

**Biological Effects of
Chronic Acceleration** A. H. SMITH AND C. F. KELLY **opp. 1**

Two centrifuges at the University of California at Davis have logged more than 40 million revolutions in studies of the effects of changes in weight on experimental animals. Some of the results of this work are discussed here.

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SeaLab II support diver Billie D. Ledford, EN2, of Underwater Demolition Team 12, receives final checkout from diving supervisor Carl O. Schultz, GMC, of UDT-11, prior to making a 200-foot dive required in conjunction with the SeaLab II operation. A summary report on the ocean-bottom-residence experiment, including illustrations, begins on page 11.



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Biological Effects of Chronic Acceleration

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With the recent developments in bioastronautics, it has become apparent that man may soon be faced with long-term residence in environments with different dynamic properties than those of Earth. Such situations may range from the weightlessness of space and orbiting vehicles through the hypodynamic environments of smaller astronomic bodies (Moon, 0.18G; Mars, 0.38G) to the hyperdynamic environments of larger planets (Saturn, 1.53G; Jupiter, 2.65G). At present, the biological consequences of prolonged exposure to these strange environments are poorly understood. Since our biological science is classically terrestrial and the Earth's gravity is quite constant, little attention has been given to the possible biological effects of the ambient accelerative force. However, it has now become necessary, if not urgent, to investigate and understand the biological effects of chronic exposure to accelerative forces of various intensities.

In addition to its pertinence to bioastronautics, such understanding is of philosophic importance to environmental and regulatory biology. Other physical environmental factors—known collectively as “climate” or “weather”—are variable; the biological responses to their changes have long been recognized, and for many of them, the regulatory mechanisms are well known. It is likely that these mechanisms developed slowly, through evolutionary processes. Over periods of geological time, populations have been subjected to extreme and prolonged changes in environment—such as the temperature differences of the ice ages and the Carboniferous period and the temperature and oxygen-level variations that accompany migrations to and from high altitudes. Each of these extremes has had a selection effect upon developing species which should influence the physiological response of modern progeny to environmental variation. Consequently, studies of the nature of the response and of the physiological adaptation to simulated changes in gravity—an environmental variation not experienced previously by modern animals or their predecessors—should be quite informative.

Weight, Mass, and Acceleration

Accelerative forces are recognized by their tendency to change the condition of rest or motion of affected objects. Forces and acceleration are mutually defined in Newton's Laws of Motion: $F = m \times a$. However, if a restrained body is exposed to an accelerative force, the result is the phenomenon of weight, rather than an actual acceleration. The relationship between weight, mass, and accelerative force is derived from Newton's Laws:

$$W = m \frac{a}{g}$$

Where: W is the weight (as lb., kg., etc.);

m is the mass (also as lb., kg., etc.);

a is the accelerative force (as dynes, ft/sec², etc.);

g is the Earth's gravitation (in the same units as " a "; 32 ft/sec², 980 dynes, etc.).



Thus, it is possible to change weight in two ways: naturally, by changing the mass, and artificially, by changing the accelerative force. Also, the dynamic properties of various environments can be compared in terms of the weight-to-mass ratio (the operational principle of accelerometers)—which is equivalent to the accelerative force in multiples of the Earth's gravitation. It has become conventional to express the dynamic aspects of the environment as "G"—which, being a ratio, is dimensionless. There are no standard terms that describe environmental conditions with respect to accelerative force. We have called the prolonged exposure to fields greater than Earth gravity "chronic acceleration." Although this terminology has limitations, it does seem to be understood readily. "Environmental dynamicity" also appears acceptable, because it is descriptive of forces—both those that involve movement (kinetic) and those that do not (static). The term "gravitational" has been used, presumably to indicate "gravity-like." However, gravitation is a specific property of matter, so it is improper to apply it to forces developed by motion.

