Semi-Annual Status Report - NASA Research Grant NsG-327 - October 1, 1967

Mayo Associates

STUDIES OF THE EFFECTS OF GRAVITATIONAL AND INERTIAL FORCES ON CARDIOVASCULAR AND RESPIRATORY DYNAMICS

I.   This report will summarize the progress made in investigative projects receiving support from this grant during the period, October 1, 1966 to the present.

1. **Effects of gravitational and inertial forces on intrathoracic pressure relationships in chimpanzees** - with Dr. A. C. Nolan.

The first phase of an investigation of the cardiopulmonary effects of forward $(+G_x)$ and backward $(-G_x)$ acceleration in chimpanzees is nearing completion.

The last procedure in this current series of experiments (total of 9) was done May 10, 1967 and was successful in all respects, with prompt and complete recovery of the chimpanzee afterwards.

Computer programs for real-time analysis for monitoring purposes during the experiment and for final analysis of the data on-line from analog tapes recorded during the experiments are nearing completion.

Real-Time Computer Analysis: Programs have been written for real-time analysis of arterial and mixed venous (pulmonary artery) blood oxygen saturation, vascular, intrapleural and esophageal pressures, and cardiac output (indocyanine green dilution). These programs average selectively filtered (to eliminate artifacts introduced by centrifuge rotation) data over one-second intervals and display the results on-line during the experiments. Successive oxygen saturation values are displayed on a storage oscilloscope; dye curves corrected for recirculation and derived values of cardiac output are similarly displayed. Such analysis and display are vital to the conduct of these experiments since the effects of such factors as the magnitude and duration of acceleration imposed can be continuously assessed and appropriately altered, greatly increasing the efficiency of experimentation.

N67-37113

FACILITY FORM 602

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19

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CR#88529

(NASA CR OR TMX OR AD NUMBER)

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(CATEGORY)

The results of real-time analysis are also stored on magnetic disc packs. Subsequent to a given exposure to acceleration, other programs cause these results, corrected for shifts in zero reference level produced by acceleration, to be digitally printed out and/or graphed in a calibrated analog plot against time providing an additional data base for appropriate modification of the experimental procedure from exposure to exposure.

On-Line Analysis: The programs described have been successfully applied in nine chimpanzee experiments. Based on these programs, work is nearing completion on new and more extensive programs for analysis of these data. In particular, these new programs analyze pressure variables at selected intervals during the respiratory cycle (end-inspiration, end-expiration); because of the complexity of the analytic procedures and large volume of data involved, these programs exceed the allotted core memory of the system and, hence cannot be used in a real-time mode. They will, however, from data stored during an exposure to acceleration, generate graphic displays of analyzed data shortly after the exposure and can, therefore, be used to assess and modify the course of a variety of different physiological experiments.

2. Regional effects of gravitational and inertial forces on pulmonary arterial-venous shunting - with Dr. R. A. Vandenberg.

Differences in the specific gravity of air and blood cause hydrostatic pressure differences at the interfaces between air-filled alveoli and the blood-filled capillaries surrounding them in the normal gravitational environment, and exposure to acceleration multiplies these specific gravity and hydrostatic pressure differences in proportion to the increased gravitational force produced. Thus, intravascular pressures in compartments containing blood, with a specific gravity of approximately one in the normal environment, reach high levels in dependent regions of the lungs during exposure to acceleration. However, the pressure in the alveoli, containing

air whose specific gravity does not differ significantly from zero, remains equal to ambient atmospheric pressure independent of the site of the alveoli within the thorax or the level of the gravitational force to which they are exposed. Thus, it might be expected that alveoli in dependent regions surrounded by vessels containing blood under high pressure might be compressed and atelectatic or filled with edema fluid. If this were so, blood flowing to these regions might be poorly oxygenated or might be shunted from pulmonary artery to pulmonary vein.

