BIOLOGIC EXPOSURES TO SPACE ENVIRONMENTS

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INTRODUCTION

OF considerable importance in the planning of any exploratory program designed to carry man into new and incompletely known situations is the requirement for a valid and objective evaluation of the risk involved. Technological efforts now under way on an international basis to breach the cosmic space frontier with a manned earth orbiting vehicle have drawn a focus upon this aspect of the total program far more searching and critical by a greater variety of people than ever enjoyed before by any medical or biological program of investigation.

One of the traditional means by which any new risk to mankind is evaluated, whether it be in the exposure to a new disease or an unknown environment is through the use of biological specimens under carefully controlled experimental conditions. It is quite understandable, therefore, why animal experimentation under space-equivalent conditions would comprise, from the standpoint of the biomedical scientist one of his most reliable and useful means of estimating the human hazard involved.

There are three underlying principles for probing into space with biologic payloads.

1. There is a continuous requirement to validate physiological predictions.

2. The necessity for proving the feasibility of man's venture into space is implicit in the well-conceived biologic experiment in space vehicles.

3. The use of biological equivalents of man in evaluating the space systems adequacy to provide the life sustaining requirements, is a logical precursor to manned space flight.

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Inherent in these three objectives is the basic premise that the experiment is so conceived as to furnish reliable data for supporting man's inevitable ventures into the realm of space. It is not the purpose of this paper to review all the work accomplished by many outstanding, dedicated, ingenious scientists whose knowledge and foresight are a credit to the international bioscience community. Rather, the material analysed for the purpose of this summary was found contained in relatively few reports, since the criteria set forth required that only those experiments be included which utilized rocket engine thrust to propel the biopack into space equivalent atmospheres. This stipulation was made in order to provide pertinent data on not only the biologic effects of the space environment itself but also those induced by the dynamic vehicular forces contained in the total flight.

Three Russian[2,3,4] and three American[1,5,6] published reports (and the as yet unpublished Russian[8] orbital flight with recovery of the two canine occupants, and as yet unpublished American[9] ballistic flight of a small primate, SAM space) fell into this category. Of these the former contained the great preponderance of data in terms of both numbers of exposures and range of stresses encountered. Owing to the diversity in design and execution of these reported experiments it was not found practical to review the total results as a homogeneous package except in certain broad aspects and instead to extract the highlights from the reports of each separate working group, considered here in order of their date of publication.

LITERATURE REVIEWED

1949–1952

The Henry group[1,7] represents the pioneer work accomplished to study the biologic effects of space flight and covered eight separate rocket flights using five V-2's and three Aerobee rockets. Initially, the primary objective was to test and demonstrate the feasibility of a prototype ejection escape mechanism for use in the X-2 aircraft and secondarily to study the biologic effects of the zero gravity state. In all of the V-2 and the first Aerobee flight, recovery of the intact specimen was unsuccessful due to a complete failure of the parachute system. Apparently, the single chute was automatically deployed under insufficiently stabilized conditions of both altitude and velocity which resulted in opening shock forces of unacceptable magnitude. Between Aerobee I and II, the entire parachute system was redesigned using a 2-chute system with the drogue stabilizing the nose cone free-fall to a point where main chute deployment was successful. This modification proved successful and all animals in Aerobee II and III were recovered.

As the work of this group progressed, their objectives underwent reorientation and became one of primary interest in the zero gravity effects upon circulation. An average of 2½ min of weightlessness during which arterial and venous pressures, EKG, pulse, and respiration values were recorded. Narcotized biologic specimens were used and there were observed no significant changes in cardio-respiratory function, leading to the conclusion that in a properly secured, positioned, and anesthetized animal there were no physiological disturbances from rocket flight which provided several minutes of weightlessness.

An additional dividend from the Henry group resulted from their photographic record on the behavior of mice in rotating drums during the zero gravity phase. Although no conclusions were drawn on the basis of the two exposures, the results were extremely interesting and the reviewer was left wondering as to why initial findings were never augmented and validated by subsequent similar work. Basically, the question was, could visual and/or tactile stimuli replace whatever sensory inputs were provided by the labyrinths to maintain a sense of security and orientation in the weightless state?

