Evolution of Instrumentation and Techniques for the Study of Cardiovascular Dynamics from the Thirties to 1980, Alza Lecture, April 10, 1978

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心血管动力学研究的设备与技术的发展

1930～1980年

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Evolution of Instrumentation and Techniques for the Study of Cardiovascular Dynamics from the Thirties to 1980, Alza Lecture,* April 10, 1978

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Milestones in physiology are marked by development of new devices and techniques for dynamic measurements of bodily functions and many of the earliest contributions to instrumentation in all fields of science were made by biomedical scientists. As a result of developments since 1940 stimulated by needs to study the effects of environmental stresses encountered in aerial combat and for accurate diagnosis prior to cardiac surgery, it was possible by the late 1950s to measure practically all of the external functions of the heart and lungs. An unfufilled need still exists, however, for accurate dynamic measurements of the shape and dimensions of the myocardium required to assess the intrinsic status, i.e., the cardiac reserve of a given patient's myocardium.

A 28 X-ray source high-temporal resolution cylindrical-scanning computerized tomographic system is being fabricated to meet this need. This system, which will scan synchronously up to 250 parallel cross sections of the body over an axial range of 25 cm within 0.01 sec at a maximum rate of 60 scans/sec, promises to facilitate noninvasive studies of moving organ systems and to have dramatically beneficial effects on clinical diagnosis and health care.

As a physiologist, I appreciate very much the honor of an invitation to give a lecture at a society meeting primarily made up of engineers. This is particularly so because it is my impression that many engineers regard physiology as a rather imprecise science, and in relation to the considerable precision of most engineering disciplines there is admittedly basis for this impression. The ever present inherent variability of biologic systems, particularly in awake animals and man, plus the difficulty of making precise measurements in living intact organisms, are the major and very difficult to eliminate bases for this impression.

As bioengineers, I am sure you are more cognizant of these difficulties than are your colleagues in the more exact physical sciences and quite certainly one of your objectives which is shared by all biologists is to develop more precise devices and techniques for measurement of biologic variables.

* The studies upon which this discussion is based have been supported since 1942 by the Mayo Foundation and in part during the past two decades by a career investigatorship appointment from the American Heart Association and research grants from the U.S. Air Force, NASA, and NIH. Current support is from Research Grants RR-7 and HL-04664 from NIH.

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FIG. 1. Drawing of Stephen Hales measuring the arterial pressure in a horse, 1728 (year of observation). (Commissioned by Stathem Instruments, Inc., 1967; *Classics of cardiology*, New York: Dover, 1941. Vol. 1; reproduced with permission from E. H. Wood *et al.*, *Indwelling and implantable pressure transducers*. Cleveland: CRC Press, 1977. Pp. 21–34.)

Since the very beginning of the science of physiology, the milestones of its history have been marked by development of new devices and techniques for dynamic measurements of bodily functions.

When your President, Dr. James Bassingthwaighte, invited me to give this talk, he suggested that I discuss some of the instrumentation I have been involved in during my period as a researcher, particularly the why and how come various techniques for study of the heart and circulation were developed during the period from my start in physiologic research in the 1930s to the present. Since such a discussion would have a significant autobiographical and thus inherently an egotistical tinge, I expressed and still have some misgivings regarding this format. However, at Jim's urging and following the path of least resistance, the impersonal but rather ambitious title of this discussion was settled upon.

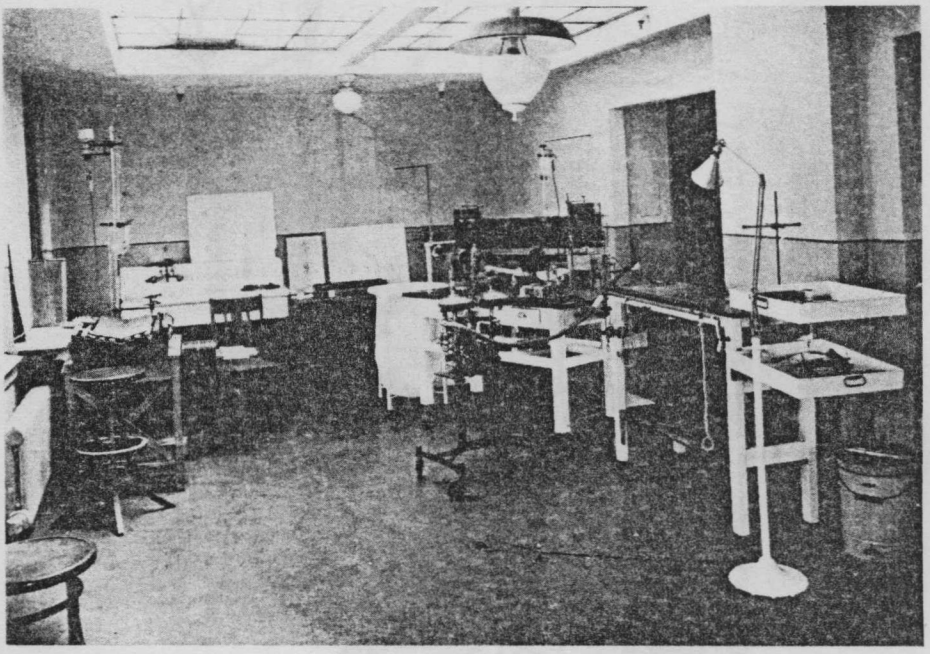

FIG. 2. The laboratory of Dr. H. E. Essex, 1940. A typical hemodynamics laboratory of that era. Note animal operating table on the right, and positive pressure respirator and smoked drum kymographic recording assembly in right midbackground.

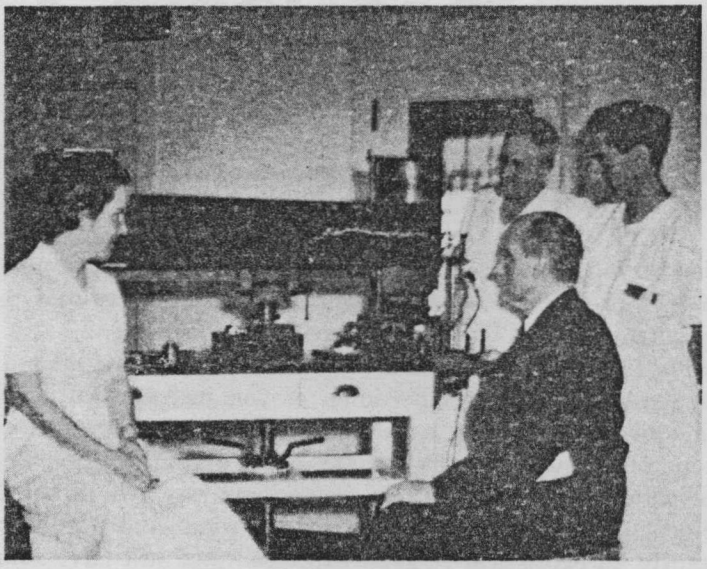

FIG. 3. Dr. H. E. Essex, midforeground, and technical staff examining blood pressure changes recorded on carbon covered (smoked) kymographic paper mounted on a kymographic recording assembly, 1940.