It has been possible to localize a pulmonary arterial-venous shunt to dependent regions of the lungs during exposure to levels of acceleration similar to those encountered by astronauts on launch and re-entry from space flight. This has been done by comparing the oxygen saturation levels, determined by cuvette oximetry, of blood being withdrawn continuously from pulmonary veins draining superior and dependent regions of the lungs simultaneously with saturation levels in the pulmonary artery and aorta in anesthetized dogs, both during respiration with air and 99.6% oxygen. Computer programs providing a continuous display in alphanumeric form of the simultaneous oxygen saturation levels in blood from three sites on an oscilloscope at a remote computer station next to the centrifuge control station, have enabled the effect of an exposure to acceleration to be monitored on-line. A printed output and Calcomp graph of oxygen saturation data, together with intravascular pressure analysis, available shortly after completion of the exposure, provide additional facility in immediate comprehension and interpretation of the results being obtained during each stage of the experiment and, on this basis, appropriate modifications of the procedure can be made, if indicated. As a result of this facility, it has been noted in some dogs that, while dependent pulmonary venous saturation usually decreases and remains similar to pulmonary arterial saturation, aortic saturation tends to recover towards the end of two-minute exposures to 5 and 7G acceleration in right and left lateral positions suggesting the possibility

that redistribution of pulmonary blood flow away from atelectatic dependent re-

gions of the lung to better ventilated areas may be occurring.

3. Effects of gravitational and inertial forces on regional distribution

of pulmonary blood flow - with Dr. J. H. Reed, Jr.

To study regional distribution of pulmonary blood flow, two methodologies

have been devised, both of which utilize the 3200 CDC digital computer as an in-

tegral part of the analysis of data obtained. The first is the use of a roentgen

videodensitometer (Mayo Clinic Proc. 39:849, 1964). This system provides a video-

magnetic tape recording of the x-ray image of the thorax during and following in-

jection of contrast media into the right ventricle and its subsequent dispersion

through the pulmonary circulation. The transmission of x-ray as recorded by this

system, bears a Beers' law relationship when the black level (i.e., the recorded

value when no x-ray impinges on the image-intensifier tube) is known. By replaying

this recorded tape, the videodensitometer provides a density-time curve at any pre-

selected rectangular site in the x-ray image.

By assuming that the contrast media is uniformly mixed as it passes through

the pulmonary valve and correcting linearly for the thickness of lung at the site

selected, the change in optical density units from the preinjection baseline, as

the result of the intravascular contrast media provides a linearized dilution curve

for each site, the area of which is related to the fraction of the cardiac output

traversing this site.

The areas of the roentgen dilution curves at the selected sampling sites are

computed on-line by the A-D converter 3200 assembly during successive replays of

the videotape using a sampling rate of 60 per second. Each data point is converted

to optical density units and the resulting optical density-time curve is filtered,

smoothed, the down slope extrapolated to correct for recirculation, and the area

computed. The results are displayed via the high speed printer.

Plots of these areas versus vertical distance show that blood flow to superior sites in the lung is decreased in proportion to the magnitude of the gravitational and inertial force to which the animal is exposed.

The second methodology utilizes radioactive microspheres with diameters of 35 $\pm$ microns. These particles are injected in the right ventricle and are assumed to mix uniformly in the blood stream as they traverse the pulmonary valve. Since the sphere diameters exceed the diameters of the capillaries, they are lodged in lung capillaries in different regions of the lung in direct proportion to the blood flow to these regions. Up to four isotopes are used in order to get four observations of flow distribution under different conditions in the same animal. These isotopes are counted by pulse height analyzers using a multiscaler mode. The counts in a particular channel are contributed to some extent by the activity in that energy range of each isotope so that the true count of any isotope must be computed by solving four equations in four unknowns. This process is carried out in the CDC 3200 digital computer by a 4 x 4 matrix inversion program. Further programs provide normalization and plotting of results of the distribution of the emboli with vertical distance so that they can be related to the conditions at the time of injection.

Data from ten animals obtained during exposures in the right lateral position to force environments of 1, 2, 4, and 6G have given the following results: Distribution of pulmonary blood flow to the dependent lung at rest varied from 50 to 73% of the total cardiac output. The lower values were associated with higher left atrial pressure and vice versa. Under increased acceleration, the superior regions showed a progressive decrease in the fraction of the cardiac output passing through it as compared to 1G (0.2 to 6.1 at 2G, 4.5 to 8.0 at 4G, and 7.5 to 18.4 at 6G). In the mid-lung region, the fraction of cardiac output increased similarly to the loss in superior region whereas the most dependent region of the lung showed

little change in spite of the fact that the greatest change in hydrostatic pressures occurred here. DPBF plus oxygen saturation data from superior and dependent pulmonary veins suggest that redistribution away from the most dependent region occurred toward the end of the 60-second exposure. These findings have important implications in relation to the inter-related factors which determine regional blood flow, alveolar size, and ventilation.