In Aerobee II, the labyrinthine treated mouse serendipitously found a firm clutch on the wall of the drum, realized his good fortune and rode out the zero-*g* period with composure while his untreated companion missed his small foothold and floundered around in mild panic. On Aerobee III both mice were normal, but only one was provided with an easily acquired foothold which he found and clung to continuously while his drum mate without the paddle repeated the performance characterized by disorientation and floundering.

Registration of data by telemetry and recovery of the photography data even after very high impact forces presented no problem and useful data on both dynamic vehicular forces and biologic parameters were obtained in all flights.

1957 Galkin, et al.[2]

The stated objectives of this group were listed as:

1. The study of safety factors in manned space flight.
2. The flight test of a hermetically sealed cabin in a missile nose cone equipped with a recovery system; both capable of sustaining life to 130 miles altitude and returning a live subject.
3. A study of immediate and delayed biologic effects resulting from rocket flight.

The general design of the experiment was reported as follows: Dogs were used uniformly as subjects in these and all subsequent USSR rocket experiments due to their practicability and ease of pre-training. Pairs of dogs, one anesthetized and one normal, were placed in similar hermetically sealed biopacks contained in the nose cone of a rocket vehicle which achieved an altitude of 130 miles with a total weightless period of $3\frac{1}{2}$ min. A parachute system was used to first stabilize nose cone altitude and terminal velocity and then reduce final impact levels to biologically acceptable values. Data is not available citing the number of failures and successes in the total programme yet the group pointed out that initial difficulty was experienced in the recovery system which necessitated some modification before successful recovery was achieved. Fourteen dog exposures (7 rocket flights of 2 each) are cited but final protocols list only 6 dog subjects by name although some dogs were flown twice.

Cabin environments were maintained as follows: Ambient pressure at 760 mm Hg with minimum at 460 mm Hg CO_2 content between 0·2 and 1·8 per cent with normal alveolar CO_2 values being maintained by demand injection of O_2 as required by respiratory depletion of the ambient pressure.

Complete pre- and post-flight physiological determinations were made including blood studies, chest X-ray, EKG, pulse, blood pressure, respiration, body temperature, weight and observation of behaviour during pre-flight confinement in capsule for periods of three hours and under acceleration forces on the centrifuge approximating launch and re-entry dynamic stresses. During actual flight EKG, pulse, respiration, and blood pressure values were telemetered, the latter sensed by indirect oscillometry using an exteriorized loop of carotid artery. Motion pictures of 24 frames/sec were taken of the subjects throughout the entire mission.

Physiological changes showed maximum change during the "active" phases of flight, during launch and re-entry with increases of all values of pulse, blood pressure, and respiration representing the most constant finding in the normal dogs. In the weightless state, all values returned quite rapidly to normal once a steady rate free fall of the nose cone was established.

In the anesthetized animals the changes were much less pronounced and lacked uniformity between the subjects; the most constant change being an increase in respiratory rate during launch and re-entry. EKG findings were generally not significant and well within limits of normal variation shown by the animals in training. The most significant EKG change noted in all subjects was a marked inversion of the *T* wave complex and this occurred in a female dog under training with no environmental stress being applied.

Behavioral changes as revealed by the photographic film were fairly constant with the predominance of increased motor activity being recorded during engine light-up and launch, and again with first impact of the deceleration forces. During the weightless period completely normal behaviour and alertness were reported.

Data recorded on the capsule environment revealed a remarkable stability of both pressure and temperature with the capsule air temperature ranging only from 25·0 to 25·5°C during the entire mission. Telemetry worked best during the coasting phase and poorest during re-entry. The group felt that considerable improvement was needed in this particular aspect of the investigations.

Conclusions reached by this group were as follows:

1. Dynamic forces during launch and re-entry have the greatest effect on the "organism of dogs".

2. Weightlessness caused no significant alterations in either vital function or behavior.

3. The hermetically-sealed cabin and components maintained a thoroughly adequate and reliable life support environment throughout the mission.

