

N79-19022

Paper No. 13

AIRCRAFT FLIGHT SIMULATION OF SPACELAB EXPERIMENT USING AN IMPLANTED TELEMETRY SYSTEM TO OBTAIN CARDIOVASCULAR DATA FROM THE MONKEY

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ABSTRACT

The utility of a multichannel implantable telemetry system for obtaining cardiovascular data was tested in a monkey with a CV-990 aircraft flight simulation of a space flight experiment. Valuable data were obtained to aid planning and execution of flight experiments using chronically instrumented animals.

INTRODUCTION

The utility of multichannel implantable systems for telemetering cardiovascular variables has been demonstrated in ground-based experiments (1,2). Previous multivariable systems were comparatively large and suitable only for animals weighing at least 20 kg such as large dogs, baboons, or chimpanzees (1,2). Advances in miniaturized, hybrid circuit modules and use of inductively coupled power have made it possible to design a multichannel unit for implantation in monkeys (or dogs) as small as 10 kg. This report describes the evaluation of this type of system in an aircraft flight test simulating a space flight experiment. Basic design features, implantation technique, and initial results are presented. A metabolic experiment performed simultaneously has been reported separately (3,4).

SYSTEM DESCRIPTION

The basic operating principle of the implanted telemetry system is conversion of analog data to a multiplexed, pulse-width-modulated (PWM) format which frequency-modulates (FM) a radio-frequency (RF) transmitter, as described previously (1). The system components placed internally include two pressure transducers, a temperature sensor, and an electrocardiographic (ECG) lead (Figure 1). The transducers are connected to a hermetically sealed mainframe package (6 cm long, 2.4 cm wide, and 1.3 cm thick) containing power converter, signal conditioner, and 88-MHz transmitter with integral transmitting antenna. An attached Silastic-covered coil receives power by inductive coupling from an external coil driven by a 250-kHz oscillator (Figure 1). Total weight of the implanted unit is approximately 40 g. The system

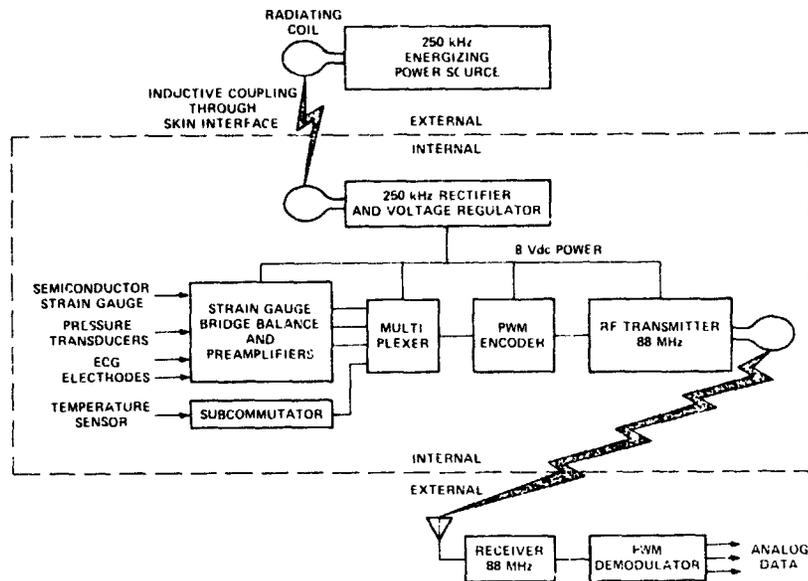


Fig. 1- Inductively powered multichannel telemetry system functional elements

is completed by a receiver and demodulator which convert the PWM signal to the original waveforms.

Transducers and Signal Conditioners

The pressure transducers are bonded semiconductor strain gauges enclosed in a titanium case. One of the transducers is 3.5 mm in diameter, operated as a 500-ohm vertical half bridge. This small size makes it especially suitable for insertion in the descending thoracic aorta. Since long-term zero drift could be a problem with this size transducer, it was a.c. coupled to provide a frequency response of 0.03 to 100 Hz. The second pressure transducer is 4.5 mm in diameter, also a 500-ohm half bridge. It has greater long-term zero stability with a frequency response from d.c. to 100 Hz, and was used for left ventricular pressure measurement. Connecting leads may be any length, but we find 20 cm suitable for monkeys and small dogs.