4. <u>Regional effects of the head-up and head-down positions on intrapleural and circulatory pressures and pulmonary blood flow</u> - with Dr. C. M. Coulam and Dr. J. H. Reed, Jr.

In previous studies of intrapleural pressure gradients, the pleural pressures were found to be dependent upon both the gravitational field vector of the earth (or a centrifuge produced acceleration vector) and also on the density of the thoracic contents and the position of the catheter tip (or other pressure measuring device) in the intrapleural space (J. Appl. Physiol. 21:1500, 1966). Recently, literature has appeared (J. Appl. Physiol., in press, Vertical Gradient of Alveolar Size in Lungs of Dogs Frozen Intact, J. B. Glazier, et al) which implies that this pressure gradient relationship may not hold in dogs positioned in a head-down state, as compared to the head-up, supine, and prone positions studied earlier.

Investigations have been instigated to study intrapleural pressure gradients in the head-down and head-up dog in order to investigate the above mentioned implication. Since the intrathoracic measurement of absolute pressure requires a knowledge of a catheter tip's exact location inside the chest cavity, biplane x-rays are required and subsequent pressure corrections needed in order to arrive at an absolute pressure value relative to some predetermined reference location. Also, the circulatory state of a dog and subsequent pulmonary blood flow are functions of body position - therefore, the calculation of cardiac output in each body

position must be made. The computer is used in this project for real-time cal-
culation of cardiac output, using the indicator-dilution method, and subsequent
on-line pressure data correction and reduction during replay of the analog tape
recordings obtained during the procedure. The correction of pleural pressures
is based on the work of Rutishauser et al (J. Appl. Physiol. 21:1500, 1966) and
yields pressure data which is corrected to some absolute body position (e.g.,
sixth thoracic vertebrae or to a mid-lung location). The computer programs de-
veloped by Nolan and Van Norman, described in another section of this report, are
used to determine pleural pressures at desired phases in the respiratory cycle on
a breath-to-breath basis.

Regional pulmonary blood flow in the two body positions is determined by the
radio-isotope embolization-computer technic described in the prior section of this
report.

Preliminary results indicate that the gradient in pelural pressure is approxi-
mately one centimeter of water per centimeter of vertical distance over the caudal
one-half of the lung in both the head-up and head-down positions and significantly
less than this (about 0.2-0.4 cm H_2O/cm vertical distance) in the cephalad half
in both positions. Pulmonary blood flow was decreased in whichever segments of
the lung were superior, increased in the mid portions and, in spite of hydrostatic
increases in circulatory pressures, little changed in the most dependent regions
of the thorax in the two body positions.

5. Studies of the nature of the pleural space - with Dr. C. C. Wunder.

An attempt is being made to resolve the different concepts concerning the
nature of the pleural space by following by gamma emission the sedimentation of
spheres of varying density and diameter. The spheres, which are filled with Yb[169],
are injected into the space through catheters inserted percutaneously. Sedimen-
tation occurs in accord with Stokes' Law for an open-fluid channel for portions of

spheres of 100 microns in diameter. Inability to distinguish impaction between
juxtaposed visceral and parietal pleural surfaces from adherence of the spheres
to these surfaces as causes of lack of sedimentation complicates the interpreta-
tion of results. Sedimentation or lack thereof of spheres 400 microns in diameter
can be followed by conventional roentgenograms. Spheres larger than 1000 microns
do not sediment. Optical measurements suggest that this may be the maximum width
of the space at mid-lung.

6. Development of biplane roentgen videodensitometry.

Videodensitometry has proved to afford important advantages over other indi-
cator-dilution technics with regard to frequency response, the precision with which
sampling sites can be selected, and the very valuable capability, following one in-
jection of indicator, of recording simultaneous dilution curves from as many sites
in the silhouette of the circulatory structures under investigation as desired.
Thus, specific sampling sites within ventricles or atria may be selected (e.g.,
near or away from valves, appendages, apices, inflow and outflow tracts, over re-
gurgitant streams, etc.) and opacity changes due to circulating indicator can be
determined during all phases of the cardiac cycle.