4. The problem of stabilizing the gyrations of the nose cone during the deceleration phase was not satisfactorily resolved during these experiments. Prior to drogue chute release, severe multi-directional *g* forces were imposed upon the subject by the oscillations and tumbling of the nose cone which imposed *g* forces in a magnitude and vector which were "unacceptable" to the subjects. Both rectal and oronasal hemorrhages were noted in some of the recovered subjects.

5. The prolonged "return to normal" time of the increased cardiac activity during the weightless period "occurs as a result of the partial adaptation of the animals to this unusual condition".

6. Since the anesthetized dogs showed little change during the mission and practically no effect during zero *g*, "it can be assumed that the changes in pulse, respiration, and blood pressure observed during the weightless period in the conscious animals were probably a non-specific vegetative reaction to an unusual stimulus".

1958 Bugrov, et al.[3]

The objectives of this group were stated as follows: To explore the feasibility of ejecting living specimens under emergency conditions at high altitudes and fast speeds without the protection of a pressurized capsule, relying upon a pressure suit and "escape truck or rack" to contain the restrained subject, support, and recovery apparatus.

The design of this experiment called for installation of two dogs, complete with pressure suits (globular transparent pressure helmets) and recovery gear, onto sliding "trucks" which could be forcibly ejected with an explosive charge at pre-set altitudes. A typical mission called for the nose cone "stabilized by rotation" to reach 70 miles altitude at zenith followed shortly after in the descending trajectory by expulsion of the right truck and animal at 50–55 miles altitude. After 3 sec the double parachute system was deployed sequentially and the dog returned slowly to earth. The nose cone continued in its descent until 24 miles altitude at which point the left truck and animal were ejected and allowed to free fall to 18–20,000 ft before deploying the parachute.

Initial failures in the equipment were experienced with loss of the subjects (possibly 11 of 18 dogs) and these were attributed to "defects in the parachute" systems. Telemetry and "registration apparatus" were adversely affected by both vibration during engine operation and "shock loads" incident to the ejection sequences. A portion of their resume included a statement that the "registration systems employed need considerable improvement".

The physiological data recorded during these experiments demonstrated basically the same changes by the Galkin group. Pulse, blood pressure, respiration and motor activity were all increased during the "active" phases of the flight. Physiological indices registered during the 2–3 min of zero gravity showed no significant departure from normal. Of interest was the finding that in some pairs of dogs subjected to identical physical forces during the launch phase, one specimen showed the unusual increase in cardio-respiratory and motor activity while the other companion subject in the same nose cone showed a decrease in all values, plus involuntary urination and defecation. The group characterized this atypical picture in their subjects as a "passive–defensive reaction to the external stimuli". In a discussion of their findings they pointed out that "the differences in plus rate (i.e. increase or decrease over the control values) observed during the active portion of the flight were determined by the individual characteristics of each animal—"by its own particular type of nervous system".

To study any possible long-term effects from these exposures this group have kept 5 dogs of this series under observation for the past 18 months, recording blood values, growth rates, depigmentation of skin or hair, and general behavior. Thus far they have observed no delayed or chronic affects in any of these subjects.

1958 Van der Wal and Young; *"MIA" Project*

The objectives of this team, working at Space Technology Laboratory, Ballistic Missile Division, ARDC, were to study the physiological response of mice to a 20–30 min period of weightlessness while free-riding in the nose cone of a Thor-Able test missile. Mice were chosen as subjects for these "minimal" space biomedical experiments because of their size and the available data on their physiology.

The experimental plan called for three individual mouse flights on three successive Thor-Able test missions and these were executed as scheduled on 23 April, 9 and 23 July 1958. Although severely restricted by factors of time and the non-interference status of their biopackage, these workers exhibited noteworthy ingenuity in the functional design of their total mouse package; particularly in the method by which they picked up and registered the electrical activity of the mouse's heart through a single commutated channel of telemetry. As an outstanding example of biomedical engineering under difficult conditions, their final report fully merits detailed inspection.

