Mayo Association

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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, October 1, 1965 to April 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.

The decrease in arterial blood oxygen saturation during and after transverse acceleration has been attributed to pulmonary arterial-venous shunting in dependent regions of the lungs considered to have become atelectatic as a result of the increased weight of the blood and thoracic contents relative to air. This postulate has been examined in anesthetized dogs exposed to 2, 4, and 6G acceleration in the supine ($+G_x$) and prone ($-G_x$) positions during IPP respiration with air and 99.6% oxygen, and also during spontaneous respiration with 99.6% oxygen. The site of the pulmonary arterial-venous shunt has been localized to dependent regions of the lungs by comparing the oxygen saturation of blood withdrawn continuously from superior and dependent pulmonary veins through cuvette oximeters with similarly determined blood oxygen saturation levels in the aorta.

Teflon catheters (#6F) were introduced percutaneously into the left atrium by transseptal puncture and manipulated under fluoroscopy so that their tips were in upper and lower lobe veins in the left or right lung. Figure 1 shows lateral and posterior-anterior pulmonary vein angiograms after injection of 2 to 3 ml. of 69% Renovist into such catheters. For oximetry, pressure recording and indicator-dilution studies, other catheters were positioned in the right atrium, both pulmonary arteries, aorta, and femoral artery. The pulmonary

vein catheters were placed so that left atrial blood could not be withdrawn retrogradely and contaminate the venous sample. Absence of contamination was confirmed by injecting 2.5 mg. indocyanine green into the contralateral pulmonary artery and recording indicator-dilution curves from the pulmonary vein and aorta. If no deflection occurred in the venous curve during inscription of the primary femoral artery curve, the siting of the pulmonary vein catheter was considered satisfactory. Using the same technic during 6G acceleration, it was demonstrated in two dogs that blood sampled through catheters correctly located at 1G remained uncontaminated. In all dogs, stability of catheter positions was checked by thoracic roentgenograms exposed approximately at the middle of every period of acceleration. Catheters positioned in the left or right lower lobe (dependent in the supine position and superior in the prone position) provided the most consistent data. Before, during, and after exposures to acceleration of 60-90 seconds, blood was withdrawn continuously at constant rate (4 to 9.9 ml./min.) using Harvard withdrawal pumps from pulmonary artery, pulmonary veins, and aorta. After "on-line" analog-digital conversion, the double-scale oximetry and pressure data were analyzed in real-time with a CDC 3200 digital computer programmed to calculate oxygen saturations, systolic, diastolic, and mean vascular pressures, acceleration, and respiratory excursion. The experimental data were also recorded on photokymographic paper and magnetic tape. Periodically throughout the study and between each exposure to acceleration, the dogs were hyperinflated. With increasing levels of forward ($+G_x$) acceleration, both dependent pulmonary vein and arterial blood saturation decreased, and the pulmonary vein saturation fell to a lower level than arterial (see Figure 2). Note that during 6G acceleration, dependent pulmonary vein saturation fell from a mean control of 86.5% (82-98) to a mean low of 61% (48.5-79.5) while the arterial sample fell from a mean control of 94% (88-98) to a mean low of 71% (60-90). Thus, the dependent pulmonary vein-systemic arterial oxygen saturation difference increased from a mean control of 7.5% to 10% at the mean low. In the immediate post-6G period, arterial saturation

rose more rapidly than dependent pulmonary vein saturation so that pulmonary vein-arterial systemic oxygen saturation difference increased to a mean maximum of 14.5% sixty seconds after stopping acceleration. These observations at 6G related to pulmonary vein sampling sites and dependent lung borders at mean hydrostatic distances of 17.4G·cm. (9.9-27.6) and 39G·cm. (33.3-45.6), respectively, below mid-lung. The effect of graded backward acceleration on superior pulmonary vein blood saturation was in marked contrast to the effect of forward acceleration on dependent pulmonary vein saturation (Figure 3). Although there was a similar decrease in arterial blood saturation with increasing acceleration, superior pulmonary vein blood saturation showed little or no change. Note that during 6G acceleration, arterial blood saturation fell from a mean control of 89% (82-96) to a mean low of 74% (64-87), but superior pulmonary vein saturation changed only from a mean control of 98% (96-99.5) to a mean low of 97% (94-99). The maximum mean superior pulmonary vein-systemic arterial oxygen saturation difference (23%) occurred 20 seconds after stopping acceleration. These observations at 6G acceleration relate to pulmonary vein sampling sites and superior lung borders at mean hydrostatic distances of 11.5G·cm. (-1.8-17.7) and 37.8G·cm. (33-45), respectively, above mid-lung. It is concluded from these data that little or no arterial-venous shunting occurs through superior regions of the lungs during transverse acceleration and IPP respiration with air.