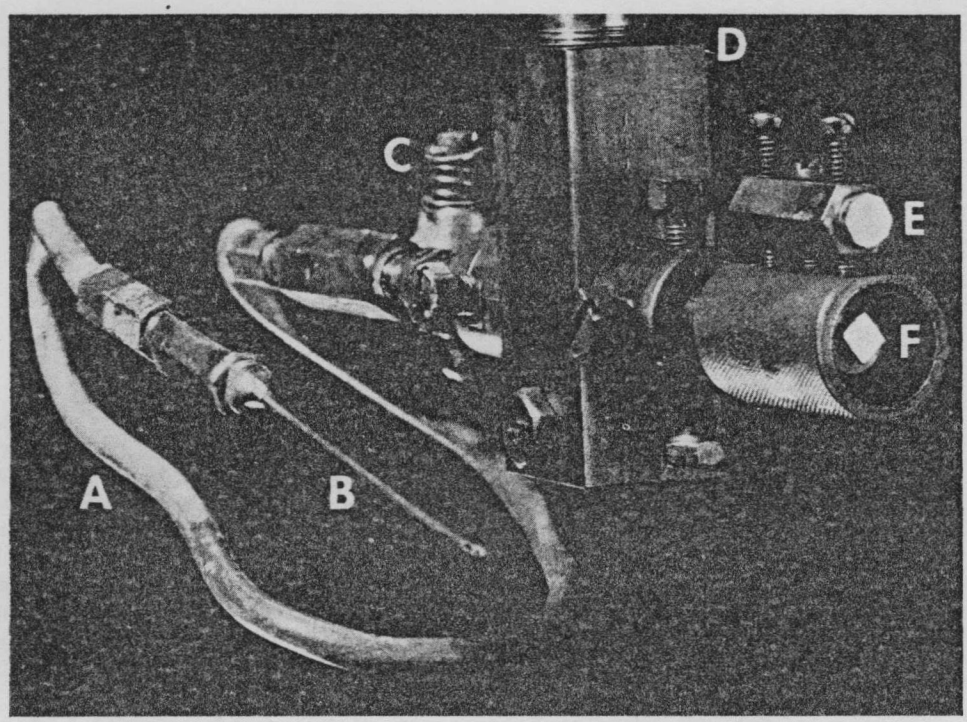

FIG. 4. Hamilton hypodermic manometer (Hamilton *et al.*, 1934). Malleable lead tubing (A) connecting hypodermic needle (B) via stopcock (C) to the manometer which is fixed in an adjustable position by the rigid mounting assembly (D). The mirror (F) is mounted eccentrically on a flexible copper–beryllium membrane, which is subjected to and flexed by the pressures transmitted to its back surface via the noncompliant, gas-free, liquid-filled hypodermic needle lead tubing systems. The mirror (E) is rigidly attached to the manometer frame to record any physical movement of the manometer assembly or the imaging light source on the photokymographic recording. Hence, it serves as the baseline trace for measurements of the pressure pulse tracings imaged by mirror F, 1932. (Courtesy of Dr. Phillip Dow, Department of Physiology, Medical College of Georgia; Reproduced with permission from E. H. Wood *et al.*, *Indwelling and implantable pressure transducers*. Cleveland: CRC Press, 1977. Pp. 21–34.)

Although the 1930s are indicated as the starting point in this title, I cannot resist pointing out that many of the earliest contributions to instrumentation in all fields of science were made by biologists. In this regard the names of Helmholz, Leeuwenhoek, Einthoven, Otto Frank, and others come to mind.

One of the earliest of these is illustrated in Fig. 1 which is a 20th Century artist's concept of Stephen Hales' very direct method of measuring the arterial blood pressure in a horse in the early 1700s (Hales, 1733). Although a tremendous fund of information concerning cardiovascular and respiratory physiology has been amassed in the more than two centuries that have elapsed since this experiment, the instrumentation for study of circulatory dynamics in the 1930s was certainly unsophisticated and relatively crude in relation to current standards.

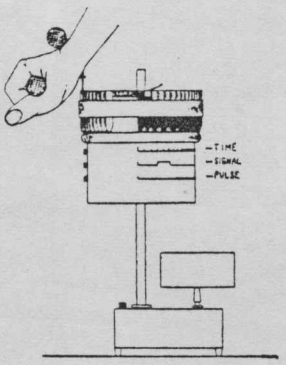

FIG. 5. Assembly for collecting rapidly successive samples of blood flowing directly from the radial artery into a series of small test tubes mounted on the circular surface of a rotating kymographic assembly. This, arterial blood sampling procedure was carried out before, during, and after injection of a circulating indicator dye into another, usually systemic venous, site in the circulation. The concentration of the dye (usually Evans Blue) in each arterial sample was then determined colorimetrically and these concentrations plotted against the time at which each sample was collected. The fastest and mean circulation times and circulating blood volumes within temporally equivalent segments of the circulation between the injection and sampling sites and also the blood flow (cardiac output) between these sites could be calculated (Hamilton *et al.*, 1932), 1928.