The single ECG lead consists of a bipolar pair of Silastic-covered, 100-strand, 50-gauge stainless steel wires terminating in 3-mm uninsulated loops. Frequency response at the output is 0.1 to 100 Hz.

Signal conditioning includes bridge completion and balancing for the pressure cells, and amplification of pressure and ECG signals prior to multiplexing. Two additional d.c.-to-100-Hz channels are available if desired.

The sixth channel is subcommutated to provide a total of eight additional subchannels; four of these are active. One is used for temperature, and the other three for system monitoring, although all could be used for physiological data if required. The thermistor temperature sensor is positioned to project approximately 1 cm from the main package in order to detect deep body temperature. The stainless steel case required for thermistor sealing results in a 30-sec time constant. The engineering variables monitored are the unregulated voltage from the internal receiving coil, and the ± 3.7 -V regulated output from the power supply. After subcommutation, these channels are amplified and multiplexed.

The hybrid signal conditioner modules contain differential amplifiers with adjustable gain to a maximum of 300. Higher gain can be provided for applications with very low-level signals such as EEG. Gains are adjusted to meet the ± 1 -V range of the multiplexer. The pressure channel gains are 120, and the ECG amplifier gain is 50. Pressure transducer signal conditioning requires approximately 11 mA at 3.7 V, and the remainder, approximately 2 mA.

Multiplexer, Transmitter, and Receiver

Time-division multiplexing of the analog signals is achieved with a low powered CMOS device. This technique converts the polarity and amplitude of the original signal into the width or duration of a pulse (PWM). The basic clock rate for system timing is 10 kHz. Time frames containing eight pulses or "words" are generated at 120 Hz (Figure 2). One of the eight words is a

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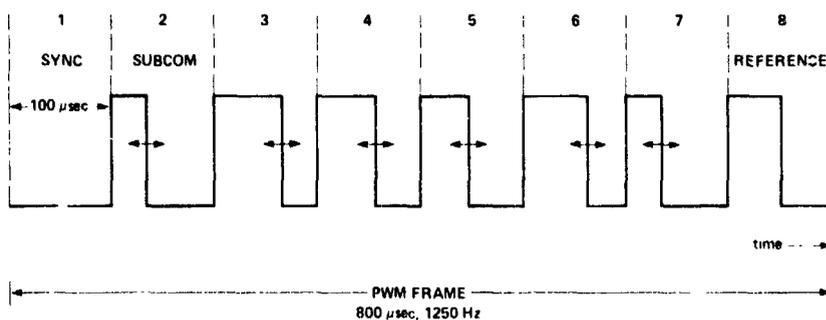


Fig. 2- Pulse width modulation logic of the implanted unit multiplexer

blanked pulse denoting the initiation of the sampling sequence. A second is a system zero reference. The other six words are used for the physiological and system monitoring data. The five high-frequency channels are each sampled at 1250 Hz, providing a signal frequency response of at least 100 Hz. The sixth word samples each of the eight subcommutated channels at 156 Hz, providing a frequency response of at least 15 Hz on each of the eight possible subchannels.

The maximum desired modulation of $\pm 80\%$ alters channel pulse duration ± 40 μ sec. Signals exceeding the ± 1 -V multiplexer range will cause overmodulation with saturation and clipping; excessively low level signals will contain noise.

The train of PWM information then frequency-modulates (FM) the 88-108-MHz RF carrier of the transmitter, which broadcasts from the internal loop through the tissue to an external antenna and telemetry receiver. The receiver bandwidth is 500 kHz to provide an acceptable rise time for the PWM signal. The transmitter operates within the maximum allowable field strength of 50 μ V/m at 15 m for noncommercial applications. Despite this constraint, the transmitter easily achieves a 5-m range even in a noisy RF environment.

