AIR1.941130.025c

PROTOCOL OF EXPERIMENT INVOLVING
HUMAN VOLUNTEERS

Title: Measurement of Cardiac Stroke Volume Using an External Coincidence Counting System and Albumin Tagged Cobalt-58

Project 7755-01-005

Principal Investigators: Major Malcolm C. Lancaster, Chief of the Internal Medicine Branch will be the principal investigator and will be designated as Responsible Medical Officer. In addition, Captain Raymond A. Schwegler and Captain Paul L. McHenry, both of the Internal Medicine Branch, will be directly involved in the performance of this study.

Medical Consultant: Captain Raymond A. Schwegler

Technical Objectives: This study will be a clinical evaluation of the method of measuring cardiac stroke volume by means of precordial coincidence counting utilizing albumin tagged Cobalt-58.

Background: Techniques for measuring cardiac output and stroke volume using precordial singles counting and albumin tagged isotopes have been thoroughly investigated and clinically utilized(1). However, it is felt that coincidence counting techniques made possible by the more recent development of coincidence counting apparatus will make this method of measuring cardiac output a much more reliable and efficient clinical procedure. The present study is necessary to compare the values obtained by this technique using coincidence counting equipment with other standard non-isotopic means of measuring cardiac output such as the use of cardiogreen dye curves.

The theoretical advantages of this technique in measuring cardiac output during non-steady states such as during exercise must also be evaluated including the practicality of obtaining instantaneous and repetitive measurements of cardiac output over short intervals of time.

These studies are to be performed to determine the feasibility of using this technique in the routine clinical evaluation of outpatients with known or suspected cardiac disease. The applicability of using this method in the cardiovascular evaluation of normal subjects such as those undergoing various conditioning and deconditioning studies will also be determined from the results obtained in the initial studies.

Hazards: The potential hazards to the volunteer subjects are negligible. The maximal total body radiation dose received by any one subject will be 0.2 roentgens and the retained isotope (Cobalt-58) will amount to less than 25% of the permissible body burden for occupational exposure (based on calculations for a 70 Kg man).

The only additional procedures required of the volunteer subjects will be transcutaneous arterial and venous catheterization on one occasion only, just prior to injection of the isotope. The venous catheter will not be advanced beyond the superior vena cava and the arterial catheter will be placed at some point distal to the subclavian artery. The catheters will be in place for a maximal period of 3 hours during which time they will be utilized to make the necessary dye measurements of cardiac output which are needed to correlate with the radioisotope measurements. The use of transcutaneous catheters for cardiac output measurement is a standard clinical procedure and in the hands of experienced personnel there are no significant hazards to the subject. The hazards which might arise would include minor hematoma formation at the site of the transcutaneous puncture and transient arterial spasms at the site of the arterial puncture. These potential hazards will be thoroughly explained to the subject prior to testing. The blood withdrawn in performing dye dilution curves will amount to no more than a maximum of 50 cc's and as such will present no hazard.

The subjects will also be instructed as to the amount of radiation which they are to receive and it will be pointed out to them that the total dose utilized will amount to approximately that received by two chest x-rays.

Since the human volunteers are to be utilized on only one occasion for a maximum period of 3 hours, hazardous duty pay will not be required.

Requirements for Human Volunteers:

a. Number Required: A total of 30 subjects without manifest disease will be studied. These subjects will be volunteers obtained from the United States Air Force Training Command Basic Training Program at Lackland AFB, Texas, for specific participation in this study.

These subjects will be exclusively males between the ages of 18-25 years and will be selected on the basis of a negative history and physical for cardiovascular disease.

A total of 10 subjects with manifest cardiac disease will also be studied. These patients will be selected from the USAF Consultation Service patients with the prerequisite being the presence of cardiomegaly. The subjects will be studied

in the same manner as the normal subjects to determine if variations in heart size and geometry appreciably alter the reliability of the technique. The age range of these subjects will be between 30 and 60 years.

Specific consent of all human subjects used in this study will be obtained. All normal subjects will be obtained by solicitation of volunteer participants.

b. Date and total number of days required, including convalescent leave: Exact time sequences for study are yet to be determined pending final installation and check-out of the coincidence counting equipment and pending specific arrangements for procurement of the necessary radioisotope material for human usage.

The volunteer subjects from the USAF Training Command Program, Lackland AFB, Texas will undergo a complete cardiovascular evaluation on the day of their arrival at Brooks AFB. The subjects will then be studied on the same day or the following day after which they will be returned to Lackland AFB. No convalescent leave will be required.

The volunteer subjects selected from the USAF Consultation Service will be studied during their scheduled stay at the School of Aerospace Medicine and it is anticipated that no additional time will be required of these subjects over that for which they are already scheduled.

c. Schedule of Experiment: After the initial insertion of the transcutaneous catheter the procedure first involves the intravenous injection of approximately 0.1 uc/Kg of albumin tagged Cobalt-58 into the subject followed by a 10-15 minute period to allow the isotope to equilibrate in the intravascular compartment. In no instance will any additional isotope be administered to the subject and no other drugs will be utilized.

After equilibration of the isotope the subject is positioned on a table in such a way that a coincidence pair of scintillation crystals are alligned directly anterior and posterior to the heart. Precordial count rates are then recorded simultaneously with the recording of an electrocardiogram. The differences in count rates during systole and diastole can then be determined. By determining the activity of the Cobalt-58 isotope from a blood sample drawn during this time, the differences in systolic and diastolic count rates over the heart can be expressed in terms of volume changes in the heart.

In each subject the minute stroke volume obtained by this method will be compared with the minute cardiac output determined simultaneously by a standard dye dilution technique. In addition, multiple one minute precordial isotope counts will be carried out on each subject to determine the reproducibility of the calculated cardiac output measurement made. In

some subjects these repeated one minute precordial counts will be carried out with the subject at complete rest. In others, similar measurements will be determined after repeated periods of graded exercise using the same workload. With the data collected in this way the accuracy of the calculated stroke volume over intervals considerably shorter than one minute can also be determined. By taking precordial counts during the actual period of recumbent exercise the accuracy of the calculated stroke volume during exercise can likewise be evaluated.

The final analysis of this data will be carried out in coordination with the Department of Biometrics.

d. NA

e. Special Requirements: The intellectual, educational and physical profile requirements of the subjects can be met by any individual who is accepted for or retained by the United States Air Force for active duty. All subjects will be required to undergo a complete medical history and physical examination. In addition, a baseline electrocardiogram will be obtained as will a routine chest x-ray.

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MEMO ROUTING SLIP	NEVER USE FOR APPROVALS, DISAPPROVALS, CONCURRENCES, OR SIMILAR ACTIONS		ACTION
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		DATE	COORDINATION
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3			NOTE AND RETURN
			PER CONVERSATION
4			SEE ME
			SIGNATURE

REMARKS

Attached experimental protocol to be reviewed at the next [illegible] research committee meeting

FROM	DATE
IRVING DAVIS, Lt Col, [illegible] Chief, Biosciences Branch	6 Nov 67
	PHONE 22150

DD FORM 1 OCT 60 95 Replaces DD Form 94, 1 Feb 50 and DD Form 95, 1 Feb 50 which will be used until exhausted. GPO 1961 0—596753