Figure 2 is a picture taken in 1940 of a typical hemodynamics lab of that era. This was before the days of human cardiac catheterization so that practically all direct hemodynamic measurements were made in experimental

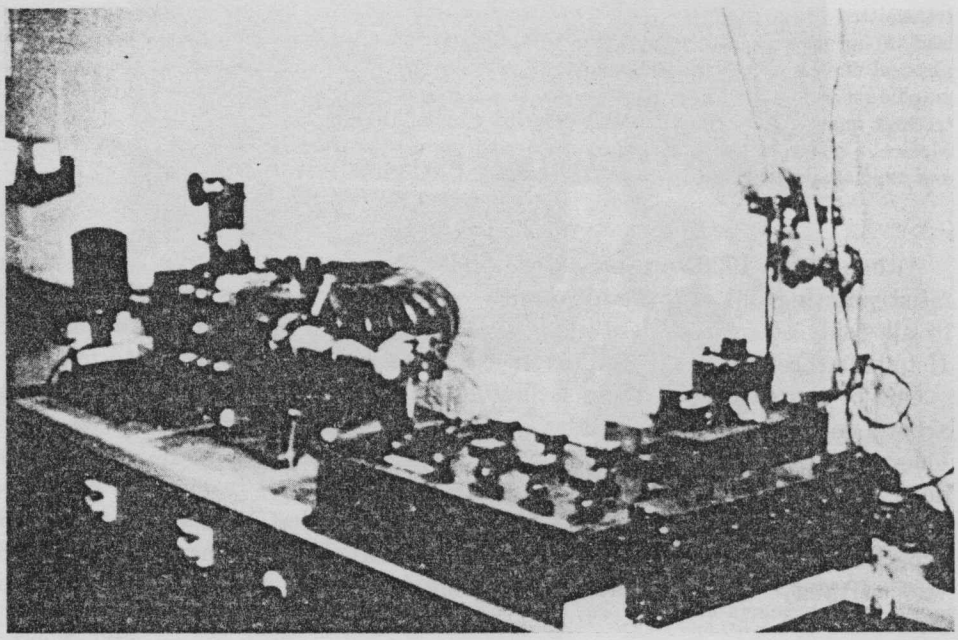

FIG. 6. Early model Einthoven string galvanometer used for the first recordings of the electrocardiogram at the Mayo Clinic about 1915.

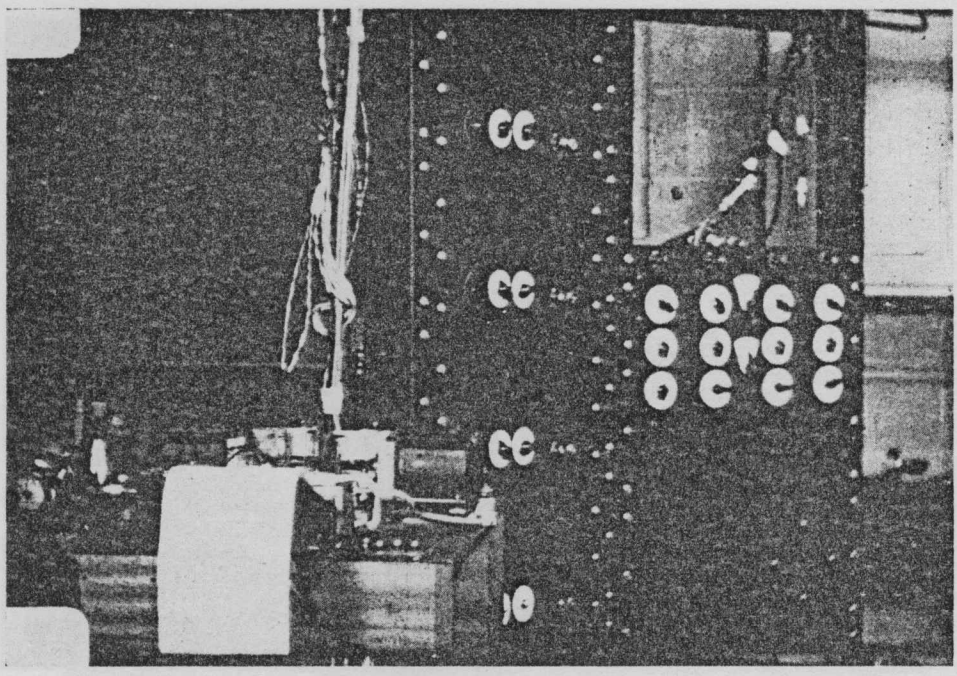

FIG. 7. Four-channel electroencephalographic recording assembly (Albert Grass) used to record brain waves in the 1930s.

animals. The almost universally used recording medium was a smoked drum kymographic assembly. Usually, several stylus-tipped mechanical lever assemblies adjusted to write on the carbon-covered kymographic paper were directly coupled to a moving anatomic part such as the apex of an exposed beating heart, or to floats above the menisci of mercury or water U tube manometers, or to rubber membrane tambour assemblies air coupled to various volume measuring devices. These relatively low-frequency, variably damped mechanical systems served as the routine transducers for studies of cardiovascular physiology at that time. Figure 3 shows Dr. Hiram Essex, a former president of the

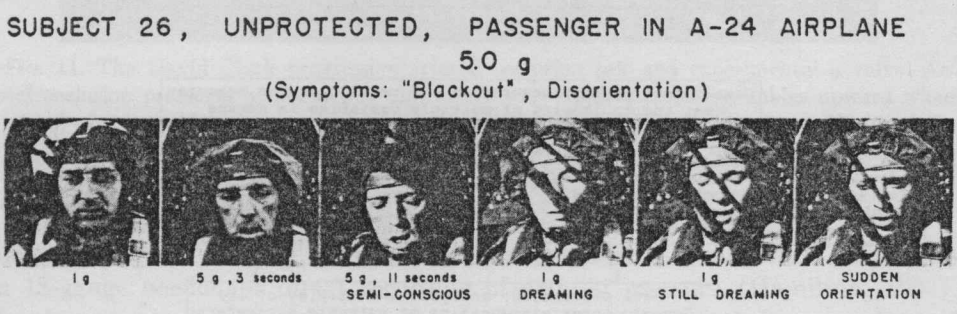

FIG. 8. Frames from a motion picture of a passenger in a dive bomber losing consciousness during a 11-sec exposure to an acceleration of 5*g* and recovering therefrom about 7 sec after return to level flight, i.e., 1*g*, 1945. (Reproduced with permission from E. H. Lambert, *Journal of Aviation Medicine* 1949, 20, 38.)