The encoding chain is designed to be independent of minor RF oscillator frequency drift and small variations in signal strength. Since the data are coded into the duration or width of each pulse, a highly linear frequency response in the transmitter and receiver is not required.

Demodulator, Display, and Recording

The received signal is coupled to a demodulator which reverses the encoding process (1,5). The receiver output is clipped and limited in the demodulator to remove effects of amplitude variations. The individual decoded analog waveforms are then displayed on a CRT and processed in a standard manner with onboard direct writing and analog tape recorders, and a digital computer.

Power

No active power source is implanted. All energy for system operation is inductively coupled from an external energizing coil (7 cm o.d.) to an internal receiving coil (5 cm o.d.). The power source for the external coil supplies 250 kHz and operates at 20 V, 150 mA. A vest maintains the external coil position, and the coil power supply operates from the 115-V a.c. line. Alternatively, the coil supply can be powered by rechargeable batteries, with the entire assembly contained in the vest, to obtain data from the unrestrained animal.

The internal coil and power rectifier-regulator combine to provide an 8-V-d.c., 15-mA supply for operation of the internal system components. Total power consumption is approximately 150 mW.

System Accuracy

The primary determinants of accuracy in this system are environmental RF interference, transmitter-receiver distance, percentage channel modulation, nonlinearity, and drift. At 80% modulation, 5-m range, in a relatively noisy environment, noise at the output is less than 0.1% of full scale, nonlinearity 0.25%, and zero gain instability less than 1% for a nominal accuracy of the total system of approximately $\pm 2\%$, excluding transducer drift. Assessment of transducer stability requires periodic calibration and comparison with a reference standard (Figure 3).

IMPLANTATION

A completed unit ready for implant is shown in Figure 4. The entire unit is placed within the thoracic cavity, using surgical techniques similar to those reported previously (1,2). In our laboratory, the pressure transducers are coated with TDMAC-heparin complex (Polysciences, Inc.) prior to implant to minimize the possibility of thrombus formation. The main unit is stabilized on the rib cage in the intrapleural space deep in the posterior thoracic gutter just above the diaphragm. The internal coil is positioned just cephalad to the main unit in an area where the chest musculature is minimal. Antibiotic coverage is begun the day of surgery and continued 5 to 7 days after surgery.

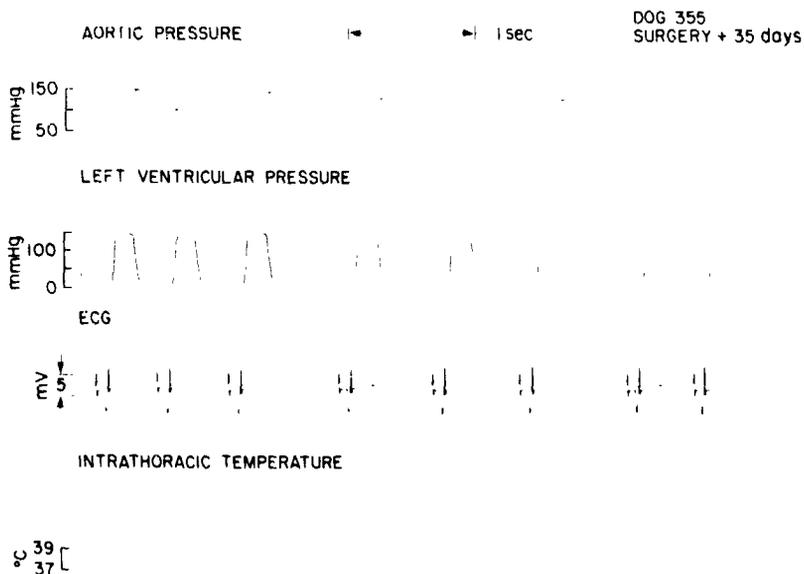


Fig. 3— Representative data from a 10-kg dog 2 weeks after implantation with comparison waveforms from a manometer-tipped catheter

