave records from astronaut Borman on day 2 of the Gemini GT-7 flight. These shifting behavioral states were also accompanied by marked lability of heart rate, blood pressure, and respiration—phenomena also seen in Borman.

Detailed analysis of nervous and cardiovascular data will continue for many months, but it is clear that the monkey retained all basic features of his terrestrial patterns in these systems.

However, important signs of pathophysiology first appeared in early days of the flight. For the first time in man or animals, pendular eye movements were recorded in the first 3 days of weightlessness and indicate a vestibular-ocular disturbance. The eyes swung slowly and rhythmically from side to side about once per second with progressively increasing amplitude. After four to six such movements, they ceased abruptly, often with strong activity in trunk muscles, which was indicative of brief struggling and probably aversion to sensations associated with these eye movements.

The monkey was trained in two tasks. One involved delayed matching of symbols (DM task), and tested recent memory and perception. The other tested coordination of eye and hand in detecting coincidence of two rapidly rotating objects (VM task). By comparisons with preflight performance, including tests in the spacecraft a few hours before launch, flight tests twice daily elicited only desultory responses. Physiological evidence clearly indicated that the animal alertly watched the tasks that he did not perform. He unfailingly retrieved the single pellet offered "free" at the onset of each task session even when no subsequent responses occurred in that session. The DM and VM tasks were presented in consecutive sessions until day 5, and it was noted that the monkey made some responses to DM task until day 4 of flight. The VM responses must await detailed analysis of the on-board tape recorder data.

Since very little food was acquired as task rewards, virtually all food was taken in "free" feeding sessions at 4:00 p.m. each evening. Twenty pellets were offered and taken in less than 3 minutes on the first days of flight. Usually the oral pouches were filled with four to six pellets before chewing began. The pellets were then masticated in the following 1½ hours.

The monkey consumed all water offered until day 8 of flight. The daily ration was 360 ml in the day period and 120 ml at night. A ground command on the fourth night gave additional water for a total water intake of 720 ml for 24 hours. This was done in an attempt to stimulate task operation.

The animal's condition deteriorated sharply on day 8. Food and water were no longer taken during this period, and the heart rate slowed to 70 beats per minute with an accompanying sharp drop in blood pressure. Brain wave records showed increased slow waves but were consistent with a sleeping rather than a comatose condition. This situation occurred at the end of a period in which the only telemetered signs of a progressive decline in general condition was a slow fall in brain temperature to 35°C compared with 38.2°C at launch.

The blood pressure sustained until day 6, despite a decline in heart rate from 170 beats per minute early in the flight, to 110 beats on day 6. Thereafter, diastolic blood pressure fell below ground base-line values and continued to decline until recovery. Central venous pressure (measured in the right atrium) clearly indicated changing central vascular patterns. From a preflight mean pressure of − 0.5 mm, there was a rise during the early hours of flight to + 0.75 mm. This higher level waned slightly in the first 4 days. On day 5, central venous pressure again rose to + 0.75 mm, which was interpreted as a cardiovascular adjustment. This did not alter either heart rate or blood pressure. It coincided with a high fluid intake, and is interpreted as an attempt at restoration of venous volume. Central venous pressure declined to negative levels in the last 2 days of flight. Photographic records have confirmed that the animal was alert and active until day 8. Immediately prior to deorbit the heart rate had fallen to 39 beats per minute.

Recovery occurred in the vicinity of Hawaii 8½ days after launch. The capsule was opened at Hickam Field approximately 3 hours after reentry. The monkey was noted to be cold and vital signs scarcely perceptible. Capsule temperature had remained at 20°C throughout the flight, below the desired mean of 24°C. The significance of this factor and associated movement of air over the immobilized animal is to be tested further since preflight simulations did not indicate an environmental hazard for animals so tested in a 1 *G* environment.

Careful resuscitation was attempted with blood transfusion, intravenous fluid, and electrolytes. There was a good response, and 6 hours after recovery the heart rate was 75, and blood pressure was 75/26. However, blood pressure remained labile and was stabilized only by judicious administrations of dextran. The monkey's general condition continued to improve, his pupillary reactions were brisk, and he frequently attempted to raise himself off the couch with well-coordinated movements of head and all four limbs. Twelve hours after recovery, brain temperature had risen to 35.8°C from 34.2°C, and the brain wave record resembled that of light sleep. At this stage ventricular fibrillation occurred with sudden onset and further attempts at resuscitation were unsuccessful.

The animal lost considerable weight, approximately 1 kg between launch and recovery. At autopsy no major pathology was detected in heart, lungs, gastrointestinal, renal, or nervous systems. All tissues appeared healthy and are being subjected to a detailed histological examination. Small bruises on the liver and some bruising of the heart, both of recent origin and attributed to reentry, were the only signs of injury. X-ray bone densitometry studies, before and after flight, have shown a greater loss of calcium in the test monkey than in control animals similarly restrained on the ground.

The fluid loss, approximating 20 percent of the original body weight at launch, has been closely investigated, both from physiological data and data on water condensed in the spacecraft. The following account of circumstances leading to the animal's collapse implicates weightlessness as a prime factor and is relevant to environmental constraints, task requirements, and mission durations currently planned for manned spaceflight.

Spacecraft data clearly indicate an early and profound loss of fluid by insensible perspiration. After day 4 this mechanism was no longer as severe. The urine output increased steadily to almost diuretic levels by day 8 of flight. As nearly as can be determined, the net negative fluid balance over the 8-day period was 1250 to 1280 ml. A primary mechanism of the continued loss of water in the later stages of flight appears to relate to a redistribution of blood volume in the thorax as a consequence of weightlessness. This redistribution would evoke a diuresis with a concomitant electrolyte loss. In addition, part of this loss was from intracellular water from tissue and was confirmed by radioactive potassium measurements.

The critical measurement from this study in relation to manned flight is the finding of a high fluid loss, even in a sedentary resting subject. This loss is related to shifts in blood volume and its distribution and involves perturbations in body fluid balance, electrolyte metabolism of sodium and potassium, and, ultimately, the stability of the cardiovascular system.

There have been a number of reports by astronauts of sweating and vasomotor instability associated with subjective feelings of heat and cold. Marked distress with tachycardia and respiratory embarrassment have been widely reported on exercise during extravehicular activity. The well-documented sequence of events leading to collapse in this monkey suggests the need for a guarded approach to design of missions for man that might involve extreme effort after a considerable exposure in weightlessness.

The findings from Biosatellite III presented here are necessarily preliminary. However, the important findings listed above characterize this mission as highly successful in revealing physiological effects of weightlessness in spite of the reduced duration of the experiment. They also indicate the great value of carefully designed animal experiments in collection of important biomedical data relevant to manned flight, particularly where the physiological sensors and required experimental control are difficult or impossible to secure in manned flight.

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19 August 1969