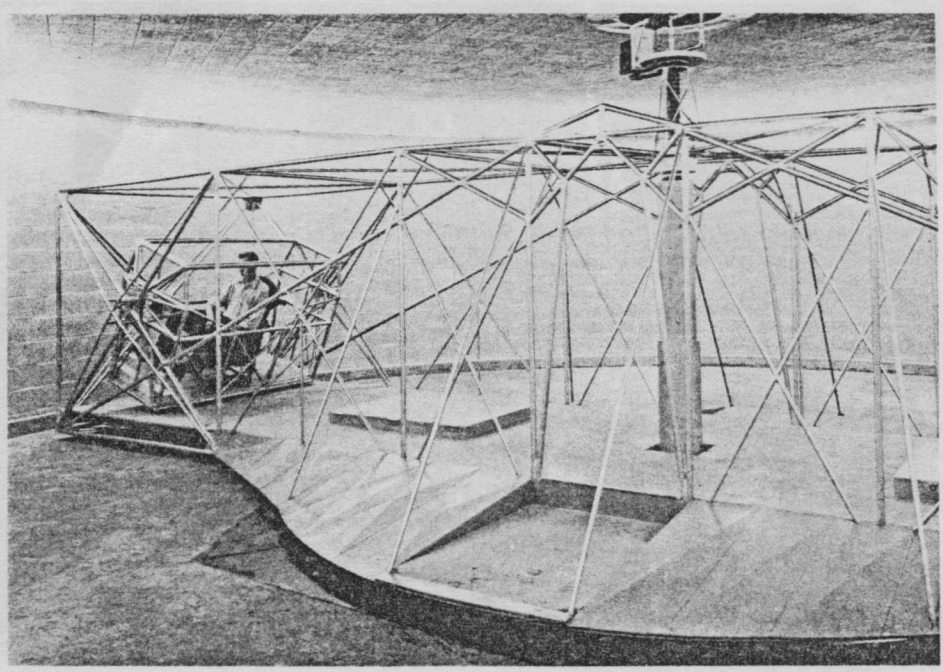

FIG. 9. The Mayo Human Centrifuge undergoing initial trial just after its installation in the Medical Sciences Building, Rochester, Minnesota, 1942. (Reproduced with permission from E. H. Wood *et al.*, *Federation Proceedings* 1946, 5, 327.)

American Physiological Society, examining a smoked drum kymographic recording of arterial pressure recorded by a mercury U tube manometer assembly. Obviously, the dynamic response characteristics of such systems are far removed from the requirements for a high fidelity recording of cardiac mechanics or arterial pressure pulses. However, during this era Gasser and Erlanger (1922) had pioneered the use of the cathode-ray tube to record nerve potentials and Hamilton had developed a high-frequency, low-compliance membrane ma-

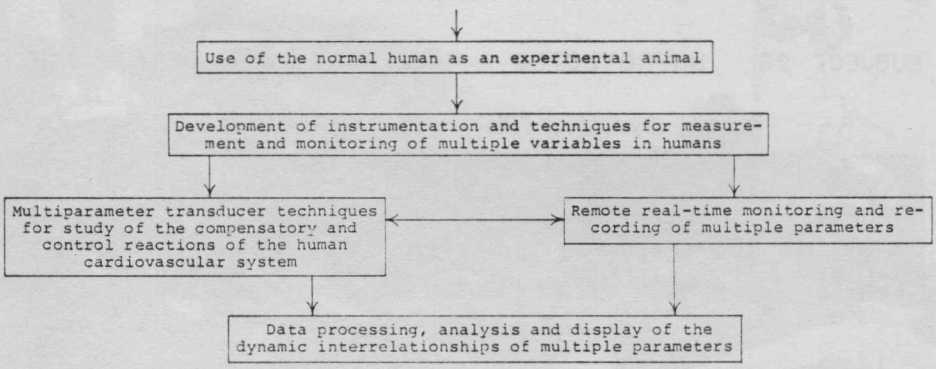

FIG. 10. Biomedical developments expedited by the Mayo Human Centrifuge project (1942–1978).

FIG. 11. The David Clark progressive arterial occlusion suit and experimental g valve. Arterial occlusion pressures of about 200 mm of Hg were applied from the ankles upward when the level of $+g_z$ acceleration reached 1.5g and were increased automatically about 52 mm of Hg per g above this level by the g compensated valve, lower left, being activated manually in this picture, 1942. (Reproduced with permission from E. H. Wood *et al.*, *Federation Proceedings* 1946, 5, 327.)

nometer (Fig. 4) directly coupled via a water-filled malleable lead tubing to an 18-gauge needle for direct recording of arterial pressure (Hamilton, 1934). He also proposed and used the system illustrated in Fig. 5 for recording of arterial dilution curves of Evans Blue in successive blood samples collected from blood flowing directly from the radial artery into a series of small test

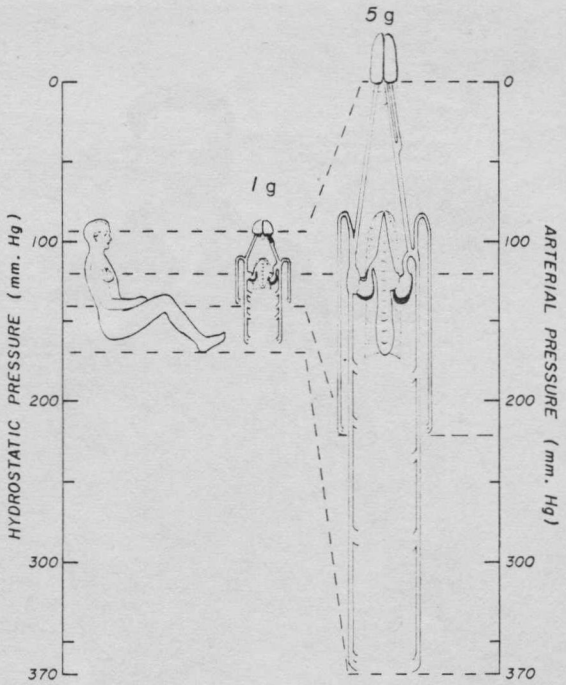

FIG. 12. Diagrammatic representation of hydrostatic pressures in vascular system of a man in upright sitting position at 1*g* and during headward acceleration of 5*g*. Left panel: Average position of pilot in present day aircraft. Center panel: Diagrammatic representation of vascular system of seated pilot at 1*g* indicating that, with an arterial pressure of 120 mm of Hg at heart level, arterial pressures at head and foot levels are calculated to be 96 and 170 mm of Hg, respectively. Right panel: Illustration of the fivefold increase in hydrostatic pressure differences in the arterial and venous circulations imposed by 5*g* of headward acceleration. Assuming that arterial pressure at heart level was maintained at 120 mm of Hg, arterial pressure at base of the brain would be zero, while at the heels it would be 370 mm of Hg. Under this circumstance and in the absence of muscular activity, a venous pressure of 250 mm of Hg would be required to return blood from the heels to the level of the heart. See Fig. 19 for verification of these differences in arterial pressure at heart and head levels with subject in upright seated position at 1*g* and during exposures to headward acceleration, 1942. (Reproduced with permission from E. H. Wood *et al.*, *Federation Proceedings* 1963, **22**, 1024.)

tubes mounted on a rotating drum (Hamilton *et al.*, 1932). The Einthoven string galvanometer (Fig. 6) had been in use for more than a decade for recording of the electrocardiogram without electronic amplification, for research and clinical diagnostic purposes and the Albert Grass 4-channel, ink pen writer (Fig. 7), used mainly for recording of brain waves, was in use in some medical centers.