Two Types of Responses

Any effects that alterations in the ambient accelerative force may have on biological systems will result from the artificial change in weight

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which occurs simultaneously. Biological responses to such changes can be anticipated on several grounds. Some of the responses would be nonspecific, resembling the effects of exercise. The work required for movement against an accelerative force is proportional to the weight and distance moved. Within the Earth's gravity, this relationship is expressed as follows:

$$\text{Potential Energy} = \text{height} \times \text{mass} \times \text{gravitation.}$$

So, in a hyperdynamic environment, more work will be required for locomotion, maintenance of tonus, *etc.* However, any biological changes resulting from this aspect of chronic acceleration should be similar to those resulting from a greater degree of exercise under a lesser accelerative force.

Other responses to changes in the ambient accelerative force will be quite specific, and their effects should not resemble those of exercise or other natural activities. Some of these will result from changes in the specific weight (wt/vol). For example, in a 5G environment, the heart must handle a fluid with the normal specific weight of iron. Other tubular organs having fluid contents, such as the gut, will experience similar difficulty. Organs with density gradients will be particularly susceptible to changes in the environmental accelerative force. The brain, for example, is less dense than the surrounding cerebrospinal fluid; consequently, it is buoyant (in humans, at normal gravity, its buoyancy is 50 gms). Brain buoyancy will be proportional to the ambient accelerative force—it will be zero under conditions of weightlessness, 150 gms in a 3G environment, *etc.* This buoyancy appears to be borne inelastically by the brain, placing the tissue under a mechanical stress. The classical work of Claude Bernard ("Piqûre," 1848) and the metabolic sequellae observed in some individuals recovering from brain concussion indicate a likelihood that the application of mechanical forces to at least some areas of the brain will cause a general metabolic alteration. Consequently, prolonged changes in brain buoyancy—especially those caused by the phenomenon of weightlessness—may have important neurophysiological implications, if normal buoyancy is a factor in the functional regulation of the brain.

In understanding the biological effects of chronic acceleration, it is important to distinguish between the specific and non-specific phenomena. This can't be done with experimental animals; however, it can be estimated by maintaining exercised as well as sedentary controls. Such exercised controls will be particularly useful where selection over several generations is involved.

Changes at the molecular level (*i.e.*, molecular sedimentation or direct influence on thermochemical reaction) are not anticipated. The forces

involved in chronic acceleration are very weak compared to the thermal energies (“Brownian” movement) of molecular and colloidal particles. Any metabolic alterations that are observed will result from changes in regulatory processes, including, perhaps, those of the endocrine system.

Centrifugation

A major problem in studying the effects of chronic changes in the ambient accelerative force is technical—finding a suitable method of obtaining the desired environment. Perhaps the best method would utilize gravitation, with the establishment of research stations on our Moon (0.18G), Mars (0.38G), Saturn (1.53G), and Jupiter (2.65G). However, this kind of development is not immediately feasible. Also, it would present other complications, such as variation in daily and seasonal cycles.

To do such research on Earth, it will be necessary to deal with only “super-gravity fields.” Gravity is the most constant and pervasive factor in our environment—and it is unique in that no way is known to interfere with or limit it. However, there are ways to increase the ambient accelerative force: by changing the rate of motion (“linear acceleration”) or by changing the direction of motion (centrifugation). For experiments covering long periods of time, only the latter is feasible. If one maintained a field of 2.5G by linear acceleration, the object involved would go into an earth orbit in 5.8 minutes, escape the earth’s gravitation in 8.4 minutes, and “attain” the speed of light in 154 days! Consequently, centrifugation must be employed for producing long-term artificial changes in weight (simulating changes in gravity). This procedure necessarily involves turning, which has its own biological effect. However, this effect can be kept at a minimum by elongating the centrifuge arms. Also, if the cages are hinged, the accelerative force—the resultant of the centrifugal force and gravity—will be perpendicular to the cage floor. Changes in weight produced by centrifugation are considered to be the same as those produced by gravitation. Einstein’s “Principle of Equivalence” states that the effects of accelerative forces are indistinguishable, irrespective of their physical bases.