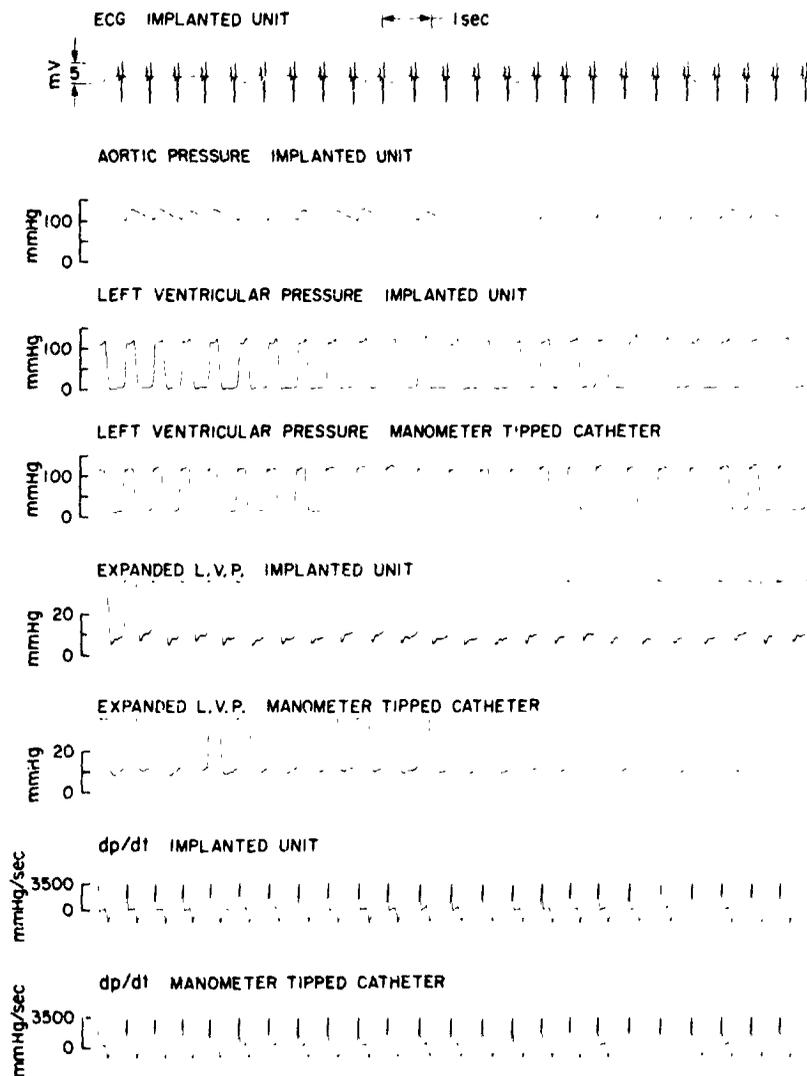


Fig. 3(b)— Concluded

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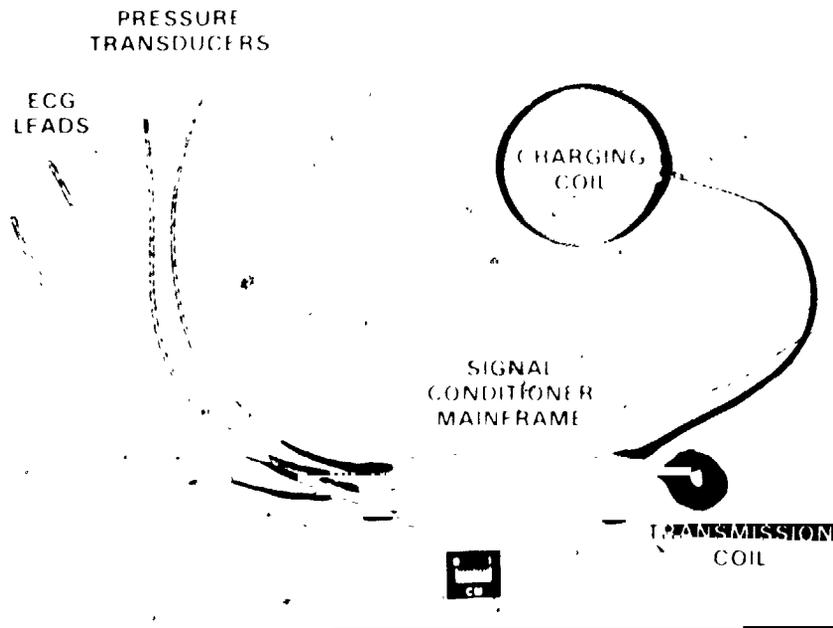


