

4 cgs

R-136
Department of Health,
Education & Welfare

PROGRESS REPORT NO. 3

A Longitudinal Study of Naval Flight Students With Particular
Attention to Cardiovascular Disease

1 April 1965 to 30 September 1965

N 66 131655

FACILITY FORM 602

(ACCESSION NUMBER)	(THRU)
20	1
(PAGES)	(CODE)
CR 68541	04
(NASA CR OR TMX OR AD NUMBER)	(CATEGORY)

RECEIVED
NOV 2 9 31 AM '65
OFFICE OF CONTRACTS
RESOURCES CONTRACTS

GPO PRICE \$ _____

CFSTI PRICE(S) \$ _____

Hard copy (HC) \$ 1.00

Microfiche (MF) .50

Third and Final Report of Work Done Under Contract R-136

Contract R-136 between the Office of Advanced Research and Technology, National Aeronautics and Space Administration and the Division of Chronic Diseases of the U. S. Public Health Service was established 1 July 1964 and officially terminated 30 September 1965. Two progress reports have been submitted, and the present ^{third} report also serves as the final progress report. Although the contract is terminated, all of the scientific reports which will appear over the coming months will be issued as joint U. S. Public Health Service, National Aeronautics and Space Administration, and U. S. Navy publications, thus ^{TP} acknowledging the combined efforts of the three agencies. The purpose of the contract was to implement the third follow-up of the "Thousand Naval Aviators," by far the most costly and ambitious of the three. This purpose has been served; the medical evaluations have been carried out, the findings are on IBM punch cards and magnetic tapes, and the work of analysis and report writing has begun. We trust it is appropriate to state that the assistance provided by the contract was essential to insure success of the present undertaking.

Personnel. The following lists comprise the participants during the period under review.

Principal Investigators

Dr. Samuel Fox
Captain Ashton Graybiel, MC, USN

Primary Investigators

Captain Robert E. Mitchell, MC, USN
Lieutenant Commander Albert Oberman, MC, USPHS

Special Consultants

Lieutenant R. J. Wherry, Jr. MSC, USN - Statistician
Dr. William R. Harlan, Jr. - Lipid Protein Metabolism
Dr. James E. Banta - Epidemiology of Cardiovascular Disease
Dr. Albert Damon - Anthropometry
Dr. Stuart Rosner and } - Computer Analysis of Cardiopulmonary Measurements
Dr. Caesar A. Caceres }
Dr. Gerald Cooper - Hematology and Biochemistry

Associated with Special Aspects of the Study

Captain N. W. Allebach, MC, USN
Lieutenant D. H. Jackson, MC, USNR
Lieutenant R. F. Smith, MC, USNR
Mr. James K. Colehour
Dr. Alfred R. Fregly
Dr. Harlow Ades
Dr. Vernon C. Bragg
Dr. Earl F. Miller, II
LTJG Norman E. Lane, MSC, USNR

Technical Staff

Mrs. Margaret Duty
Mrs. Wilma Bredt
Mr. Richard Irons
Miss Mary Ann Overman
Miss Edna Marques
Hospital Corpsmen Coyle, Gubanich, Kars, Redmond, Sampia, Valverde, Van Cleave and Young
Miss Mary Duvall
Miss Emogene Resmondo

MEDICAL EVALUATIONS

A very considerable effort was involved in locating the subjects and sometimes in persuading them to come to Pensacola. At the conclusion of the previous follow-up, all but three had been located of the 839 survivors of the original group of 1056. Twenty had died, leaving 815 known survivors. In the present follow-up all but four of the 815⁸¹⁵ were located; 17 had died (five, after receiving the preliminary questionnaire), 675 were

Some information was obtained,
reexamined, at least vital statistics was obtained on 89¹, and the remaining 30 did not
respond to our letters of enquiry. *9*

With few exceptions, among those reexamined data were collected on all items in the test battery listed below.