Research Approach to Chronic Acceleration

At the present time, only a remarkably few chronic acceleration research programs are in progress. These include investigations at NASA’s Ames Research Center (Dr. J. J. Oyama), at the University of Iowa (Dr. C. C. Wunder), and ours at the University of California, Davis. The chronic acceleration research program on the Davis campus

was started in 1955, supported initially by funds provided by the Office of Naval Research and subsequently by funds provided by ONR and NASA. The objectives of this program include the development of apparatus, techniques, and biological materials for studies of the anatomical, physiological, and pathological changes involved in physiological adaptation and de-adaptation to chronic acceleration. The experiments last from several months to a year, with centrifugation stopped only a few minutes a day for observation of the animals. Most of the experiments have been conducted with chickens, which are bipeds and which possess a circulatory system more adaptable to the effects of chronic acceleration than that of quadrupeds. Also, other environmental experimentation (involving high altitude, thermal extremes, *etc.*) is being carried out on this campus with chickens, which extends the usefulness of the chronic acceleration research.

The centrifuges (Figures 1-3), which were provided recently by a grant from NSF and designed by Mr. S. J. Sluka, are 18 feet in diameter and "double-decked" to carry 16 cages. The cages are arranged for the normal husbandry of chickens. They have a total of 120 square feet of floor space per centrifuge, which will accommodate about 150 mature birds. However, the cages can be modified readily to accommodate a larger animal, such as a dog, or filled with smaller cages to accommodate rats or other small animals. One of the centrifuges has a mechanical drive with an operational capacity of 4.5G (considerably in excess of the tolerance of kilogram-size animals, which is about 3G). The other centrifuge has a hydraulic drive with an operational capacity of 6G (approximately the tolerance of rats). On July 1, 1965, the mechanical drive had logged 21,198,281 revolutions (equivalent to 491 days at 2.5G), and the hydraulic drive, 20,310,587 revolutions (equivalent to 471 days at 2.5G). No major mechanical difficulties have been encountered with either machine.

"Chronic Acceleration Sickness"

The exposure of animals to chronic acceleration may result in a substantial mortality. For example, only 70 percent of a group of chickens introduced gradually to a field of 3G may survive after three months. The pathology involved in this "chronic acceleration sickness" has been investigated by Dr. R. R. Burton. The debilities developed by birds in hyperdynamic environments are rather discrete, and two syndromes have been recognized. One of them, which involves leg paralysis, is uniformly lethal, but the other one may be reversed spontaneously with the bird returning to a quasi-normal (asymptomatic) condition.

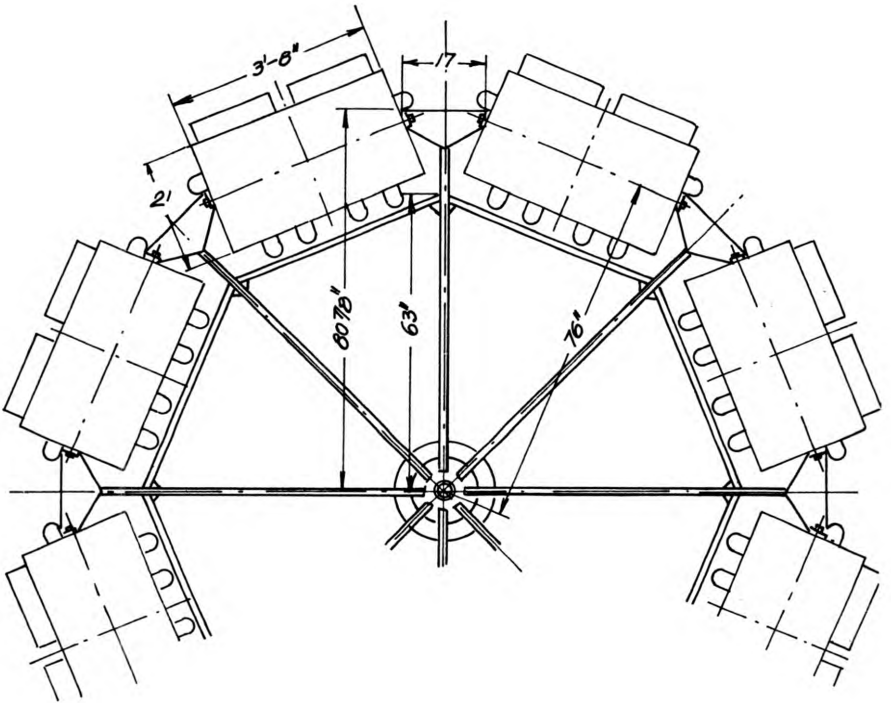
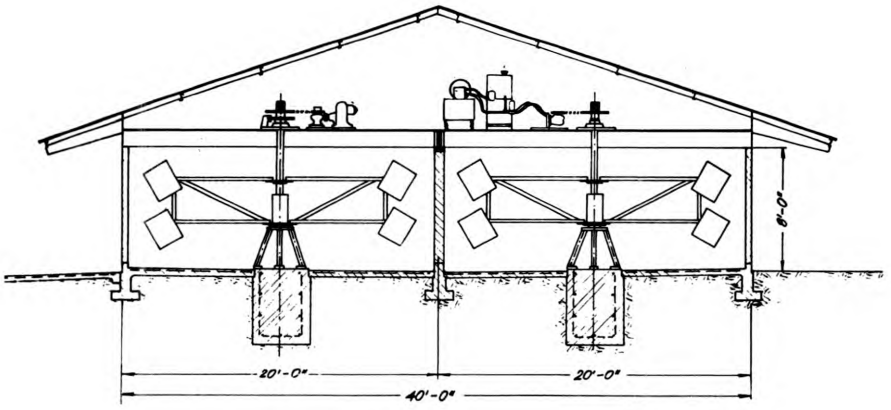