Fig. 4— Multichannel telemetry unit prepared for implantation

RESULTS OF OBSERVATIONS FROM FLIGHT TESTS

To date, units have been implanted in eight monkeys and three dogs. Implant durations with healthy animals have ranged from 64 to 490 days. Durations of full signal output from the units have ranged from 31 to 231 days. The shortened survival times resulted from deliberate sacrifice of the animal to study the effects of the implant and to recover the unit for evaluation, not from long-term or delayed illness caused by the presence of the device.

The postoperative course was generally smooth except for late breakdown of the skin at the incision site in the two flight animals. Detailed hematological and related data on the two *Macaca nemestrina* animals prepared for the flight test are contained in Table 1. These data are representative of the findings from all animals. The most consistent changes were decreased weight, subsequently remaining stable, and anemia, resulting from blood loss during surgery. Progressive recovery and return to normal is apparent. The magnitude and duration of leucocytosis was variable, with little change in three of the rhesus monkeys. X-ray examination has shown a left lower lobe infiltrate which gradually clears. The time to recovery with normal hematology and X-ray findings was 6 to 8 weeks. The tissue

Table 1- History of the Experimental Monkeys
M. nemestrina

| Animal no. | Date, 1976 | Year acquired | Est. age, yr | Weight, kg | Hct, % | Hgb, g% | RBC, $\times 10^6$ | WBC, $\times 10^3$ | Plasma protein, g% | BUN, mg% | Comment | | | | | | | | | |
|------------|------------|---------------|--------------|------------|--------|---------|--------------------|--------------------|--------------------|----------|-----------------------|-------|-------------------|------|-----|------|-----|----|--|--|
| 603 | 3/23 | 1969 | 15 | 16 | 44 | 15.0 | 5.5 | 8.9 | 7.4 | | Flight animal Surgery | | | | | | | | | |
| | 3/24 | | | | | | | | | | | | | | | | | | | |
| | 3/31 | | | | | | | | | | | 14.25 | 32 | 10.5 | 4.0 | 13.3 | 6.9 | 13 | | |
| | 4/2 | | | | | | | | | | | | 33 | 11.5 | 5.5 | 19.1 | 7.7 | | | |
| | 4/8 | | | | | | | | | | | | 34 | 9.8 | 4.8 | 11.4 | 7.4 | | | |
| | 4/27 | | | | | | | | | | | | 39 | 13.4 | 5.0 | 11.9 | 7.8 | | | |
| | 5/5 | | | | | | | | | | | | | | | | | | | |
| | 5/10 | | | | | | | | | | | | | | | | | | | |
| | 5/17 | | | | | | | | | | | | | | | | | | | |
| | 5/24 | | | | | | | | | | | | | | | | | | | |
| 604 | 7/26 | 1974 | 9 | 14.4 | 38 | 12.7 | 5.7 | 10.6 | 7.5 | | End flights (5/21) | | | | | | | | | |
| | 8/9 | | | | | | | | | | | 13.8 | 47 | 13.1 | 6.1 | 6.9 | 7.0 | 13 | | |
| | 3/31 | | | | | | | | | | | 11.8 | 42 | 11.8 | 6.2 | 14.9 | 8.2 | 15 | | |
| | 4/6 | | | | | | | | | | | | 42 | 13.0 | 5.9 | 6.7 | 7.2 | | | |
| | 4/15 | | | | | | | | | | | 10.5 | (42) ^a | 10.6 | 5.0 | 21.0 | 7.9 | | | |
| | 4/27 | | | | | | | | | | | 10.5 | 32 | 10.4 | 4.2 | 11.6 | 8.3 | | | |
| | 5/24 | | | | | | | | | | | | 34 | 11.6 | 5.0 | 11.6 | 8.1 | | | |
| | 7/9 | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |

^a Accuracy questionable.

changes were those expected with thoracic surgery and placement of an implanted device, and the unit is satisfactorily tolerated.