Interview--Personal and Medical History. Each participant completed a medical history form containing 225 questions. This provided a detailed review of systems and past history with special attention to respiratory and cardiovascular symptoms. The examining physician scored a review-of-systems summary sheet after discussing the replies with the subject. A family history of cardiovascular disease, diabetes, and cancer in parents, siblings, and children was also included. A pulmonary questionnaire* included details of cardiopulmonary disease and exposure to pulmonary irritants. It was also used in another study apart from the Thousand Aviators, necessitating some repetition of questions. The personal history covered such diverse topics as smoking, physical activity, both on and off the job; hours of sleep; diet; socioeconomic status; ethnic origin; and geographical residences. A separate questionnaire regarding flight status and previous flying experience was also available.

Physical Examination. A complete physical examination was performed and recorded on a standard form. Any questionable noncardiac findings on the physical examination were referred to the appropriate consultant at the Naval Hospital in Pensacola. In addition to routine "casual" supine and sitting blood pressures taken during the course of the physical examination, a "basal" blood pressure was taken in the following manner:

*Limited to those subjects who had pulmonary measurements recorded on magnetic tape.

Immediately after arrival at the laboratory the subject rested in a quiet room. Shortly thereafter the supine blood pressure was taken on the right arm with a Bauman sphygmomanometer from which the back had been cut out so that the column of mercury was visible from front and back. The examiner auscultated (fourth phase diastolic), viewing the mercury column from the unmarked side; at the appropriate time he signaled to another observer who recorded the reading. Three trials were used for the supine; then the procedure was repeated for the sitting blood pressures.

spread
out



All clinical diagnoses on each subject were coded according to the World Health Organization's classification of diseases. It might also be mentioned that a complete summary of the findings of each participant was sent to him complete with recommendations, if any.

Special criteria were set up for establishing the diagnosis of coronary heart disease for present, past, and future evaluations. These standards, agreed on by two observers, graded the diagnosis as indeterminate, possible, probable, and definite.

Electrocardiography. A basal 12-lead electrocardiogram modified by the equated lead selector was taken at standard speed and deflection on a Sanborn 100 Viso Cardiette. Standardized measurements of the amplitudes of P, Q, R, S, and T; of the durations of PR, QRS, and QT; and of the mean frontal QRS and T axis were made in selected leads. Also, values for the peak-to-peak QRS voltage and duration from the onset of the Q to the peak of the T wave were determined in the frontal plane. All resting tracings were also classified according to Blackburn's system for population studies. The scheme was modified to include a lesser classification for T waves < 1.0 mm upright. A conventional 12-lead electrocardiogram at standard speed and amplitude was also recorded on a magnetic tape apparatus, Sanborn 211. These tapes were then analyzed by the Instrumentation Unit of the Heart Disease Control Program by conversion to a digital form suitable for their established electrocardiographic programs.

Exercise electrocardiograms were taken at opportune times during the testing schedule. Each participant underwent a graduated battery in the following sequence: double Master's, a Harvard step-test at 20 steps per minute for three minutes, and at 20 steps per minute for four minutes. Individuals with physical disabilities, recent coronary symptoms, or with acute electrocardiographic changes were excused from the complete sequence though some of these men did participate in the less rigorous exercise tests. Leads I, II, III, AVF, V2, V4, V5, and V6 were recorded simultaneously in two groups on a four-channel Sanborn 964 at standard speed and deflection. A timed sequence of tracings consisted of baseline, immediately after exercise, 1 minute, 2 minutes, 3 minutes, and 5 minutes after exercise.

2
9
A number of parameters were measured in leads II, AVF, V4, V5, and V6: amplitudes-P, Q, R, S, T, and J point; durations--PR, QRS, QT, and QX. Special attention was given to the ST segment measurements. The procedure for locating the reference points on the ST segment was as follows: A baseline was drawn from the PR segment immediately preceding the Q wave to the analogous point on the QRS complex following the ST segment to be measured. The J point and X point (where the ST segment crosses the isoelectric line) were defined; then a third point, the Z point, was established by the intersection of two straight lines, a straight line coincident with the initial part of the ST segment and another coincident with the proximal ascending limb of the T wave. Although one or more of these points may be absent in a given situation, the ST segment can still be characterized by the remaining points in terms of slope or area.