Figure 1 – Cross section and top view of animal centrifuges.

Both syndromes are reversed readily upon return to normal gravity, indicating that they do not depend on organic lesions. This indication is supported by a lack of specific lesions at autopsy. Also, if birds that have become acceleration-sick are taken off the centrifuge and returned later to an accelerative force, the syndromes do not necessarily reoccur.

Death from chronic acceleration sickness generally occurs in 3 or 4 days after the onset of symptoms. Simple inanition does not appear to be a factor, since acceleration-adapted birds deprived of feed and

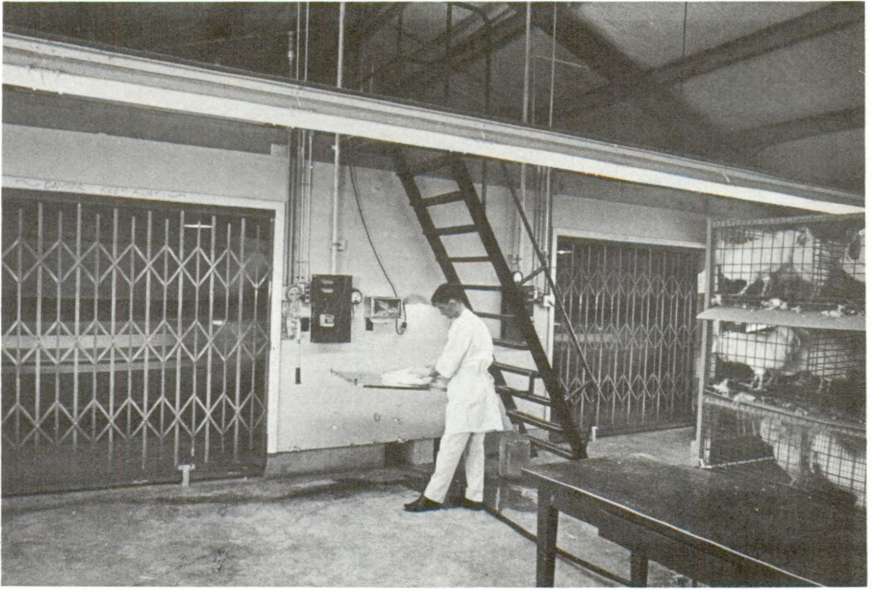
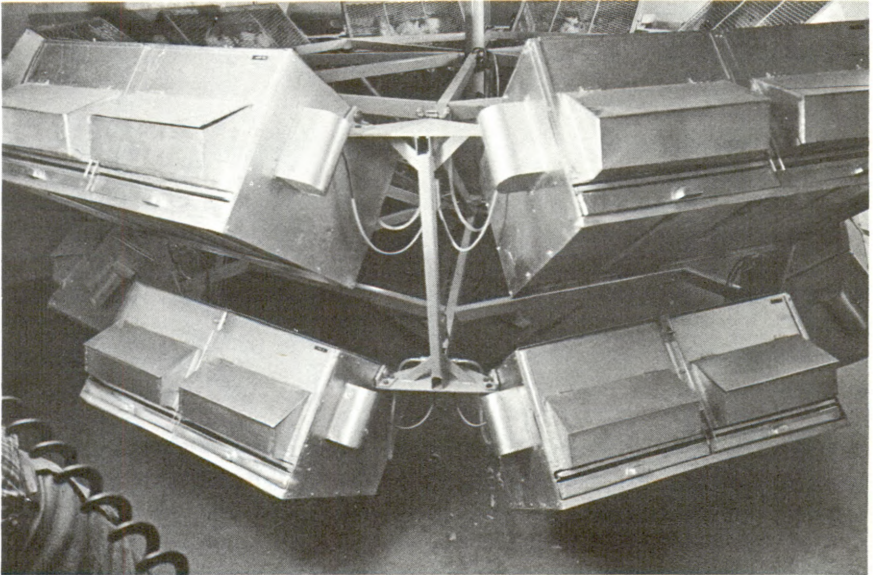