Failure modes of the telemetry system have been variable and of the type likely to occur with any instrumentation inside the body for a long period. In three cases, transducer leads eroded at a tie-down point. Occasionally, internal electronic components have failed. In general, the implant experience indicates the type of improvements needed in future units. Overall, the system operated as designed.

Data have been obtained repeatedly from dogs during treadmill exercise and from awake, chair-restrained monkeys in ground-based tests. In the airborne simulation of a space flight experimental environment, eight flights with over 50 takeoffs and landings were conducted over a 16-day period. The five initial flights were made primarily to check out the onboard recording system. Signals from the implanted unit were always present. For the final week (three flights), the monkey (#603) was fitted with a vest containing the energizing coil and sealed into the pod. Data were obtained and recorded on each of the three flights.

A typical in-flight record is shown in Figure 5, and the effect of lower body negative pressure (LBNP) in Figure 6. The aircraft configuration would not permit the LBNP test in flight, so it was performed with the aircraft on the ground. In-flight heart rates averaged 135 beats/min, and arterial blood pressures averaged 135/90 mm Hg.

Distance between the coplanar external and internal coils could vary about 2.5 to 4 cm, with small degrees of relative motion tolerated without loss of signal. Larger variations in these relationships caused transient signal loss.

During the prolonged period of confinement, the jacket and oscillator supply for the energizing coil within the pod caused skin irritation, and on one occasion, a pressure point over a vertebral process produced a slough of a 2-cm-diam area of skin. This has since cleared without complications.

DISCUSSION

The results indicate that the simulation was successful. The telemetry system operated within the design limits, there were no radiofrequency interference problems, and valuable experience was gained which will aid future planning for flight experiments.

A major improvement for future development of the telemetry system is circuitry with even less power consumption. Decreased power requirements would decrease the amount of energy to be transferred and permit greater latitude in placement of the energizing coil. An increase in the energizing coil size and the power supplied to it is also important, as well as providing a longer cable length so the energizing oscillator can be located outside the pod. These changes are relatively easy to implement.

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CV 890 SIMULATION

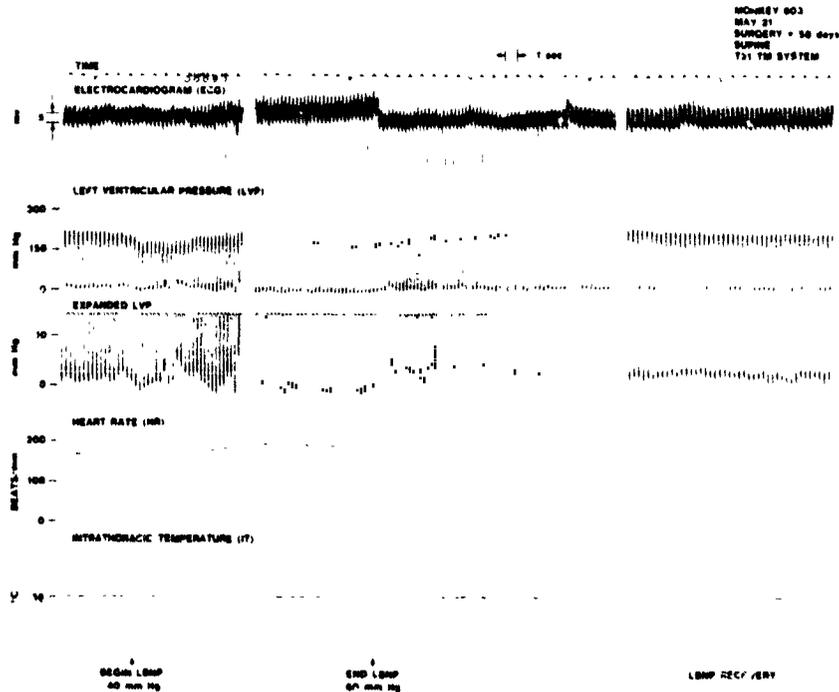


Fig. 6— Changes with lower body negative pressure recorded onboard the aircraft from the pod with the test *Macaca nemestrina* (#603)