Quantitative exercise electrocardiograms were recorded on a Sanborn 350 recorder, after work on a Lannoy bicycle ergometer, by means of a special purpose analog computer. The subject underwent two minutes of exercise (150 watts of work) after which orthogonal leads using the Frank lead system were analyzed for spatial mean QRS vector, mean T vector, ventricular gradient, and ST parameters.

Plethysmography. For evaluation of peripheral pulses a mercury strain-gauge plethysmograph (Model 250, Parks Electronics Laboratory) was used. This device was placed over the base of the fingernail to obtain a standard pulse wave for that particular individual since upper extremity pulses are rarely affected by peripheral vascular disease. This tracing was compared absolutely and then with those obtained from the toes with respect to amplitude, time required

for the ascending limb of the curve, and contour of wave. A heat lamp was used to relieve any vasospasm brought on by emotion, temperature, et cetera.

Ballistocardiograms. These were taken on the Astro Space Air Suspension and the "Reeves" swing bed, both ultra-low frequency ballistocardiographs, using the Sanborn 964 recorder. All tracings were taken simultaneously with lead II of the electrocardiogram, and the air suspension tracings also were recorded simultaneously with a carotid pulse wave. The majority of the participants had records taken on both machines. Using the trough of the G wave as the baseline, amplitudes of GF, GH, GI, GJ, GK, GL, GM, and GN were measured. The durations of Q-H, Q-I, Q-J, G-H, J-K, H-L, and P-Q were measured as was the time from the Q wave of electrocardiogram to the upstroke and incisura of the carotid pulse. Other values were derived from these basic parameters.

Vectorcardiograms. The vectorcardiogram was obtained from a Sanborn 350 apparatus with a three-plane scalar recorder. Frontal, horizontal, and left sagittal loops were inscribed at intervals of two milliseconds employing the Frank lead system. Orthogonal tracings in the three planes using the same lead system were also taken. Detailed measurements on spatial vectors from these tracings have been made to date on the initial 200 subjects.

Laboratory Determinations. Hematocrit, white blood cell count, and differential cell count were done in routine fashion from a finger "stick." The urine was microscopically analyzed and tested for albumin and sugar with "Uristix." Serum cholesterol was determined by the method of Abel et al. Serum lipoproteins were determined by ultracentrifugation at the Institute of Medical Physics. Protein bound iodine and uric acid measurements were also carried out on the fasting blood. Triglyceride values were unsatisfactory for the initial

391 participants; the solvent in the initial method did not adequately eliminate the phospholipids. Determinations employing the method of Carlson proved quite adequate for the remainder of the group. Cholesterol and the later triglyceride studies were standardized by the Heart Disease Control Program lipid laboratories in Atlanta, Georgia. Glucose values both fasting and two hours after a 100 gram glucose load were analyzed by the method of Somogyi. Glucose determinations for the first 384 members of the study group ran approximately 12 milligrams per cent below later standards. This was corrected by improving preservation methods since the determinations were not carried out on the same day. All abnormally high glucose results were substantiated by a repeat complete glucose tolerance test performed by the subject's own physician, if necessary. Triglyceride determinations two hours after the carbohydrate load were also available on a sample of 230 subjects.

Pulmonary Function and Metabolic Studies. Routine spirometry was done with a 13.5 L Collins apparatus. In a sitting position the subject performed the following maneuvers after runs of tidal breathing; maximal inspiration, maximal expiration, and finally a maximal expiration after a maximal inspiration (vital capacity). The readings were made at two speeds, 32 mm per minute and 160 mm per minute. A separate determination of these parameters was made on a Med-Science Wedge Spirometer 370 adopting the procedure of Bartlett. A velocity-volume loop was photographed with a polaroid camera from the oscilloscope. This loop was produced when the sitting subject after breathing normally into the spirometer then inhaled maximally and as rapidly as possible after which he exhaled in the same manner.

All maneuvers were photographed superimposed on each other. In addition to the measurements obtained from the routine spirometry, maximal inspiratory and expiratory velocity could be calculated by this method.