Considerable electronic development work is still underway to improve the quan-
titative capabilities of the device and to provide somplete versatility in the size
and shape of the sampling window.

Methods of calibration of the device for studies of changes in concentration
of contrast medium in the blood stream in absolute units are being developed.

The analog output of the instrument approximates a Beers' law relationship
when the black level is known. Calibration experiments have been carried out in
vitro using known concentrations and depths of Renovist solution and calibration
curves obtained using a variety of x-ray kilovoltages and thicknesses of background
x-ray absorbing media.

The model used to test the system was based on the transmission being equal to a double exponential of the following form:

$$T = \exp(-E_W\ C_W\ d_W) \cdot \exp(-E_I\ C_I\ d_I)$$

where T = transmission
       E – extinction coefficient
       W = water
       I = iodine
       C = concentration
       d = depth

A two-dimensional search routine to find the best fit, based on statistical correlation coefficient, for extinction coefficients for iodine and water (or tissue equivalent) have been obtained by the use of a CDC 3200 digital computer in this variety of circumstances. The extinction coefficients for iodine were approximately 0.9 cm^2/gm and those for water were 0.02 cm^2/gm. Since the extinction coefficient for water is small compared to that for iodine, contrast media, such as Renovist, can be considered to follow a single exponential and thus follow closely a Beers' law relationship.

7. <u>Development of time shared on-line and real-time electronic data processing and computer technics</u> – with Mr. W. Van Norman.

A Control Data Corporation general purpose 3200 digital computer and Philbrick analog computer coupled via a 32-channel analog-to-digital and 16-channel digital-to-analog converter assembly to eleven remote stations in various laboratories in the Mayo Medical Sciences Building has been in operation for sixteen months. Each of four remote stations allocated to the cardiovascular laboratories consist of an alpha-numeric keyboard for immediate input of data to the central computer on a time-shared basis and a storage oscilloscope for immediate display of instructions and output of information from the computer in alpha-numeric or analog form.

Progressive development of the software and related technics for investigative application of this powerful laboratory tool, including closed-loop operation, are

underway. It is envisaged that this type of on-line analysis of data transmitted directly from the laboratory and the immediate return display in the laboratory of the computed results will facilitate on-line comprehension by the experimenters of the nature of the results being obtained during the course of experiments and, hence greatly increase the efficiency of performance of such procedures.

The tedious task of retrospective search and retrieval of recorded data and its analysis after completion of the experiments will be reduced by these technics, and the tendency for such experiments to swamp the investigator with menial data analysis tasks, at the expense of his conceptual analyses, is minimized.

8. Study of technics for beat-to-beat determination of end-diastolic left ventricular pressures in dogs during different circulatory states - with Dr. C. Russ.

End-diastolic pressure is one of the most important determinants of left ventricular function. Its measurement from high sensitivity recordings, at first glance, appears to be a relatively straight forward determination. However, critical evaluation of this measurement from such recordings usally reveals a hemodynamically important rarge of indeterminancy of one to several centimeters of water due to the pressure wave caused by atrial systole. This pressure wave normally occurs just prior to and is fused to a variable degree with the onset of the pressure wave produced by ventricular systole. Therefore, the exact pressure at which ventricular systole begins (i.e., ventricular end-diastolic pressure) is difficult to determine with an acceptable degree of precision. Furthermore, a search of the literature has failed to reveal a description of acceptable criteria for measurement of this important determinant of ventricular function.

Study of dogs with heart block in whom the atrial and ventricular rates can be controlled by coupled electronic pacemakers offers the possibility, by selectively omitting single ventricular or atrial beats, of isolating and recording

the respective segments of the ventricular pressure pulses generated by atrial systole and those caused by ventricular systole. Therefore, by comparison of such recordings, the instant and the pressure at which the onset of the pressure wave, due to ventricular systole (i.e., the ventricular end-diastolic pressure) should be measurable with a considerable degree of precision.