World War II intervened at this time, and the associated extensive use of high performance military aircraft capable of flying at high altitudes and/or generating high accelerative forces was a very strong impetus for study of the pathophysiologic effects of the environmental stresses of low atmospheric pressure, low oxygen tensions, cold, and high *g* forces on the healthy young pilots and crews of such aircraft.

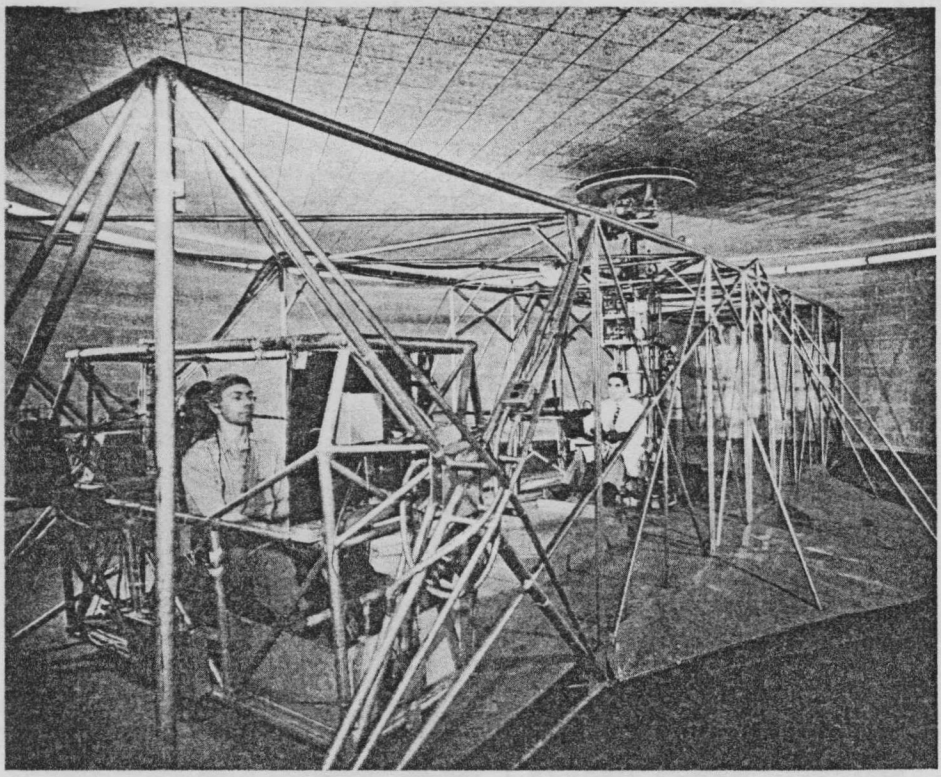

FIG. 13. Mayo Human Centrifuge in 1946. The cockpit, in the foreground, rotates during centrifuge rotation so that the resultant vector of the gravitational and inertial forces to which the subject is exposed is along the heart to brain axis (g_z acceleration).

Pilot blackout and unconsciousness during aerial combat and dive bombing maneuvers was a particularly pressing problem. The seriousness of this problem for pilots of high performance fighter planes is illustrated in Fig. 8 which consists of frames from a motion picture taken in the sky over Rochester, Minnesota, showing a passenger in a dive bomber losing consciousness and recovering therefrom during an exposure to a gravitational-inertial force environment five times greater than the force environment of planet Earth. Human centrifuges were built in Canada, the U.S. and the axis nations to study these phenomena under more controllable laboratory conditions. The first modern human centrifuge in the U.S., which was built and supported by private funds, went into operation in 1942 in the Medical Sciences Building of the Mayo Foundation in Rochester, Minnesota (Wood *et al.*, 1946).

Figure 9 is a picture of this device just after its installation in a specially built 40-ft diameter circular room. A human centrifuge is, in fact, a very large biomedical tool which, among other things, is uniquely suited for study of the compensatory and control reactions of the cardiovascular system of awake human beings. Although at that time no one had that degree of foresight and the device was not built with that purpose in mind, this machine has had an

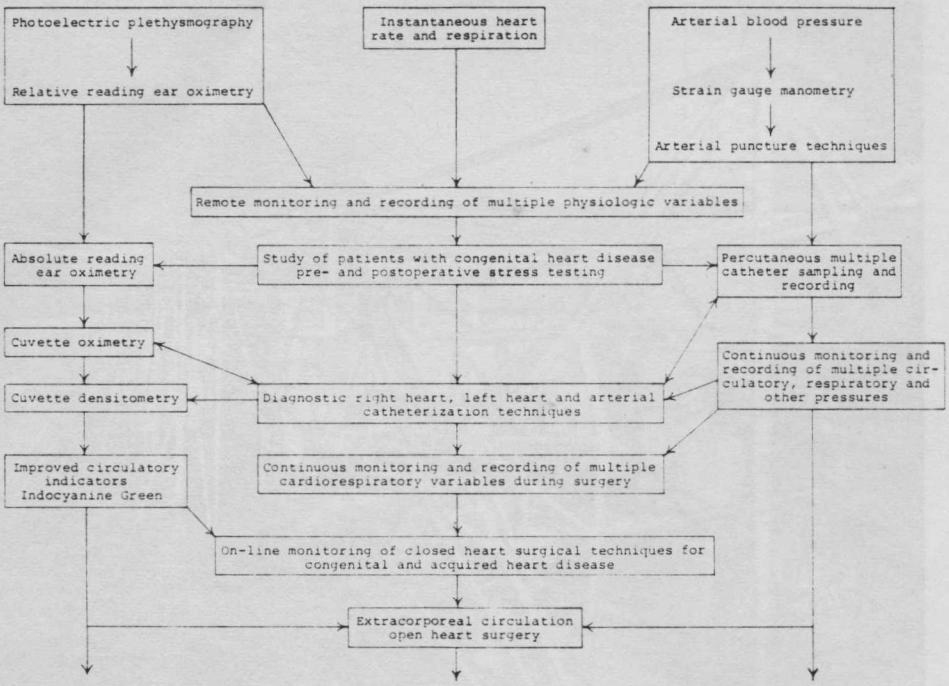

FIG. 14. Descendants of Mayo Human Centrifuge Instrumentation techniques (1942–1960).

important influence on new developments in the practice of medicine, particularly in cardiology and cardiac surgery.

