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STUDIES OF THE EFFECTS OF ACCELERATION ON CARDIOVASCULAR AND RESPIRATORY DYNAMICS

This report will summarize the progress made in investigative projects supported by this grant during the period, April 1, 1966 to October 1, 1966, and outline plans for investigative activities planned for the second twelve-months of the three-year period specified in the original grant request.

I. Specific Projects

1. Regional pulmonary arterial-venous shunting during exposure to transverse acceleration.

A major phase of this project has been completed and a final report of the results has been prepared. By continuous recording of the oxygen saturation of regional pulmonary venous blood sampled via cuvette oximeters through catheters introduced by transseptal punctures, it has been demonstrated that the decrease in arterial oxygen saturation during exposure to acceleration is caused by a pulmonary arterial-venous shunt through dependent regions of the lungs. In order to study this phenomenon more thoroughly when breathing 99.6% oxygen, additional experiments are to be carried out during longer duration (3 to 5-minute) exposures to acceleration. One-minute exposures were used in the prior experiments.

The use of longer duration exposures requires development of technics for continuous sampling and concomitant reinfusion of the sampled blood from three vascular sites simultaneously for periods of five or more minutes. The three sites are the pulmonary artery (mixed venous blood), the femoral artery (mixed arterial blood), and a ventral or dorsal pulmonary vein (regional pulmonary venous blood). Use of special roller type pumps for this purpose is being explored.

2. Pleural and pericardial pressure measurements during G_x acceleration in primates.

Studies have been carried out in four chimpanzees. It is anticipated that additional studies on four additional chimpanzees will provide the data to complete the first phase of this study.

Continuous recordings are made of airway (endotracheal tube), aortic, pulmonary artery, right atrial, dorsal, and ventral right pleural and left pleural, and esophageal pressures, along with centrifuge RPM, and angle of tilt of the cockpit during several series of exposures to 2, 4, and 6 G_x when in the prone and supine positions supported by individually molded half-body casts. In some exposures, the oxygen saturations of femoral artery (mixed arterial) and pulmonary artery (mixed venous) blood were recorded continuously and in others cardiac output determined by the dye-dilution technic.

Completion of these observations requires that the chimpanzee be maintained under anesthesia for a period of about fifteen hours. All of the animals studied have survived the procedure. However, one animal was sacrificed about one month after the procedure due to thrombo-arteritic complications resulting from femoral artery catheterization.

3. Development of on-line time-sharing electronic data processing and computer analysis technics.

A Control Data 3200 computer coupled with an Adcomp read-writer interface was installed in January 1966 at a site in the Medical Sciences Building in close proximity to the human centrifuge. This assembly's fast cycle time (1.25 μsec) and multiplexed read-write interface, permitting random access sampling at rates up to 10,000 samples per second, have improved time-sharing of the facility and also extended the range of on-line data analysis.

Programs have been developed for analysis of pressure data, accelerative force, phases of respiration, cuvette oximetry, and indicator-dilution curves input to the computer in analog form during centrifuge runs. These programs are stored on disc files and called into use by interrupt of the computer from a "remote" station in the centrifuge control and monitoring area. After initial

elimination of high frequency vibrational artifacts by smoothing through 8th order Butterworth filters set up on a Philbrick analog computer, the pressure data is digitally corrected for baseline shift caused by accelerative forces on the manometer assemblies. Pleural pressures are automatically referred to the site of the respective catheter tips in the thorax. A computer generated plot from the Calcomp incremental plotter of corrected pressures from multiple sites and oxygen saturation data from three double-scale cuvette oximeters, recording continuously throughout the period of acceleration, is available for study immediately after each centrifuge run. These data now enable the investigator to modify the experimental design in the light of results being accumulated during the course of the experiment rather than after retrospective data analysis. They may indicate the need to adjust the sampling sites or suggest the desirability and manner of obtaining additional information to support or amplify the experimental procedure.