Figure 2 — Centrifuge rooms. The centrifuges are located behind the gates. Adjacent to them is an animal room which houses controls and facilities for other operations, such as autopsy examination.

Figure 3 — View of animal centrifuge.



water at 3G survive 6.3 ± 0.4 days (as compared with 12.8 ± 0.4 days at normal gravity), and without exhibiting the typical signs of chronic acceleration sickness (Burton's Disease).

No qualitative differences in chronic acceleration sickness have been observed between stocks that have and have not been selected for tolerance of chronic acceleration; the incidence is merely greater in the latter. Also, no qualitative difference in sickness is evident between the more susceptible individuals (those that die after a few days at 1.5G) and the more resistant individuals (those that die after many months at 3G).

Physiological Adaptation

Survival in hyperdynamic environments requires physiological adaptation. A group of birds transferred rather gradually to a 3G environment may suffer a 30 percent mortality. However, if hatchmates are introduced abruptly, all will die within 72 hours. Adaptive changes may be induced by very low fields; for example, ten days exposure to a 1.1G environment greatly reduces the mortality of birds that are exposed later to a greater accelerative force (e.g., 3G).

Physiological adaptation to hyperdynamic environments may be retained for long periods and perhaps indefinitely. Most physiological responses to chronic acceleration disappear in a relatively short time—3-5 weeks after return to normal gravity. However, adapted animals returned to normal gravity can be re-introduced to hyperdynamic environments 3-4 months later without apparent discomfort or decrease in body mass. This finding indicates that astronauts may be able to tolerate Earth gravity directly after fairly long periods of weightlessness. It also implies that very long periods of weightless exposure may be required before the full consequences of the gravity de-adapted state become known.

The factors which permit animals to tolerate hyperdynamic environments are heritable. When unselected stocks of chickens are exposed to accelerative forces in the order of 3G, they suffer a mortality of 6 percent per day, whereas when survivors of such trials are reproduced serially through five such selections, the mortality rate is reduced to less than 1 percent per day. (However, this reduction in mortality is not accompanied by a great increase in the toleration limit, which remains at about 3G, as it does for unselected stocks.) Such selection also eliminates the disorientations and postural difficulties seen in some centrifuged birds upon return to normal gravity. However, rapid selection in the converse occurs also; for example, in centrifuged birds that have been selected through several generations on the basis of these disorders, the frequency of the disorders approximately

doubles. Such rather rapid selection progress is generally considered by geneticists to indicate a metabolic basis to the processes involved.