The evolutionary influence of the human centrifuge on biomedical technology in the Mayo Medical Complex is diagramed in Fig. 10. This influence stemmed mainly from the requirement for use of normal humans as experimental animals. One such is shown in Fig. 11 of Ralph Sturm as he looked back in 1942 wearing an early model progressive arterial occlusion antiblackout suit designed and fabricated by Mr. David M. Clark (Wood *et al.*, 1946).

The cardiovascular problems posed by an increase in the gravitational–inertial force environment are diagramed in Fig. 12 which illustrates the five-fold increase in hydrostatic distances in the circulatory system of a seated pilot caused by the increased weight of the blood associated with a force environment of $5g$. Because of this effect, systolic arterial pressure is reduced to zero at head level, in spite of maintenance of a normal value of 120 mm of mercury at the heart.

Use of normal humans to study these effects required development of instrumentation and techniques for measurement and monitoring of multiple variables in healthy individuals. This necessitated development of new transducer techniques, suitable for use in normal humans, which would produce electronic analogs of multiple physiologic parameters such as respiration, the heart beat, and blood pressure. Electronic transduction, i.e., generation of electronic analogs of these variables, was a mandatory requirement for these

studies since their monitoring and recording had to be carried out remotely from the whirling cockpit in which the subject was seated (Fig. 13). The only recordings registered in close proximity to the subjects were obtained by a movie camera mounted in the cockpit.

The next series of figures have been selected to illustrate the instrumentation and recording techniques developed for human centrifuge studies in the early

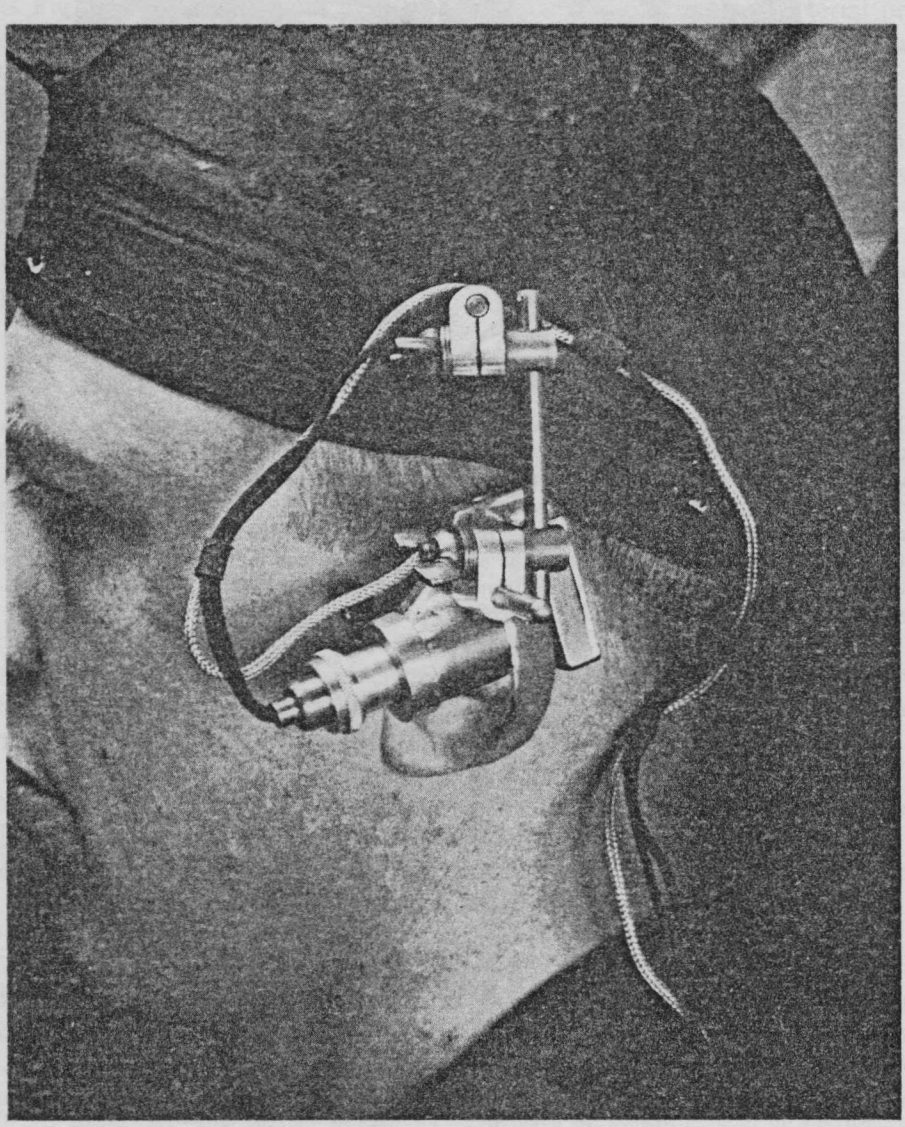

FIG. 15. Photoelectric earpiece in place on the pinna of the ear and attached by means of a special universal clamp to a plaster helmet custom made for each subject. This assembly was used to maintain the position of the earpiece which detected the variations in opacity of the ear associated with the changes in its blood content produced by exposure to acceleration, 1945. (Reproduced with permission from E. H. Wood *et al.*, *Journal of Applied Physiology* 1963, 18, 1171.)