By means of the Sanborn 211 and the Med-Science Wedge Spirometer 370, expiratory and inspiratory curves were also recorded on magnetic tape for computer analysis. While standing, the subject inhaled maximally from room air through a three-way valve, then exhaled with maximum force and speed into the spirometer. He then inhaled as quickly and rapidly as possible from the spirometer, exhaling into the room air. A paper recording immediately demonstrated the validity of the curve. Final analysis of total volumes, forced expiratory and inspiratory volumes (one second, two seconds, and three seconds), and flow rates (maximal, 200-1200 ml, and 25%-75%) rested with the computer.

Anthropometry. All weights and measurements were taken in the afternoon with the examinee completely disrobed. An average of two readings was taken for each parameter. All measurements of an extremity were made on the right side.

Heights. A special device was used for measuring body height. With head oriented in the horizontal eye-ear (Frankfort) plane, and back flat against the support, the subject stretched to maximum height and inspired deeply. This procedure was used for both standing and sitting heights taken to the nearest tenth of an inch.

Weight. Was taken on a calibrated balance scale to the nearest pound.

Skinfolds. Four areas were measured: 1) midway between the right acromial process and the olecranon, 2) at the inferior tip of the scapula, 3) the right mid-axillary line at the

level of the nipple, and 4) right mid axillary line at the level of the umbilicus. A full thickness of skin was pinched up from the underlying tissue parallel to the natural folds of the area. Lange skinfold calipers were then applied to the fold about one cm below the fingers and halfway down the fold. Values were recorded after the indicator had settled (Figure IV-13).

Circumferences. Keuffel and Esser Wytface tape was applied with minimal pressure for these measurements. Chest circumferences were taken at the fourth intercostal space at mid-breath, maximal inspiration, and maximal expiration. The relaxed abdomen was measured at the level of the umbilicus just superior to the "fat roll." The biceps was assessed at the mid-point of the arm between the right acromial process and olecranon, first with the arm and forearm relaxed at the side, and then with the arm perpendicular but the forearm placed parallel to the floor while the fist was tightly clenched. The maximal circumference of the forearm was measured with the entire arm extended parallel to the floor, volar surface upward, and hand open. That portion of the wrist just distal to the styloid process of the ulna was measured again with the arm in the same position. The maximal circumference of the calf was measured while the subject stood on a chair with his legs slightly apart.

Diameters. All diameters were evaluated with a Hardlika anthropometer; the blades were pressed firmly against the bony prominences. For the biacromial diameter the subject stood with his head slightly bent forward and shoulders "slouched." Measurement was made from the most lateral aspects of the acromial processes (Figure IV-15). Both breadth and

anterior-posterior diameters of the chest were measured at the level of the nipples. The bi-iliac measurement was made just inferior to the anterior superior iliac spine in the horizontal plane, with the legs together. While the subject held this position the anthropometer was also placed on the trochanteric prominences. The diameter of the wrist was measured from the styloid process of the radius to that of the ulna with the arm hanging at the side, hand open and parallel to the sagittal plane. Maximal diameter between the maleoli was measured with the subject standing on a chair dividing his weight equally between both feet. The anthropometer blades were 45 degrees to the horizontal plane for this measurement.

Hand Grip. Strength was measured in both right and left hands with a dynamometer with the forearm parallel to the floor and at right angles to the arm. The maximal recording of two trials was used.

Somatotype. Photographs were taken with the subject posed in three standard views by rotating a turntable 90 degrees. All pictures were made at a standard distance of 14 feet with a Rembrandt portrait camera (Model II) using a Tessar 6.3/2 10 lens. Scoring as described previously was on a 7-point scale for each of the components: endomorphy, mesomorphy, and ectomorphy. Dysplasia (heterogeneity of build) and gynandromorphy (femininity) were also evaluated. The somatotypes were rated by Doctor Albert Damon, Harvard University, who fortunately also scored the original somatotype in 1940.

Teleoroentgenograms. Standard cardiac series consisting of posterior-anterior, left lateral, and right and left anterior oblique views were taken. Other than the immediate clinical evaluation, measurements of the transverse, broad, and long diameters of the heart were made calculating frontal area and cardiothoracic ratios. Chest films available from 1952 and 1958 were also evaluated in this manner for comparison.