Other refinements needed in future units include increased stability of the oscillator frequency with less susceptibility to failure at low power levels, improved transducers with decreased zero drift and longer leads, reinforcement at stress points, and smaller overall size of the implanted electronics package. Frequency stability will reduce the need for receiver tuning and will simplify operation. More stable miniature transducers will remove the need for capacitive coupling and the associated long time constant following power interruption. Smaller overall package size will reduce the extent and duration of the intrathoracic changes.

Monkey skin does not tolerate trauma nearly as well as dog skin. At least 2 months should be allowed for surgical recovery before pod insertion to reduce susceptibility to skin irritation from jackets or other items placed on the animal. Foreign materials over the skin should be minimized, and if used, a protective layer should be provided with extensive padding coupled with careful skin hygiene. An access port must be provided to permit this care. A suitable approach could be the arrangement used in the glove-box or germ-free animal enclosure.

Some other details regarding the working environment should be noted. In the confined quarters of an aircraft or similar situation, device controls, recorder displays, and similar items directly related to the specific experiment must be clustered with minimal distance between them, and such items must be located at a convenient work height.

The technologic advances permitting the miniaturization needed for the implanted telemetry unit and its successful operation without an implanted power source forecast similar units for even smaller animals, with energy received from coils located in the wall of the cage (6). Alternatively, for larger animals, a selection of modules with a range of transducer types can be made available. The necessity of changing experimental designs can then be met by implanting various combinations of modules without requiring a completely new multichannel system for each type of experiment.

This system expands the capability to obtain the more meaningful data provided by study of awake animals in a wide variety of conditions, particularly onboard future space flights and in similar stressful environments. Other obvious applications include study of the effects of drugs, analysis of psycho-physiological interactions, and similar investigations requiring long-term observation with minimal interference. The unit is available commercially (Konigsberg Instruments, Pasadena, Ca., Model T 21).

CONCLUSIONS

The simulation was useful in demonstrating the following:

1. Cardiovascular instrumentation can be chronically implanted in *Macaca nemestrina* and operated successfully in aircraft flight experiments simulating space flight conditions. Many hours of data were telemetered from all channels of a representative implanted unit on each of eight flights over a 16-day period, thus fully satisfying the basic purpose of the simulation.
2. Improvements are needed to maintain continuous operation of the implanted unit. The proper relative position must be maintained between the internal and external coils. The implanted device was designed to operate in an attended mode with ready access to the animal. The fact that any data could be obtained from a completely enclosed animal even after 5 days without adjustments represents a highly significant achievement. Solutions to the coil positioning problem are a) inclusion of an access port in the pod enclosure, and b) provision of an external energizing coil with a greater field strength over a larger area. The latter approach has been implemented; evaluation is continuing, but current results indicate satisfactory operation.
3. The investigator work space and the data processing capability are important factors in efficient conduct of the experiment and are additional elements requiring careful planning.

4. Postoperative recovery time for macaques after intrathoracic implantation is 6 to 8 weeks, approximately 4 weeks longer than for dogs. The long lead times with chronically instrumented animals must be considered in planning for flight experiments.

5. The knowledge gained from the simulation should permit successful accomplishment of this experiment in a space flight environment.

ACKNOWLEDGMENT

Many people contributed to the successful outcome of this simulation. The pod enclosure, animal insertion and maintenance, and the simultaneous metabolic experiment were provided by A. M. Kodama, R. C. Mains, D. F. Rahlmann, and their assistants at the Environmental Physiology Laboratory, University of California at Berkeley; their efforts are greatly appreciated. For the large number of Ames Research Center personnel whose dedicated work made the test possible, particular thanks are given to S. Kurasaki, J. Connolly, and C. Muehl, as the representatives of this group, and to Mrs. Carol Meaney, who prepared the manuscript.

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