With 99.6% oxygen breathing, patterns of change in dependent pulmonary blood saturation during and after forward ($+G_x$) acceleration and superior pulmonary vein saturation during and after 6G backward ($-G_x$) acceleration were directionally similar to those when the dogs were breathing air. In four dogs during 90-second exposures to 6G forward acceleration, dependent pulmonary vein saturation fell from a control of 100% to a mean low of 89.5% (76-100), while arterial saturation fell from a mean control of 98.5% (96-100) to a mean low of 96.5% (89-100). Since oxygen breathing should offset a contribution to pulmonary vein desaturation from abnormal ventilation perfusion

ratios, or a diffusion limitation, if any, resulting from acceleration induced pulmonary edema, the decreases in dependent pulmonary vein and systemic arterial blood oxygen saturation demonstrated in this study during and after exposure to transverse acceleration have been attributed primarily to arterial-venous shunting past atelectatic areas of the dependent lung.

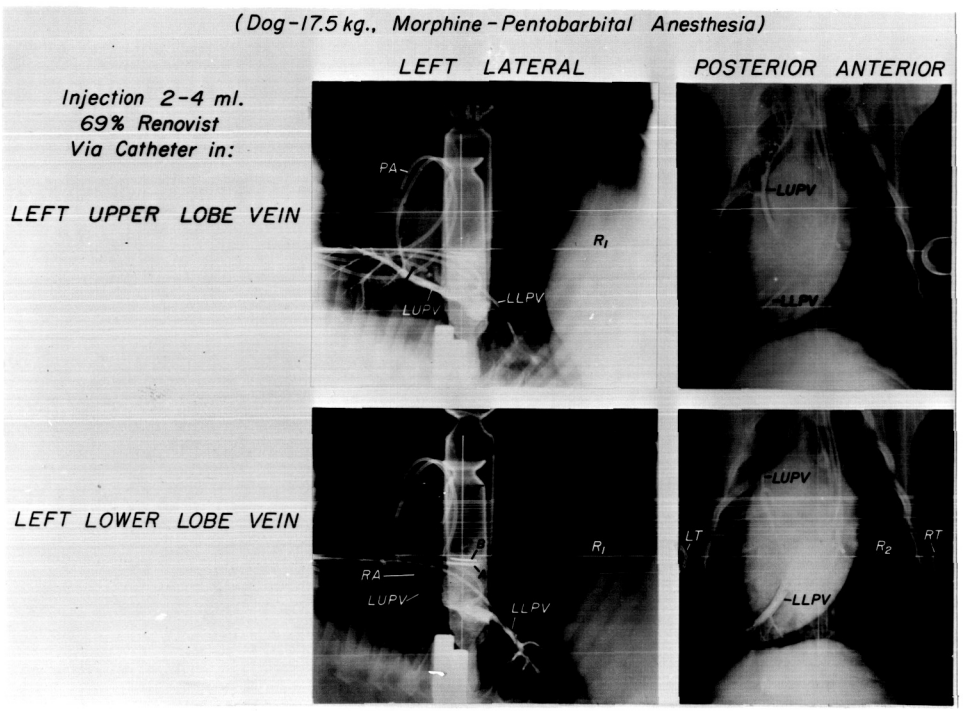

Figure 1 Left lateral and posterior-anterior pulmonary vein angiograms following injections of 2-3 ml. Renovist into sealed-end catheters (#6F) with one side hole 1.5 cm. from the tip. The catheters were positioned in left upper (LUPV) and left lower (LLPV) pulmonary veins in a dog supported supine in a half-body cast.

Distances of catheter sampling sites and lung borders to mid-lung were determined from similar thoracic roentgenograms taken at approximately the middle of periods of acceleration.