Guilford Zimmerman Temperament Survey. This was a paper and pencil personality test in which the subject answered 300 questions about himself with a yes, no, or question mark reply. According to his response he was given a percentile ranking in the following categories: general activity, energy, restraint, seriousness, emotional stability, ascendancy, sociability, objectivity, friendliness, thoughtfulness, personal relations, and masculinity. Administration and interpretation of the test are discussed in an instruction manual.

Graybiel-Fregly Ataxia Test. The three distinct ataxia tests (57) consisted of 1) walking a 3/4" wide rail with eyes open, 2) standing on a 3/4" wide rail with eyes open, and 3) standing on a 2 1/4" wide rail with eyes closed. The correct body position for all three tests is body erect, feet in heel-to-toe position, tandemly aligned, with the arms folded against the chest. The subject first walked the 3/4" wide rail with his eyes open, then he stood on the same rail with his eyes open, and finally stood on a 2 1/4" wide rail with his eyes closed. The walking test is scored on the number of consecutively correct steps to a maximum of 5 steps per trial. The scores on the standing tests depend on the number of seconds a subject is able to maintain his position to a maximum of 60 seconds with eyes open and 180 seconds with the eyes closed.

Tilt Chair Test*. A special chair was used to determine the subject's ability to estimate the postural upright; it was designed to minimize proprioceptive clues when the subject was tilted with respect to the vertical plane. He was seated in the apparatus and asked to manipulate the chair by controls to a "true" vertical position. This setting was used as the "zero point." The subject was then blindfolded and the room darkened.

*Testing was discontinued after 100 subjects.

The examiner at a separate control center tilted the chair and the subject attempted to correct his position to the vertical reference point. Deviations from this "zero point" were recorded for each trial and constituted the score.

Tonometry. A Schiøtz tonometer with a 5.5 gm plunger load was used for measuring ^ointraocular pressure. This was usually done on the second morning, occasionally after the Harvard step-test. Readings were transferred from tonometer scale to mm Hg. All borderline and abnormal values were rechecked at the local Navy Ophthalmology Clinic.

Retinal Photographs. Photographs were taken with a Noyori Fundus Camera after pupil dilatation. The subject was seated and told to fix his gaze on a reference point. Two exposures of each fundus were made at an aperture of 2.4.

Electroencephalograms. Electroencephalograms were taken either on a Grass Model III D or Model 6. Three tests were made in a standard fashion while the subject was resting; then a hyperventilation run was completed with three minutes of pre-hyperventilation, three minutes hyperventilation, and three minutes posthyperventilation. If the electroencephalogram appeared suspicious, photic-stimulation was carried out; there were twenty seconds of continuous stimulation at frequencies of 7, 10, 12, 15, 18, 21, 24, 27, and 30. A clinical interpretation was made for each record; no quantitation has been attempted to date.

Standard Threshold Audiogram. This test was administered using the Rudmose ARJ-4 automatic audiometer. It measures thresholds at 500, 1000, 2000, 3000, 4000, and 6000 cycles per second. A reversible electric motor drives an attenuator which controls the

level of presentation of each test tone in succession. This motor is controlled by a switch held by the subject. As long as the subject does not press the switch, the tone gets progressively more intense. Holding the switch in the depressed position reverses the electric motor and causes the tone to become softer. A pen records the action of the motor-driven attenuator. Thus, by holding the switch down when he heard a tone and releasing it as long as he did not hear the tone, the subject caused the recording pen to swing from slightly below to slightly above his threshold, and recorded his own audiogram in this manner.

High Frequency Audiogram. This test was one which was especially prepared by Rudmose for study of the high-frequency threshold in man. It was accomplished in the same manner as the preceding test. However, the following test frequencies were substituted for the standard tones: 4,000, 6,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, and 18,000 cycles per second.