Programs and communications have been developed also to allow similar on-line computer analysis of data transmitted from two experimental laboratories equipped for remote console computer interrupt and program selection. Analog vascular and pleural pressure data may be analyzed for mean, maximal, and minimal values, and cardiac output or stroke volume, heart rate, cycle length, duration of systolic ejection and peripheral resistance derived by real-time analysis of the contour of central aortic pressure pulses. Indicator-dilution curves can be analyzed on-line directly after inscription and oxygen saturation data computed during withdrawal of samples through double-scale cuvette oximeters with logarithmic response characteristics. Digital outputs from the computer through the Adcomp write-interface have been programmed to provide triggering pulses to coupled electronic cardiac pacemakers so that the rate, sequence of, and interval between atrial and ventricular contraction can be automatically regulated by the computer in whatever manner the investigator may direct through octal switch settings at "remote" station interrupt boxes. These technics have been

utilized in a study of the optimal atrial-ventricular stimulus interval at heart rates from 80 to 200 beats/minute. Additional programs, now being developed, will allow computer analysis of videodensitometer indicator-dilution curves derived from angiocardiograms recorded on videotape following injections of Renovist into selected sites in the heart and circulation. These programs will permit immediate assessment by videodensitometer technics of circulatory parameters such as regional pulmonary blood flow during exposure to acceleration.

The installation of a high-speed access digital computer in close proximity to the animal experimental and centrifuge areas in the Medical Sciences Building and the successful development of associated hardware and software has markedly augmented the laboratory's data handling capacity and considerably extended the range and complexity of the experiments it can undertake.

4. Modification and strengthening of the centrifuge.

Structural reinforcements of the centrifuge superstructure have been completed so that the special biplane roentgenographic concentric cockpit assembly can be accelerated safely to levels of 10G.

Servo control of the cockpit angle has been added.

Improvement of the clutching and braking mechanism has allowed adequate acceleration to and attainment of satisfactory flywheel speeds with the current electrical power facility.

II. Plans for investigative projects to be completed or initiated in the period October 1966-October 1967.

Work will continue on the projects described herein:

1. Studies of effects of acceleration on regional pulmonary blood flow using roentgen videodensitometry and radioisotope embolization technics have been reinstated using an improved roentgen videodensitometer and isotopically labeled microspheres of variable specific gravity.

Anesthetized dogs and chimpanzees will be studied on the human centrifuge while supported in the prone and in the supine positions by means of half-body molded plastic casts.

Pulmonary arterial, left atrial and systemic arterial pressures will be recorded via percutaneous catheters and cardiac output determined while at 1G and during centrifuge rotation by injection of indocyanine green dye into the pulmonary artery with continuous densitometric sampling of descending aortic blood via a percutaneous femoral artery catheter.

Lateral videoangiograms of the heart and lungs will be recorded with 4-6 ml injections of roentgen contrast media (69% Renovist) in the right ventricular outflow tract while the dog is supported in the prone position at 1G and at levels of acceleration of 2, 4, and 6G.

An injection of isotope-labeled albumin aggregate will then be made into the right ventricular outflow tract during a repeat exposure to 6G. The distribution of the radioactive emboli in the lung will then be determined using a specially adapted scanning mechanism which moves a scintillation probe so that its vertical and horizontal position in the scanning plane is continuously recorded in relation to the disintegration counts obtained from the sodium iodide crystal detector. This produces a matrix of the lung region from which activity curves in the plane of the resultant vector of the centripetal acceleration and the 1G gravitational field of the earth can be obtained and shifts in activity computed. One or more injections of labeled albumin aggregates will be made in the same animal while supported in the same body cast at 1G at intervals of one week prior to the centrifuge exposure. Identical injections will be repeated at successive similar intervals when the animal is exposed to 1, 2, and 4G, respectively, following the initial centrifuge experiment when the injection of the albumin aggregate was made at 6G. Mapping of activity throughout the lung fields will be carried out after each of these injections so that comparisons of the distribution of labeled aggregates can be made at levels of acceleration from 1 to 6G. Since the number of data points per scan is very large, reasonably complete analysis of the data along with correlation with other variables requires use of electronic data-processing and computer technics. The plots obtained of the distribution of the labeled albumin aggregate emboli

in the lungs are presumably directly proportional to the regional pulmonary blood flow.

The regional distribution of pulmonary blood flow at the same levels of acceleration will be determined independently by roentgen videodensitometric analysis of the video angiograms recorded under these condtions. This will be done by replaying of the tape recorded angiograms for recording dilution curves of the contrast media using the roentgen videodensitometer developed in this laboratory. For this application, the sampling window of the videodensitometer will, during successive replays of the videotape, be placed over as many different superior, mid and dependent regions of the lungs as desired. Regional mapping of contrast media from these videodensograms will be done similar to the radioisotope maps and the results of the two compared.