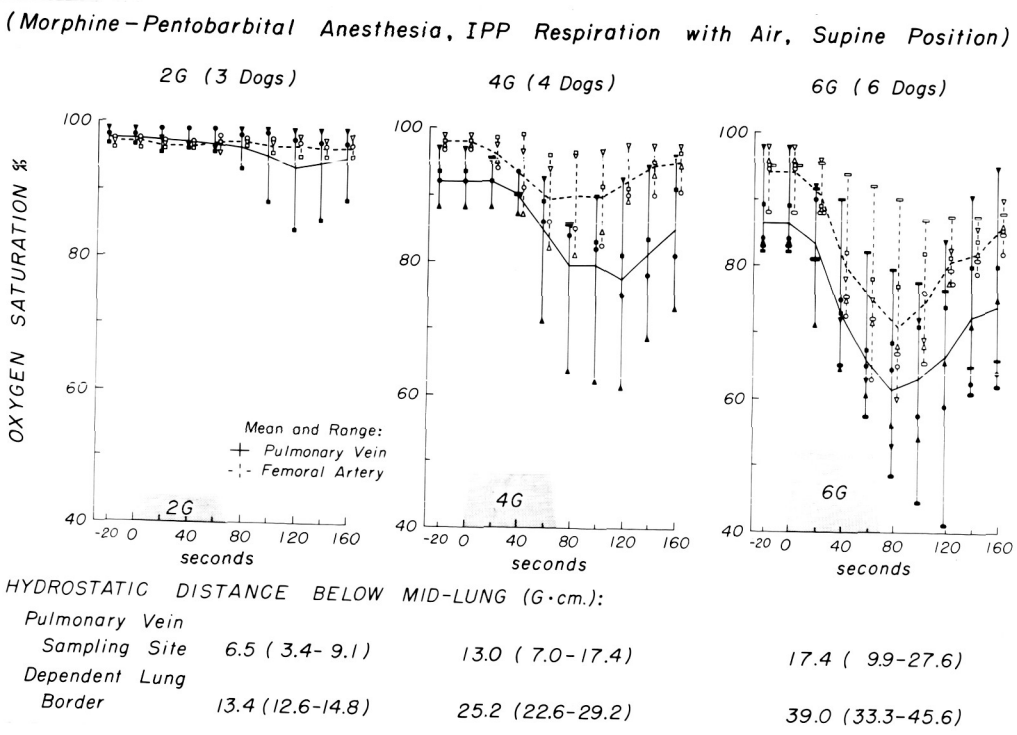

Figure 2 Summary of effect of successive exposures to 2, 4, and 6G forward ($+G_x$) acceleration for 60 seconds on systemic arterial and right or left lower lobe dependent pulmonary vein blood oxygen saturation during IPP respiration with air. Each point is corrected for catheter delay time and is the average of the previous 20-seconds continuous sampling at constant rates of 4 to 9.9 ml./min. Each dog is identified by a symbol. Note that dependent pulmonary vein blood oxygen saturation decreases and remains persistently lower than systemic arterial saturation during and after each successive exposure to increasing acceleration.

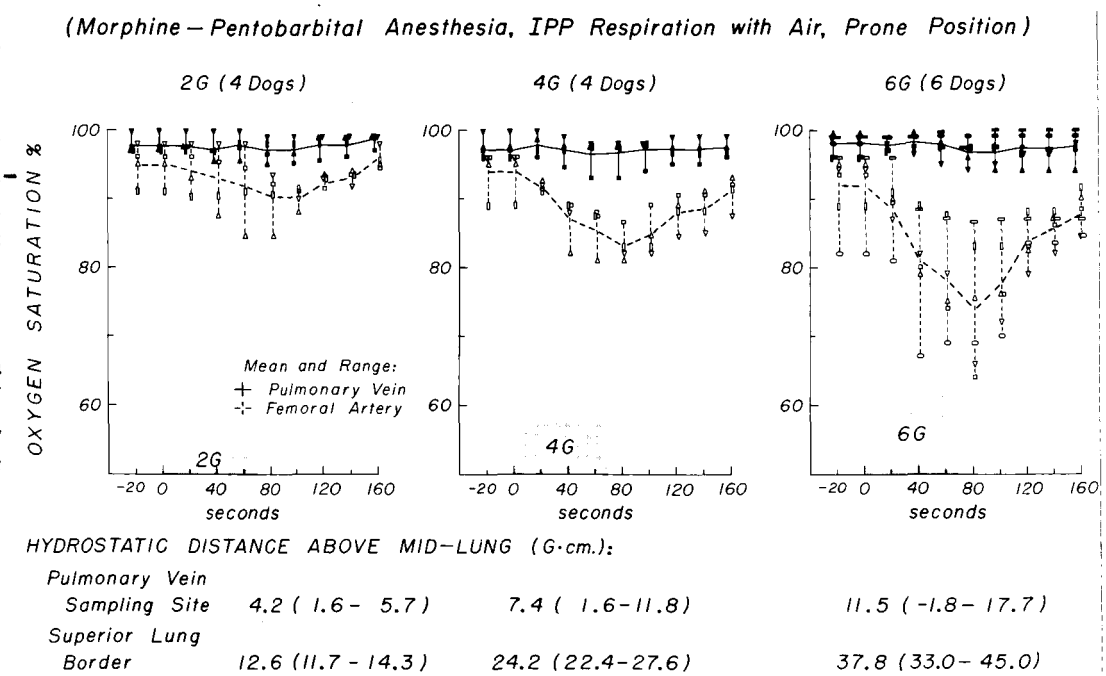

Figure 3 In dogs respired with air by IPP and subjected (in the prone position) to 2,4 and 6G backward ($-G_x$) acceleration, superior pulmonary vein blood oxygen saturation remained at control levels although systemic arterial oxygen saturation decreased progressively with increasing acceleration as shown in Figure 2. Comparison of these two figures illustrates the effect of the direction of transverse acceleration on the saturation of the regional pulmonary venous drainage.