The actual biomedical results of their experiments were somewhat inconclusive, yet the evidence at hand supports their deduction that mouse No. 2 and probably No. 3 withstood the rigors of launch and re-entry plus 45 min of weightlessness with mouse viability still remaining at the time the nose cone hit the water. None of the subjects were found but some electrical heart races were obtained during various portions of the mission on the latter two mice, No. 1 having flown the mission unwired for registration.

Analysis of fairly authentic heart traces failed to reveal any common pattern of cardiac response during the various phases of the mission; and it even appeared that the responses observed during each stress period were in opposite directions to each other. It may turn out that this strain of mice, like Bugrov's dogs, react physiologically to the stresses of rocket flight according to their own individual nervous system make-up.

1958 Joint Army Navy Bioflight Project No. 1. "Gordo" A South American Squirrel Monkey in IRBM Jupiter Nose Cone

The objectives of this experiment were given as follows:

1. To prove the basic requirements for survival and consciousness in the primate family during rocket flight.

2. To determine the physiological variants and responses in a primate to stress factors similar to those involved in escape from earth's gravity.

3. To establish a basis for further experimental studies.

The experimental plan provided for the flight of a 1 lb. unanesthetized male monkey, protected and instrumented in a completely self-contained biomedical package secured in the nose cone, through the typical flight trajectory of a Jupiter IRBM missile. On 13 December 1958 the first planned bioflight was accomplished and was considered highly successful and biomedically productive despite failure of the recovery sequence and loss of post-flight examination of the specimen.

During the pre-mission training and conditioning period considerable differences were found among the candidate subjects regarding their acceptance of restraint and confinement and only those specimens able to accept the situation for the time required with reasonable composure were chosen for further pre-mission training and physiological evaluation.

The biomedical data recorded on six telemetry channels included the EKG, respiratory rate, heart sounds, skin temperature plus capsule temperature and pressure. On the whole, registration and transmission of these data up to time of re-entry was successful, with minor exceptions noted. The thermistor package for sensing the respiratory rate was displaced downward (away from the animal's face) during the launch acceleration phase of the flight and therefore no respiratory activity or pattern was recorded during the imposition of increasing accelerative loads on the subject. In addition, this group reports that, although chest microphones attached to pick up heart sounds became overloaded with extraneous noise which obliterated the normal heart sound trace, in the final analysis this pickup provided an unexpectedly good sensor of the animal's total motor activity.

The group reported that they observed an increase in heart rate during the launch accelerations with partial return to control levels during the zero *g* phase. The character of the EKG tracing were considered within normal limits throughout the flight until telemetry failed prior to re-entry. Capsule temperature and pressure readings remained well within design specifications and the lack of dust contamination in the capsule (as evidenced by lack of dyspnea) was cited as an important accomplishment in the design and function of the carbon dioxide and water vapor absorbing elements.

In summation, the group felt that a considerable amount of biomedical data was collected from this experiment which "when completely evaluated will contribute materially to the ultimate flight of man in space".

1958 (*Reported*) *V. N. Chernov and V. I. Yakolev, USSR*[4]. *The Dog "Laika" in Orbit*, 3 *November* 1957

The stated objectives of these workers were as follows:

1. To study the behavior and condition of living organisms throughout the protracted period of the satellite's orbital motion. With the aid of artificial satellites, conditions can be created which, from the biologic point of view, approach (or duplicate) the conditions of cosmic flight. In continuing the preliminary discussion, the authors made several general observations regarding space biological investigations which would seem worth repeating and emphasizing in this review.

First, they point out the urgent necessity for exercising strict economy as regards the weight and volume of all biopack components and also in the electrical energy required to operate the total unit. Next, that biological research with satellites takes two basic forms, i.e.:

1. The development of equipment and its regulatory control which will guarantee conditions required for the normal viability of the animal at all stages of satellite flight.

2. The study of the biologic effects of the various factors involved in cosmic flight.

To the reviewer it seemed somewhat unusual that the authors did not cite a third category, namely the use of a satellite to provide a space environment for the conduction of fundamental biological investigations incapable of duplication in terrestrial laboratories.