Atrial and ventricular pulse pressures at various rates and atrial-ventricular stimulus intervals controlled by coupled electronic pacemakers have been recorded photokymographically and on magnetic tape. Computer programs have been written for on-line analysis of left ventricular and left atrial pressure pulses using the analog-to-digital, digital-to-analog conversion and Control Data Corporation 3200 digital systems juxtaposed to the laboratory. The computer generates, via a high-speed incremental plotter (Calcomp), an extended time-base replot of these pressures for selected series of heart beats simultaneously with their difference, the first derivative of the left ventricular pressure and the electrocardiogram.

Preliminary results suggest that comparison of these computer generated recordings of left atrial and left ventricular pressure pulses and the study of the temporal relationship of the electrocardiogram to the onset of the pressure wave indicated by the first derivative of the left ventricle will allow assessment of various criteria for measurement of end-diastolic pressure with precision.

9. Studies of mitral valve function using roentgen videodensitometry - with Dr. R. A. Vandenberg and Dr. J. C. P. Williams.

The roentgen videodensitometer samples and integrates, sixty times per second, the voltages on the videolines crossing any preselected area of a videoroentgen image stored on videotape. The voltage readout has been found to be logarithmically related to changes in contrast if the output of the instrument over lead (i.e., black level) has been set at zero, both in vivo and in vitro. This relationship is linear if, as described elsewhere in this report, the change in signal

with change in contrast is computed in optical density units. Mitral valve function has been assessed by analysis of left ventricular angiograms stored on videotape. Videodensograms have been recorded from left atrial and left ventricular sites immediately upstream and downstream to the mitral valve and the areas of the density time curves computed in optical density x seconds units. The recirculation during the latter part of the videodensogram has been excluded by computing the area under the extrapolation of the initial part of the exponential washout. The area of the left atrial as a percentage of the left ventricular videodensogram has been called the regurgitant index.

Regurgitant indexes, so calculated, have been found to be similar if the ventricle is primed by a normally sequenced effective atrial contraction, if the atria and ventricles have been driven simultaneously, or the atria caused to fibrillate. Thus, the widely held belief that the atrium plays a dominant role by preclosing the mitral valve prior to ventricular systole has been questioned. Studies of the isolated atrial and ventricular extrasystoles, made possible by the production of acute heart block by a percutaneous technic enabling atrial and ventricular contractions to be controlled independently have confirmed these observations. Mitral regurgitation was uncommon with left or right ventricular extrasystoles introduced at times varying throughout the cardiac cycle with the next beat included or excluded. Conversely, isolated atrial systoles were always followed by diastolic mitral regurgitation in the phase of atrial relaxation, the amount of regurgitation decreasing as ventricular systole was approached from either direction. The importance of ventricular systole in mitral valve closure has been further established by measurement of mitral regurgitant indexes before, during, and after extrasystolic potentiation of ventricular contraction with a normally timed effective atrial contraction with simultaneous atrial-ventricular driving and with atrial fibrillation. During extra-systolic potentiation, ventricular

performance improved and mitral regurgitation decreased; after termination of extra-systolic potentiation, ventricular performance tended to decline and mitral regurgitant indexes tended to increase. The increase was more evident with simultaneous atrial-ventricular driving and with atrial fibrillation than with effective atrial driving. This suggests that when ventricular contraction is impaired, an effective atrial contraction may improve mitral valve function while such an effect is not demonstrable in the presence of a normally functioning ventricle.

10. Effects of selective acute sympathetic and/or parasympathetic cardiac denervation on left ventricular function - with Dr. A. G. Tsakiris.

The response of the left ventricle, including the relationship of left ventricular end-diastolic volume and pressure under conditions of varied resistance to left ventricular outflow, has been studied in nine intact anesthetized dogs before and after acute cardiac denervation. The vagi were cut in the neck and the stellate ganglia and their cardiac nerves disrupted by fine wires placed around the ganglia eight to twelve days prior to the study, thus avoiding immediate thoracotomy.