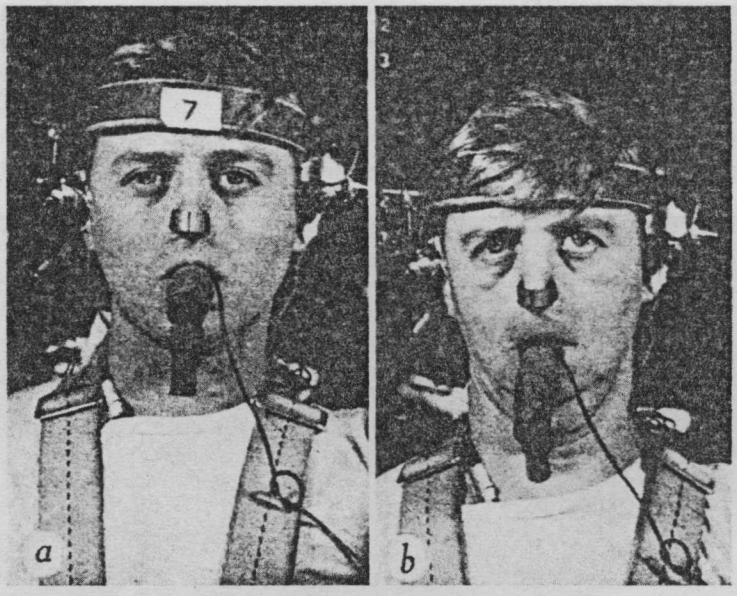

FIG. 16. Subject on the human centrifuge. (a) At 1*g* prior to centrifugation. (b) At 5*g* during rotation of centrifuge. Note that the soft tissues of the face and neck are being drawn downward, producing the appearance of increased age. The mouthpiece contains a thermocouple for recording respirations (as temperature variations) in the airway. The two photoelectric earpieces supported on the headband are used for recording the blood content of the ear (ear opacity) and the change in opacity of the ear produced by each heartbeat (ear opacity pulse). The ECG was recorded simultaneously from bilateral chest electrodes, 1945. (Reproduced with permission from E. H. Wood, *Mayo Clinic Proceedings* 1975, **50**, 497.)

1940s which, in addition to physiologic investigation, have expedited development of instrumentation techniques that have gained wide-spread use in clinical cardiology and cardiovascular surgery since that time. Figure 14 is a diagram of the temporal sequence of successive technological developments which expedited clinical progress in these fields from 1942 up through the early 1960's.

Since loss of vision and consciousness during exposure to positive acceleration is caused, respectively, by retinal and cerebral ischemia, measurements, of parameters related to cerebral blood flow were of primary importance.

Photoelectric plethysmography of the ear (Fig. 15) was used to study circulation to the head, simultaneously with (Fig. 16) respiration plus the ECG and heart rate (Wood *et al.*, 1946; Sturm *et al.*, 1947; Wood *et al.*, 1963a) recorded from chest leads. Since arterial pressure was of critical importance and it had to be measured remotely, the first strain gauge manometer (Fig. 17) for physiologic pressure measurements was adapted for direct recording of arterial pressure as illustrated in Fig. 18 which shows the assembly used for this purpose with Dr. Ed Lambert, who played a major role in its development, acting as the subject in the centrifuge cockpit (Lambert *et al.*, 1947).

A continuous, simultaneous recording of 11 physiologic variables including arterial pressure at heart and head levels during an exposure to 4.5*g* for 15 sec is shown in Fig. 19. This type of recording in a human subject or even in an

experimental animal was unique back in the mid-1940s and contributed to the very rapid developments in diagnostic right heart, left heart, and arterial catheterization techniques which occurred in the years following World War II (Cournand, 1975; Burchell, 1948; Burchell, 1956). However, when the war was on, development of methods to prevent blackout took precedence over clinical developments.

As Fig. 19 illustrates, some means of producing the increase in arterial pressure at heart level required to overcome the fivefold increase in hydrostatic distance up to the brain was required.

The simplified single pressure antiblackout suit (Fig. 20), descendants of which are still in use today, resulted. This bladder system when inflated automatically by a pneumatic valve perfected on the Mayo Human Centrifuge (Fig. 21) produced an immediate and sustained increase in arterial pressure which was sufficient to maintain arterial pressure at head level during an exposure to 5.5*g* (Fig. 22) whereas it had fallen to zero in the prior control exposure to 4.5*g* without the suit.

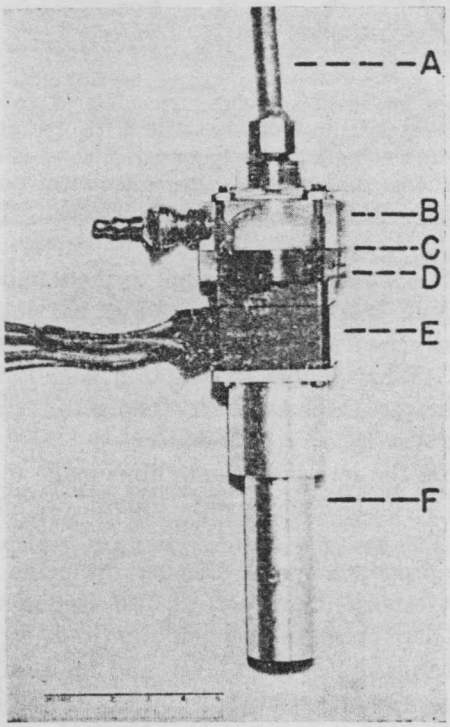

FIG. 17. Early Statham strain gauge manometer adapted for a measurement of arterial blood pressure. (A) Lead tube to which hypodermic needle is attached (see Fig. 18). (B) Lucite chamber filled with anticoagulative solution via stopcock and fluid reservoir. (C) Plastic membrane. (D) Lucite chamber filled with oil. (E) Case containing strain gauge elements connected by wire leads to battery and galvanometer. (F) Holder (from Lambert *et al.*, 1947), 1946. (Reproduced with permission from E. H. Wood *et al.*, *Indwelling and implantable pressure transducers*. Cleveland: CRC Press, 1977. Pp. 21–34.)