The experimental plan called for the placing of a pre-trained and conditioned dog of 12–15 pounds into a circumterrestrial orbit, adequately protected, nourished and instrumented within a biomedical capsule secured inside the orbital vehicle. In the light of some speculation by U.S. workers that the original intent of this group was that of attempting to re-enter and recover the biopack and subject, it is interesting to note the statement by the authors to the effect that "since we have no devices which guarantee the safe descent (and recovery) of an animal and scientific equipment we are faced with the complicated problem of recording data registering the behavior of the animal along with the pertinent hygienic and physiological indices".

The description of the biomedical package which measured 64 cm in diameter by 80 cm in length contained a number of interesting statements, particularly when one compares the components of their life support system which was apparently ready for use in 1957 with those that we have available as "off the shelf" items at this present time. The listing of these items which follows certainly gives us ample reason to pause for a somewhat sober reflection.

1. Despite the relatively small size of the biopack, it contained, in addition to 13·2 pounds of Laika, the air regeneration system, temperature regulating system, food troughs, a "sanitary arrangement" for both liquid and solid excreta and a set medical (registration) apparatus.

2. The installation for air regeneration contained a regenerative substance in the form of highly active chemical compounds which "absorbed CO_2 and water vapour and released the necessary amount of oxygen". The oxygen supply provided was calculated to be sufficient for a 7-day period.

3. The functioning of the life support components was checked by the readings of a potentiometric pressure indicator working in a range of from 200 to 1000 mm Hg, and from wire rheostat temperature indicators situated inside and outside the casing of the capsule.

4. Food and water was contained in a 3 litre metal container and considered of a gelatinous material containing the necessary amount of fluids

and nutritive ingredients. The total amount provided was computed to be sufficient for a 7-day period.

5. The animal's harness provided adequate protection against vehicular perturbations yet permitted him to stand, to sit, to recline and also to move a little back and forth along the long axis of the capsule.

6. The medical apparatus, consisting of a commutator, two amplifiers and a set of "pick-ups", provided for the registration of the following data:

(a) Bipolar EKG for the systolic frequency.
(b) Pneumograph around thorax for respirations.
(c) Maximum arterial pressure by oscillometry.
(d) Motor behavior by an actograph which indicated the presence, duration, and amount of movement.

Finally, all biopack components, both separately and as a final integrated package were rigorously tested under closely simulated stresses of actual flight such as vibration, acceleration and reduced ambient pressures.

In the preparation and training of experimental animals great care was taken through patient and exhaustive preconditioning to reduce to a minimum any abnormal physiological responses generated primarily by unaccustomed sensory stimuli. This portion of their program was exemplary from the standpoint of thoroughness and included the following interesting items:

1. Training the animal to accept without "agitation" both the burden of equipment and the close confinement of the capsule through gradual reduction in the size of the training cage and progressive increase in the time therein spent starting with a few hours and ending with 20 days. Tests of equipment for feeding and physiologic registration were carried out concomitantly with this training which resulted in "significant improvements".

2. Training the subject to accomplish normal urination and defecation without resorting to artificial drug regulation.

3. Determination of the subject's energy requirements (400–650 cal/day) and the optimal formula to provide such; 40 per cent bread crumbs, 40 per cent powdered meat, and 20 per cent beef fat.

4. Determination of the physiologic effects of noise and vibration, and a conditioning program which was considered complete "when the changes in physiological indices were insignificant; i.e. not essentially different from the level prevailing before the conditioning". It was noted that vibration caused greater functional changes than did sound.

5. Conditioning the animals to accept acceleration loads in the chest-spine direction without undue motor excitation (restlessness). The *g* time history of these conditioning loads on the centrifuge ranged from two

to ten g's and from 6 to 15 min. The average response to these acceleration loads were; increased pulse rate (2 times normal), breathing rate (3 times normal) with shallow amplitude during the higher g loads; increased arterial pressure by 50–80 mm Hg. Within 5–10 min after cessation of the accelerations all values had returned to normal and "no subsequent deterioration in the animal's health was observed".

At the same time this animal conditioning program was going on "admissable limits" in the variations of oxygen, water vapor and temperature within the capsule were being determined. From these data, the regulatory system controlling the capsule environment was perfected which established the maximum admissable concentration of constitutents at close to those equivalent values found under a normal barometric pressure. (This would imply that pressure seals and leak rates of the capsule were extraordinarily good).