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

The technic of making the half-body roentgenolucent plastic casts for support of the individual chimpanzees (25-30 kg. weight range) in the prone and the supine positions during exposures to acceleration of up to 6 G_x has been worked out in conjunction with Holloman Air Force Base.

A pilot procedure on the centrifuge to test out this body support system plus the anesthetic and handling technics to be used was carried out on November 9, 1965.

The first full-blown centrifuge experiment was completed on November 23. Airway (endotracheal tube), aortic, pulmonary artery, right atrial, dorsal and ventral right pleural and left pleural, and esophageal pressures were recorded continuously 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. In some of the exposures, the oxygen saturations of femoral artery and pulmonary artery (mixed venous) blood were recorded continuously before, during, and after the sixty-second exposures to acceleration.

In other exposures, cardiac output was recorded by the dye-dilution technic. Measurements were made while the chimpanzee was breathing air or 99.6% oxygen.

The chimpanzee, who was maintained under anesthesia for a period of fifteen hours during the conduct of these observations, recovered completely and was returned to Holloman Air Force Base in good condition.

A similar procedure was carried out on a second chimpanzee on January 12, 1966. Due to the occurrence of severe arterial hypoxemia resulting from inadequate spontaneous respiratory efforts while under anesthesia, this experiment was not fully successful although apparently valuable data concerning the effects of plus and minus G_x acceleration on intrathoracic pressures were obtained. The chimpanzee recovered completely following the 15-hour period of anesthesia required for the performance of the experiment.

The data provided by these two experiments were recorded both on photokymographic paper and magnetic tape. After selective filtering to eliminate high frequency vibrational artifacts, induced by centrifuge rotation, these data are to be relayed via a 16-channel Adcomp analog-to-digital converter to a CDC 3200 digital computer installed and available to the laboratory in January, 1966. Programs, nearly completed, are being written in the laboratory for this data-processing-computer-assembly which will allow very rapid and extensive analysis of these pressure and oxygen saturation data. In addition, it is planned to adapt a functioning program for determining beat-to-beat changes in cardiac output and vascular resistance by a combination of the indicator-dilution and pulse-contour methods to centrifuge experiments. These programs will permit much more complete analysis of these data than would be possible by manual methods and in a fraction of the time. The pressure data are selectively filtered using low band pass eighth-order Butterworth filters, set up on a Philbrick analog computer, which provide an approximate 48 decibels per octave cut-off at the desired frequency levels, thus greatly reducing the sampling rates required for the Adcomp-3200 system. When these computer programs are finished, it is anticipated by using a combination of immediate interrupt and

time-sharing (with four other remote laboratory stations) modes of operation that the full power of the Philbrick analog computer - Adcomp A-to-D and D-to-A converter - 3200 digital computer assembly can be made available for on-line analysis during and only during the two to three minute recording periods associated with each sixty-second exposure to acceleration. Thus, complete electronic data-processing of data from each period of centrifuge rotation will be available for immediate monitoring and review after each exposure to acceleration during an experiment. This system will allow much greater efficiency and flexibility in the conduct of experiments. Also, subsequent more detailed and variable modes of analysis of the magnetic tapes recording during the experiments will be possible.

Preliminary analysis of the data from the first two experiments indicates that the changes in oxygen saturation caused by $+G_x$ and $-G_x$ acceleration are similar to those previously demonstrated in man and dogs.

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

Initial experience with real-time analysis of analog data recorded in experimental laboratories in the Medical Sciences Building and transmitted 800 feet to a 7040 IBM computer facility in the Harwick Building clearly demonstrated the advances in experimental procedure to be gained by the successful development of requisite hardware and software for remote control time-sharing operation of a medium size digital computer. Programs called by setting octal switches on an interrupt box in the laboratory have allowed both input of up to 16 channels of analog data and input of digital data variables requested by the programs themselves in alphanumeric displays on a storage oscilloscope in the laboratory. After on-line digital conversion and computer analysis of the analog signals, the results of the computations are printed out in extended form on the high-speed printer and salient values also displayed both digitally and graphically on the storage oscilloscope back in the laboratory itself.

Investigator-computer interaction was, however, found to be inhibited by the considerable geographic separation of the 7040 computer and the relative unsuitability of this system for a time-sharing real-time mode of operation. Accordingly, a Control Data 3200 computer coupled with an Adcomp read-write interface was installed in January 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 not only improved time-sharing of the facility but 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 printout 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 rapid 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.

II. Plans for investigative projects to be completed or initiated in the period, April to October 1, 1966.

Work will be continued on the projects herein described.

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March 31, 1966

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