Responses to Chronic Acceleration

Repression of Growth and Development. One of the most characteristic responses of individuals that tolerate chronic acceleration is a repression of growth and development. Chickens raised in a 3G environment for several months may experience a 40 percent reduction in body mass, as compared to the body mass of normal gravity controls. Upon return to normal gravity, some but not all of this difference will be made up, the degree of recovery being inversely proportional to the maturity at the time of return to normal gravity. It is interesting that in many experiments, the maximum growth is achieved at 1.5G rather than at normal gravity.

Development, as indicated by the onset of sexual maturity, also is delayed in hyperdynamic environments. At 3G, sexual maturity in chickens is acquired in about 5 months, as compared to 4 months at normal gravity.

Anatomic Responses. Anatomic responses to chronic acceleration tend to be somewhat variable among experiments. Generally, there is a decrease in the relative carcass quantity of "soft tissue" (material which can be separated mechanically from the skeleton) and an increase in the relative quantity of skeleton and abdominal viscera (including the gastro-intestinal tract). These changes resemble the effects of starvation, except that the starvation leads to a decrease in the size of the gastro-intestinal tract. In many instances, especially those involving the centrifugation of young animals, the heart decreases in relative size. This change is the opposite of that which occurs with exercise, which generally leads to a 15-20 percent increase in heart size. However, this may be a species-specific response. In the chicken, the heart lies above the broad sternum, and it is partly covered by the liver. If the bird is young (1-2 months) when the acceleration is started, there is a tendency for a cavity to develop in the sternum, which is occupied by the heart.

Individual muscles may become hypertrophied – up to 7-fold the relative size attained at normal gravity. However, this effect is specific, occurring only in "anti-gravity" muscles, and not in the paired antagonist. Thus it is different from the effect of exercise, in which both of the paired muscles tend to hypertrophy. However, exercise is reciprocal, whereas postural maintenance in a hyperdynamic environment is not. Bones also become larger, but on a "whole animal" basis, since increases in the size of the humerus (which is non-load-bearing) equal or exceed those of the femur (which is load-bearing). This response apparently is the "other-side" of the decalcification process, which

is encountered during enforced bed rest and exposure to hypodynamic environments.

Changes in the Blood. The concentration of plasma proteins increases, which may be necessary to regulate the distribution of water between blood and tissues with increased hydrostatic pressure. Red cell numbers also increase; however, the mean corpuscular volume decreases.

Changes in Chemical Composition of Tissues. The chemical composition of tissues appears to be altered by chronic acceleration, but this has not yet been examined in detail. Generally, there is a significant increase in hydration and a rather dramatic decrease in fat content. After long-term exposure to a 3G environment, fat deposits may be virtually absent, and tissue fat may be only 15-25 percent of normal values.

Metabolic Phenomena. The metabolism also appears to be affected by hyperdynamic environments. Preliminary observations indicate that the feed intake of male chickens is increased approximately 15 percent at 1.5G, and 36 percent at 2G. Consequently an exponential relationship appears to exist between feed intake and the ambient accelerative force: The relationship can be expressed as follows:

$$F_G = F_M e^{kG} = 0.73 e^{.31G}$$

Where: F_G is the relative feed intake at a given accelerative force (i.e., relative to that at normal gravity, so when $G = 1, F_G = 1$);

F_M is the component of relative feed intake which is independent of weight (i.e., it is mass dependent. Numerically this is 0.73 of the feed intake at normal gravity).

k is the proportionality constant, which relates relative feed intake and accelerative force and which has the value of 0.31.

G is the accelerative force in multiples of the Earth's gravitation.

Assuming that this relationship would apply over a range of 0-3G, the energy requirements for environments with varying dynamicity can be estimated. For example, to furnish a caloric intake equivalent to 3000 kcal per day on Earth, the following would be required under other dynamic conditions:

<i>Weightless</i>	(0G)	2190 kcal/day
<i>Moon</i>	(0.18G)	2310 kcal/day
<i>Mars</i>	(0.38G)	2460 kcal/day
<i>Earth</i>	(1.00G)	3000 kcal/day
<i>Neptune</i>	(1.53G)	3570 kcal/day
<i>Jupiter</i>	(2.65G)	5000 kcal/day

Qualitative changes in metabolic function may occur also, as indicated by the incapability of birds raised under moderate acceleration fields to form much fat. These changes are not a simple matter of feed restriction, since the birds' feed intake is well within their feed capacity—*e.g.*, their feed intake may be doubled at low temperatures.