Biplane left ventricular angiograms produced by small amounts of contrast material (0.2 to 0.3 ml/kg) recorded on videotape allowed repeated measurements of left ventricular volume. Experiments were done at constant heart rates by driving the atria and ventricles with coupled pacemakers. Similar changes in resistance to left ventricular outflow were produced before and after acute withdrawal of vagal and sympathetic tone by the stepwise infusion of angiotensin and acetylcholine chloride into the ascending aorta. On-line measurements of cardiac output, stroke volume, aortic pressure, and heart rate by the computer were used throughout the experiments and provided an immediately available data base upon which successive steps of the experimental procedures were based and executed.

The data indicate that after acute cardiac denervation, cardiac output and

aortic pressure were closely similar to the precontrol values. However, a decrease in end-diastolic pressure associated with increased ventricular dimensions was found for comparable afterloads.

11. A closed-loop search technic for finding the optimum atrial-ventricular stimulus interval under different hemodynamic conditions - with Dr. C. M. Coulam and Dr. J. C. P. Williams.

In a previous report, a technic was described whereby the computer, in a real-time, on-line mode would calculate the beat-by-beat cardiac output of an experimental animal utilizing the aortic pressure pulse pattern recognition method described by Warner. In this report, the computer was programmed to vary the atrial-ventricular stimulus interval in dogs with induced complete block. The optimum atrial-ventricular stimulus is defined as the interval associated with the maximum cardiac output and minimal left ventricular end-diastolic pressure. Since cardiac output varies with the phase of the respiratory cycle, the animals' respirations were suspended during the periods of computer controlled stimulus interval. This, however, resulted in limitations of the time period over which the computer could search for the optimal A-V interval. The current phase of the project involves development of computer programs utilizing pattern recognition technics to monitor the animal's respiration so that cardiac output computations can be made which are based on heart beats occurring only during a selected phase (end-expiration) of each respiratory cycle. This allows cardiac output determinations over many respiratory cycles during computer controlled variations of A-V stimulus intervals. Since respiration is not suspended, the computer can be allowed to control and seek for the optimum A-V stimulus interval over any desired period.

The pattern recognition technics applied to date have been to look at the respiration pressure derivative changes, the maximum and minimum respiratory

pressure locations, and the regions of least change in the pressure contour. Once

a specified location has been reliable (and repeatably) found on the respiratory

cycle, a sub-routine is called which allows the calculation of beat-by-beat car-

diac output and the systematic change in A-V stimulus interval in an optimization

search routine based on real-time determination of cardiac output and left atrial

pressure in a closed-loop mode.

12. The determination of circulating total blood volume from indicator-

dilution curves - with Dr. C. M. Coulam.

A method is sought whereby the calculation of circulating blood volume

(CBV) can be reliably made from a three-minute recording of indicator (indocyanine

green) dilution curves. A digital model of the circulatory system, based on a

model by Nicholes and Warner (New York Acad. Sci. 115:721-737, 1964) has been

programmed in Fortran II for off-line, non-real-time computations on the CDC 32--

computer. The model is such that circulatory transfer functions (transport func-

tions) have been assumed (Poisson distributions) for the central circulation (lungs

and heart), upper body circulation drained by the superior vena cava, the lower

body circulation drained by the inferior vena cava upstream to the renal veins,

the renal circulation, and hepatic circulation. In addition, a method has been

programmed into the hepatic pathway which allows for the theoretical removal of

"injected" indicator in such a manner that the removal of dye from the central

circulation follows an exponential washout relationship.

This model makes computer simulation of indicator-dilution curves possible

so that the effects of changes in different circulatory parameters, such as cir-

culatory mixing, indicator dispersion, regional distribution of blood flow, in-

dicator removal rate, and recirculation effects can be studied and systematically

varied. The method employs a time-domain analysis utilizing the convolution in-

tegral (Mayo Clinic Proc. 42:137, 19, 1967) approach, and pattern recognition

analysis. CBV is calculated by two methods: (1) The "true CBV" of the model is the summation of the mean transit time ($\bar{t}$) of the transfer function of each circulatory pathway times the flow fraction (blood flow) passing through that pathway, (i.e., CBV = $\Sigma_i (E_i \times \text{Frac}_i)$).