The mean transit time of the contrast medium from the origin of the pulmonary artery to the left atrium will also be measured by placing the sampling window over the silhouette of these structures during successive replays of the same video angiographic tape.

The variations in distribution of pulmonary blood flow determined by these independent technics will be correlated with the simultaneously recorded pulmonary artery and left atrial pressures corrected on the basis of biplane roentgenograms to the same vertical heights (i.e., hydrostatic levels) as the selected sites in the superior, mid and dependent lungs sites at which pulmonary flow distribution was determined. Correlations with pleural pressure levels recorded at the same vertical levels while at the same resultant acceleration ($-G_x$) vector will be made as well as correlations with the degree of pulmonary arterial-venous shunting estimated from continuous oximetric determinations of the oxygen saturations of arterial and mixed venous blood under the same conditions.

Comparison of blood flow distribution results by roentgen videodensitometry and by non-embolic and embolic isotope technics is also envisaged by using

radio-opaque microspheres on the one hand and radioisotope labeled spheres of the same selected diameters on the other. In the non-embolization comparative studies, in which the blood stream is "labeled" by injection of conventional roentgen contrast media as compared to labeling with radio-opaque or radioactive microspheres, the diameters of the spheres will be selected so as to traverse the pulmonary capillaries. For the embolization studies, the diameter of the microspheres will be selected so as to be large enough to prevent traversal of the pulmonary capillary bed. The results using static radioisotopic detection subsequent to injections will then be compared with the values obtained by dynamic videodensitometric detection, during injection, of the distribution and the hold up of the embolizing microspheres in the lungs.

The capability of making studies during exposure to an increased force environment on the human centrifuge also invites study of the effect of variation of the specific gravity of the microspheres on their distribution, since such effects will be multiplied in direct proportion to the G level of the environment.

The possible effects of gravitational forces on the distribution of pulmonary blood flow and associated effects on pulmonary mechanics and regional ventilation have been a subject of great interest to pulmonary physiologists and have been recognized to be of some clinical importance for a number of years.

Development of physiologic methods for determining regional differences in pulmonary blood flow in intact man or animals will make possible further elucidation of these effects. It is currently gradually being recognized that pleural pressure varies with the vertical height in the thorax, and large regional differences in pleural pressure (greater negativity superiorly and increases to positive values in dependent regions of the lungs) occur during the increase in weight of the thoracic contents produced by acceleration.

These pleural pressure differences at levels of acceleration of greater than 4G are associated with significant arterial hypoxemia apparently due to severe disturbances in ventilation-perfusion ratios with pulmonary arterial-venous shunting through the dependent, atelectatic areas of the lung. The concomitant high alveolar-to-pleural pressure gradients in the most superior sites in the lungs apparently are responsible for the instances of physical damage to lung parenchyma which have been observed during exposure to high levels of acceleration. These effects are of practical importance in relation to the launch and re-entry phases of manned space flights. Furthermore, the exaggeration, which can be produced at will on a centrifuge, of the normal gravitational effects associated with the 1G environment offers a valuable means of magnifying these relatively small but practically important effects so that they can be readily detected and studied.

2. Development of a technic for dynamic measurements (60/second) of ventricular volume and shape using biplane roentgen videometry is underway. It is anticipated that these technics may be used to validate and calibrate the less direct methods to obtain such data which may be applicable for observations during space flight.

In brief, the measurements of ventricular volume will be made as follows: The video signals from the replay of the videotape will be fed into special electronic circuitry which will recognize the instants that each horizontal video line encounters and leaves the edges of the two projections of the opacified left ventricle. The distances (as horizontal traversal times of the video beam) of these edges from one another and from the left margins of the two video images will be measured and these four values fed into a digital computer. The computer will be programmed to calculate from these values the area of the cross-section of the left ventricle traversed by each horizontal line and to sum these areas for all horizontal lines crossing the left ventricle during

each video field, thus providing a value for left ventricular volume sixty times each second (the field repetition rate of the video system).

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