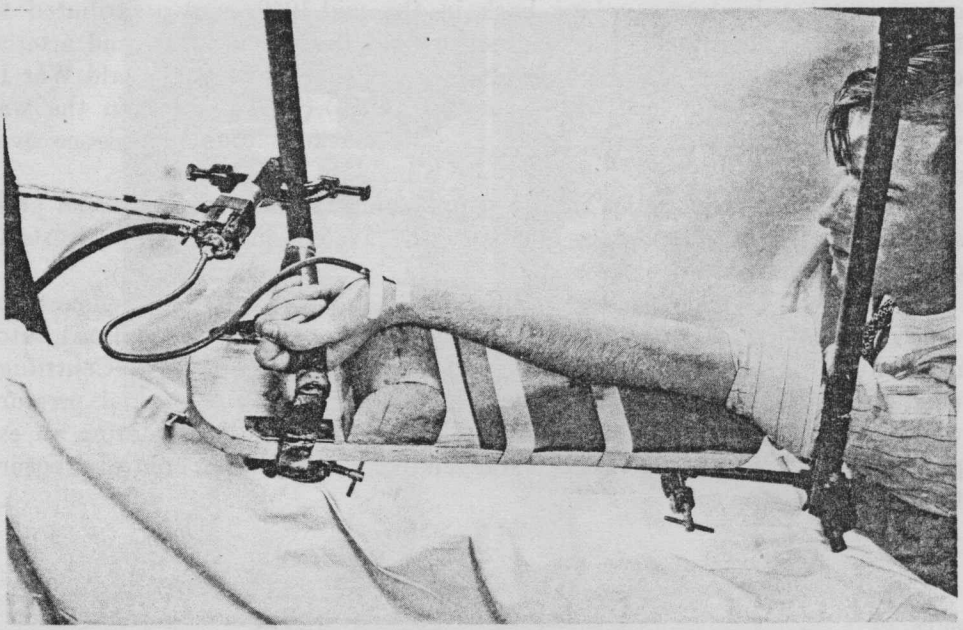

FIG. 18. Assembly used for continuous direct recording of arterial pressure in the radial artery on the Mayo Human Centrifuge. The position of the recording site was maintained at the desired level relative to the heart and/or brain during acceleration by means of the rigidly mounted arm board and wrist support, 1946. (Reproduced with permission from E. H. Wood *et al.*, *Indwelling and implantable pressure transducers*. Cleveland: CRC Press, 1977. Pp. 21–34.)

The efficacy of these devices had to be verified under actual flight conditions and this was done in a dive bomber (Fig. 23) supplied to Mayo by the Air Force and specially instrumented by Dr. Ed Lambert shown riding in the rear cockpit of the G Whiz piloted by Captain Ken Bailey who was the commander of the Rochester U.S. Air Ferry command station on the route to Russia during World War II.

Selected frames from the series of 16-mm films made in the early 1940s during these centrifuge and airplane experiments provides a more real-life impression of these studies.

One such montage prepared by Dr. Lambert from the airplane studies (Lambert, 1949; Lambert, 1950a; Lambert, 1950b) is illustrated in Fig. 24. The loss of the ear opacity pulse in the simultaneous oscillographic recordings, indicating zero blood pressure at head level, and the resulting failure to respond to light signals and disorientation of the subject are well illustrated.

That these studies carried some risks of acute sequelae is illustrated by Fig. 25 which shows the shower of petechial hemorrhages in unprotected, i.e., nonpressurized areas of the skin, following the combined use of a progressive arterial occlusion antiblackout suit and the so-called M-1 voluntary self-protective straining maneuver (Wood and Lambert, 1952) which maintained clear vision during a 15 sec exposure to a force environment nine times greater than planet Earth.

The possibility of permanent sequelae from such studies is indicated in Fig. 26 which, in the last column, lists the total accumulated periods of zero blood pressure at head level in four of the Mayo professional personnel who worked on the centrifuge from 1942 to 1945 (Wood *et al.*, 1947). Zero blood

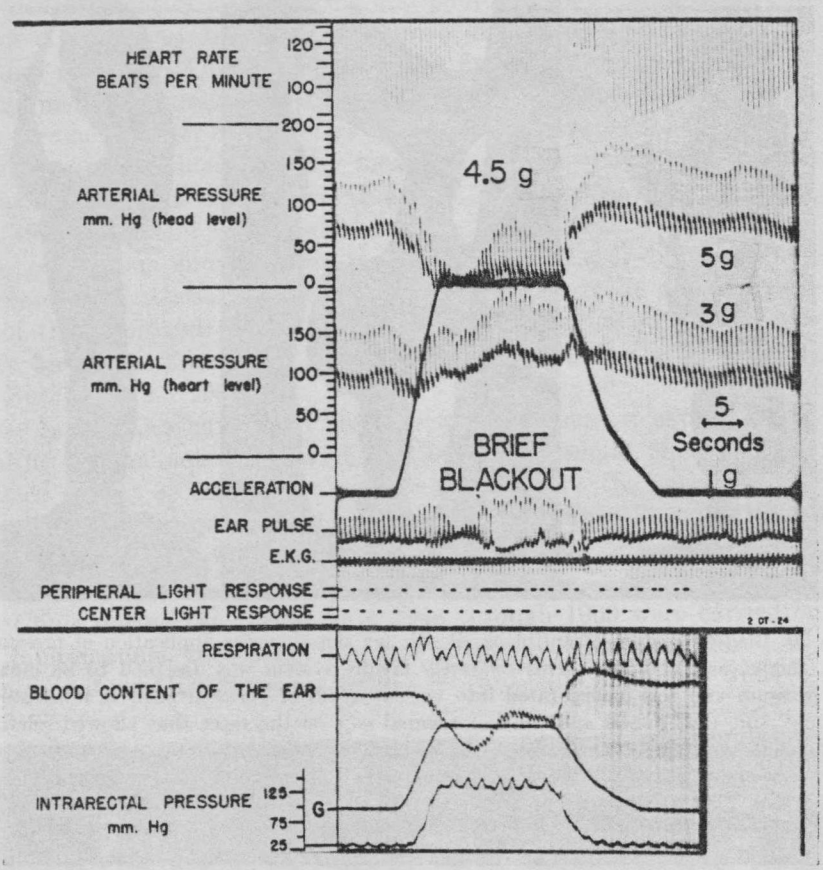

FIG. 19. Sequence of physiologic events during exposure of a healthy man to headward (positive) acceleration of 4.5*g* for 15 sec on a human centrifuge. The recordings were made by two photokymographic cameras operating simultaneously, one mounted in centrifuge cockpit (lower panel) and one in recording room adjacent to centrifuge (upper panel). Vertical white lines on upper panel delineate 5-sec intervals and were 15 mm apart before photographic reduction. Black acceleration line indicates the magnitude of headward acceleration in *g* units. Simultaneous recording of acceleration (indicated as G in lower panel) serves to synchronize the two recordings. Length of black lines designated as peripheral and center light response indicates subject's reaction times to light signals in peripheral and central fields of vision, respectively. Note initial period of progressive failure during which there are, in order of occurrence, decrease in blood pressure at head level, increase in heart rate, loss of blood volume in the ear as measured by ear opacity, reduction in amplitude of arterial pulse in the ear, and failure of peripheral vision. Then note period of compensation during latter half of exposure in which blood pressure at heart level increases to hypertensive levels to improve circulation to the head so that ear pulse recovers, blood returns to the ear, heart rate slows, and vision is restored, in spite of the fact that acceleration was continued, 1946. (Reproduced with permission from E. H. Wood *et al.*, *Federation Proceedings* 1963, 22, 1024.)