From the group of 10 dogs completing the full course of pre-mission conditioning and training, the dog Laika, a 2-year old female weighing 13·2 pounds was selected for the first canine orbital flight.

Chernov and Yakolev report the behavior remained normal during all phases of flight with the exception of the initial period of orbital flight when some increase in activity was noted. EKG also appeared normal through prelaunch, launch, and orbit except for a non-pathological configuration characteristic of increased rate during the launch phase. Heart rate increased during the first phase of launch acceleration and then decreased gradually, despite continued and in fact, increased accelerative loads. Upon reaching the subgravic state the pulse, which had returned nearly to normal, spiked transiently and then returned to normal. Probably the most significant finding here is that the return to normal rate after the initial agravic spike took nearly three times as long as it did at ground level upon removal of equal accelerative loads. Respiration increased to three times normal during launch but uneventfully returned to normal in the orbital phase. Cabin oxygen and ambient pressures apparently remained normal in all phases. The report is somewhat ambiguous in its discussion of the other parameters of cabin environment, such as CO_2, humidity and temperature, which might lead to interesting speculation on our part concerning the cause of death of the subject.

In conclusion, this group made the following points:

1. The total functioning of the capsule and life support system was considerably beyond expectations and gave complete protection even in the "region of meteor currents".

2. In considering the implications of orbital flight on "survival" there were found no immediate deleterious biologic effects observed during the time period through which Laika was observed.

3. As regards the question of long term biologic effects, specifically those from cosmic radiation, the statement was made that no pertinent evidence can be accummulated until the animal can be safely returned and studied.

4. "The accumulation of experimental data with artificial earth satellites will in the near future, we hope, permit us to arrive at definite conclusions regarding basic questions connected with the medico-biological investigations of cosmic flight".

1960 January (Unreported) C. Green, et al., U.S.A. small primate (SAM Space) in "Little Joe" Ballistic Flight

The major contribution from this biologic investigation in a missile system was the performance of the subject. This was the first successful record of a biologic subject trained to perform a specific psychomotor task that has been obtained during an entire ballistic space equivalent flight. The subject performed well except for the short period of peak acceleration and noise. The post flight performance equalled pre-flight accuracy[10].

1960 August—USSR—Two Dogs in Orbit and Recovered (Belka and Strelka)

This is highly significant and the logical extension to the Laika in Orbit effort as reported by Chernov and Yakolev. This is the culmination of the biologic and engineering sciences efforts to validate the stepwise studies that are so laboriously undertaken and fraught with disappointment. Here is evidenced the blending of all the scientific knowledge gained from earlier biologic exposures which tested fundamental principles and concepts into a final complete venture into the cosmos, orbiting the earth and returning.

This is a long way from the early work of Henry and his co-workers, who used a small room in a temporary building in the New Mexico desert to prepare their biologic experiment.

Now, the bioscientists must have extensive checkout equipment. They start their countdown 24 hr or more prior to "*X*" or firing time due to the parallel countdown of the large liquid rocket engine propulsion systems. There is constant check and recheck of each and every system, subsystem, and component. Instead of the environmental support for the few minutes of flight ten years ago, today we are confronted with days, if we include count-down, prelaunch, flight, and recovery times.

This means developing, testing, and proving environmental support systems of small size and great capacity. Oxygen must be provided with a margin of safety for unantipicated holds, additional flight time, and delayed recovery. The same holds true for CO_2 and H_2O removal, temperature control, nutritional requirements, and waste collection or disposal.

In addition to the basic physiological requirements, there is a demand for functional or performance information. Performance affects physiology and physiological alterations affect performance. Therefore, the accumulation of pre-flight data under simulated dynamic flight conditions is mandatory for the interpretation of flight information.

The complexity of the problem has challenged the biomedical investigators who have answered the challenge. It has now been demonstrated that through properly planned and progressively complex experiments exposing biologic payloads to space environments that the validation of engineering and physiological concepts can be obtained, thereby, opening the gates that lead to the path into space for man.

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