(2) The "calculated CBV" is found by fitting an exponential washout curve (with recirculation included) and locating the time t_i on this extrapolated curve such that the CBV (= injected indicator/extrapolated curve concentration at time t_i) equals the true CBV, (i.e., let the curve which describes the dye removal process from the arterial dilution curve have the form of $C(t) = C_0 e^{-kt}$ (mg/L), where C is in units of concentration, C_0 is the "zero time" concentration, k is a slope or wash-out factor, and t is time. If I is the quantity of dye injected into the circulation, then the calculated CBV is:

$$\text{Vol} = \frac{I}{C(t_i)}$$

where t_i is a particular time.

The primary objective of this research is to determine if a relationship exists between t_i and some or several parameters of dye dilution curves, such that the circulating blood volume can be calculated with acceptable reliability without the need for implicit description of each circulatory pathway. If this is possible, cardiac output, fastest and mean circulation times, plus central and circulating blood volumes could be calculated from a single indicator-dilution curve. This capability would be of great value in investigative, diagnostic, and patient monitoring applications of the indicator-dilution technic.

II. Plans for investigative projects to be completed or initiated in the period, October 1967 - October 1968:

Work will continue on the projects described herein.

Plans for continued developments of biplane roentgen videometry for dynamic studies of left ventricular function in chimpanzees and free ranging unanesthetized dogs under various types of circulatory stress are described in detail in the request for renewal of this grant being submitted with this status report.

III. Papers published or in press:

1. Rutishauser, W. J., Banchero, N., Tsakiris, A. G., Edmundowicz, A. C. and Wood, E. H.:
Pleural pressures at dorsal and ventral sites in supine and prone body positions.
Journal of Applied Physiology 21:1500-1510 (September) 1966.

2. Kenner, H. M. and Wood, E. H.:
Intrapericardial, intrapleural and intracardiac pressures during acute heart failure in dogs studied without thoracotomy.
Circulation Research 19:1071-1079 (December) 1966.

3. Coulam, C. M., Warner, H. R., Wood, E. H., and Bassingthwaighte, J. B.:
A transfer function analysis of coronary and renal circulation caculated from upstream and downstream indicator-dilution curves.
Circulation Research 19:879-890 (November) 1966.

4. Banchero, N., Rutishauser, W. J., Tsakiris, A. G., and Wood, E. H.:
Pericardial pressure during transverse acceleration in dogs without thoracotomy.
Circulation Research 20:65-77 (January) 1967.

5. Banchero, N., Cronin, L., Rutishauser, W. J., Tsakiris, A. G., and Wood, E. H.:
Effects of transverse acceleration on blood oxygen saturation.
Journal of Applied Physiology 22:731-739 (April) 1967.

6. Williams, J. C. P., O'Donovan, T. P. B., Cronin, L., and Wood, E. H.:
Influence of sequence of atrial and ventricular systoles on closure of mitral valve.
Journal of Applied Physiology 22:786-792 (April) 1967.

7. Rutishauser, W. J., Banchero, N., Tsakiris, A. G., and Wood, E. H.:
The effect of gravitational and inertial forces on pleural and esophageal pressures.
Journal of Applied Physiology 22:1041-1052 (June) 1967.

8. Banchero, N., Schwartz, P. E., and Wood, E. H.:
    Intraesophageal pressure gradient in man.
    Journal of Applied Physiology 22:1066-1074 (June) 1967.

9. Banchero, N., Rutishauser, W. J., Tsakiris, A. G., and Wood, E. H.:
    Respiratory changes in pleural pressures at different sites and body
    positions.
    Journal of Applied Physiology 22:1075-1080 (June) 1967.

10. Banchero, N., Schwartz, P., Tsakiris, A. G., and Wood, E. H.:
    Pleural and esophageal pressures in the upright body position.
    Journal of Applied Physiology (in press).

11. Reed, J. H., Jr., and Wood, E. H.:
    Use of dichromatic earpiece densitometry for determination of cardiac
    output.
    Journal of Applied Physiology (in press).

12. Wood, E. H.:
    The roentgen videodensitometry technic and its application to the study
    of mitral valve closure.
    Cardiologia (in press).

13. Wood, E. H.:
    Some effects of gravitational and inertial forces on the cardiopulmonary
    system - The Harry G. Armstrong Lecture.
    Aerospace Medicine 38:225-233 (March) 1967.

Earl H. Wood, M.D., Ph.D.
August 10, 1967

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