Therapeutic Alterations of Responses. There are indications that the biological response to a change in the ambient accelerative force can be altered therapeutically. Under chronic acceleration, drugs which limit sympathetic-nerve accommodation (*e.g.*, Reserpine) approximately double the mortality rate. The mortality rate of females is increased by androgen treatment, but only to the extent that it equals the greater rate of males. Other materials (vitamin supplements, glucosteroid, cortisone, ACTH, and estrogen) have no marked or noticeable effect. The thyroid stimulating hormone (TSH) is quite protective, practically eliminating mortality in centrifuging birds. However, thiouracil treatment, which limits thyroid function, does not have a reverse effect.

From these results and those of other investigators, it is apparent that living things can become physiologically adapted to chronic acceleration—up to some limiting intensity, which is inversely related to body size. Thus, individuals have capacities to tolerate environmental variation not previously experienced by them or their ancestors. Whether this tolerance involves the establishment of new physiological processes or merely a recombination of adaptive processes developed to meet other stresses is a question that requires much more study to resolve. It is interesting that the rate at which such adaptation is acquired in chickens is similar to the rate at which such adaptation is acquired to high altitude—but much slower than that to high temperature.

Predicting Effects of Weightlessness

Over the tolerable range, the physiological and anatomical changes appear to be proportional to the accelerative force—although neither the nature of the changes (increase or decrease) nor the kinetic relationships (rectilinear, exponential, hyperbolic, *etc.*) are uniform. Nevertheless, the response to accelerative forces can be described mathematically. From such equations, the physiological effects of gravity can be estimated, and those of prolonged weightlessness can be predicted. However, prediction and actuality must not be confused. The predictions must be tested in the weightless state. Logically, such predictions should be the basis for designing satellite experiments. If the predictions of chronic acceleration are valid, this technique furnishes a relatively convenient means of developing information pertinent to bioastronautics.

—Continued on back cover (inside).

—Continued from page 10.

Differences between the biological effects of weightlessness and the predictions made on the basis of chronic acceleration studies will occur only if different and discontinuous regulatory processes are involved in environments above and below normal gravity. Since, physically, Earth gravity is not a critical point (*i.e.*, it is not zero), such a situation appears unlikely. However, even if major deviations exist between the predicted and observed effects of weightlessness, knowledge of the responses of animals to hyperdynamic environments is quite important. If all of our information on the biological effects of accelerative forces relates only to two conditions (weightlessness and Earth gravity), few generalities will result.

Skyhook '65

The sixth annual program of Skyhook balloon flights was conducted by the Office of Naval Research in cooperation with agencies of the United States and Canadian Governments at Fort Churchill, Manitoba, Canada, between June 12 and August 14, 1965. During this time, 32 balloons were launched for ten scientific groups sponsored by the Office of Naval Research, National Aeronautics and Space Administration, NASA-Goddard Space Flight Center, NASA-Langley Research Center, and the National Science Foundation. In addition to flights made to conduct cosmic-ray investigations, four balloons were sent aloft to test satellite components, and two were dispatched to gather data for the supersonic transport program. Fourteen of the launchings utilized 10.6 million cubic foot balloons that carried experiments weighing as much as 700 pounds to altitudes between 135,000 and 143,500 feet.

A second cooperative Skyhook program was conducted between August 8 and September 24 at Flin Flon, Manitoba, during which 18 balloons were launched. These balloons carried scintillation counters for the measurement of electron activity during geo-magnetic storms or periods of maximum auroral activity. Data obtained during the flights, which were made for Dr. K. Anderson of the University of California, will be integrated with information obtained from Nike/Apache rocket shots and IMP (Interplanetary Monitoring Platform) satellites.

Fish pack a porthole of SeaLab II during the recent long-duration deep-diving experiment conducted off the coast of southern California. A summary report on the undertaking and other photographs appear on pages 11-15, this issue.