Naval Aviators Speech Discrimination Test. This test was developed at the Naval School of Aviation Medicine in 1962. It was designed to test the aviator's ability to discriminate loud speech in the presence of high-intensity noise such as that found in the cockpit of an airplane. The test was presented through earphones from a specially modified tape recorder. Text material consisted of 100 single-syllable words constituting a phonetically balanced sample of common American speech sounds. The words were presented at 115 db in a background of airplane noise (Beechcraft SNB cockpit)

which reached the ear at 100 db. The subject was required to write each test word, and the number of words written correctly represented his "NASDT Score," a measure of his discrimination in noise.

DATA PROCESSING

Routine data processing was brought up to date on all members examined, and a special scheme was devised for analyses of the exercise electrocardiogram.

Dr. T. J. Reeves, University of Alabama, was consulted regarding the most profitable use of our ballistocardiographic data. Computer programs have subsequently been developed for the evaluation of exercise electrocardiograms and ballistocardiograms.

Processed data on each member of the "Thousand Aviator" study group has reached the proportion of more than 95 punch cards per person.

<u>Item</u>	<u>Punch Cards</u>
Medical History and Questionnaires	9
Personal History	1
Physical Examination	1
Diagnoses	5
Laboratory	1
Anthropometry	2
Roetgengrams	1
Pulmonary Function	1
Electrocardiograms	15

<u>Item</u>	<u>Punch Cards</u>
Exercise Electrocardiograms	51
Ballistocardiogram	3
Vestibular Function	1
Guilford Zimmerman Personality Inventory	1
Audiometrics	2
Plethysmography	1
Storkle	3
Flight Time	1

SUMMARY OF PRINCIPAL ACCOMPLISHMENTS

The chief accomplishments under the contract were (1) the medical evaluations and (2) data reduction. This was completed so near the termination date as to leave little time for the preparation of reports. Twelve or more scientific articles will be forthcoming and, as indicated above, will bear the contract number R-136.

1. The first will deal with methodology of the entire study with emphasis on the present follow-up. It is about ready for the printer and served as the source for much of this summary report.
2. Distributions and intercorrelations of 100 selected variables. These data are presented in the form of descriptive statistics and all preliminary work is completed including Pearson correlation coefficients and histograms of frequency distribution.
3. A twenty-three year follow-up study of healthy young men. This would summarize the principal clinical and epidemiological findings.
4. Factors associated with rise in blood pressure in the third and fourth decades.
5. The serial electrocardiographic changes over a period of 23 years in a group of healthy young men.
6. Leftward shift in frontal QRS vector as an apparent function of ageing.
7. The exercise electrocardiogram and its prognostic value: A prospective study.
8. The effect of startle on the electrocardiogram as a measure of reaction to stress and its prognostic significance.

9. The standardization of the ballistocardiogram with reference to body build.
10. Interplay of blood uric acid, serum lipoprotein, and glucose tolerance test values and their clinical significance.
11. Lipid patterns: correlation with pathophysiologic factors.
12. The constancy of somatotype based on a long-term follow-up in healthy young men:
Its predictive value in the epidemiology of degenerative disease.
13. The relationship between personality and physiological variables in apparently healthy men.
14. Comparative pulmonary function measurements in healthy young cadets and middle aged naval aviators.
15. Thousand Aviator Study: Nonvestibular contributions to postural equilibrium functions.

OVERALL EVALUATION

The so-called "Thousand Aviator Study" began in 1940 as an attempt to evaluate the significance of psychological and physiological variables in terms of "success" in Naval aviation. The scores made on certain psychological and psychomotor tests were found to have predictive value for success in flight training, whereas the physiological test findings had almost no predictive value. As a consequence, the former were exploited and extended while the latter were largely forgotten. Only after many years, when degenerative disease either became evident or in doubt, was there a renewal of interest in the original baseline findings. Repeated follow-up studies have fully endorsed the great value of the early medical and physiological evaluations, but little attempt was made to relate the medical and

psychological findings until now. There are some good indications that the two are interrelated in terms of the ageing processes; hence, we are almost back at the starting point, both conceptually and in practice. It is predicted that in future follow-up studies of this group there will be a balance of interest on the part of physicians and those in the behavioral sciences.