Short Title:

Cardio-respiratory Functions during Growth and Training.

ANDREW

THE EFFECTS OF GROWTH AND ATHLETIC TRAINING ON CARDIO-RESPIRATORY FUNCTION IN EXERCISE

BY

George M.Andrew, B.Sc.(P.E.),M.Sc.

A thesis submitted to the Faculty of Graduate Studies and Research, McGill University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Physiology.

Joint Cardiorespiratory Service of McGill University and the Royal Victoria Hospital and the Department of Physiology, McGill University.

Montreal, P.Q. July 25,1967

ABSTRACT

The effects of athletic training during growth have been studied on the same children, over three years, while engaged in swim training. Resting lung volumes and expiratory flow rates as well as cardio-respiratory functions in exercise were measured and comparison made with 83 normal children. In addition, 14 young adults were studied before and after seasonal athletic training. Swim training during growth was found to significantly increase vital capacity and expiratory flow rates. Exercise diffusing capacity was greater than controls in boy, but not girl, swimmers while exercise cardiac output was consistently lower in swimmers. No group difference in stroke volume was found but swimmers had a lower heart rate for given exercise load. Seasonal training in young adults was found to lower exercise cardiac output in relation to oxygen consumption, a consequence of a reduced heart rate since stroke volume was unchanged by training. Exercise diffusing capacity was unaffected by seasonal swim training although the mean values for swimmers was greater than predicted.

TABLE OF CONTENTS

PART I:

THESIS INTRODUCTION AND PLAN

Contents:

A. INTRODUCTION: AND PURPOSE

During the past 50 years there have been many studies made on the cardio-respiratory adaptations to exercise and on the effects of training on these adaptations (326, 16). Accordingly, it is not surprising that physiologists have defined clearly some of the functional differences which account for the superior physical performance of the trained athlete. These studies have shown that there are distinct dimensional differences, in adults, between the trained athlete and untrained non-athlete with respect to some cardio-respiratory functions.

However, from the review of the literature (below), the following facts become apparent:

1) Little is known on the effects of athletic training during growth on these functions. In particular, exercise diffusing capacity studies have not been made on young growing athletes (eg. swimmers), nor on normal children. Likewise, exercise cardiac output measurements in normal children are few while the effects of chronic, strenuous athletic training during childhood on this function have not been documented.

2) The consequences of athletic training per se on these functions, in adults, are controversial. For the post part, the differences in such functions have been ascertained by comparison between groups of trained and untrained subjects. Such comparison does not specifically define the effects of

training as distinguished from endowment -- a factor which may be a most essential component in the development of fine athletes. Group comparison permits valid conclusions to be drawn when some maximal functions are examined (eg. $\dot{V}O_2$ Max) and where group differences are distinct. However, at submaximal exercise levels, where regulation of function is involved and where interindividual variation of a measurement is wide (eg. cardiac output), the only approach which can reliably indicate the effects of training on such measurements is to make repeat determinations on the same subject, before and after a training program. Accordingly, the present study was designed to investigate the following:

1) a comparison of group differences in cardio-respiratory functions between athletically trained and untrained children and by re-studying the child athletes at intervals of one year, to determine the effects of training on normal growth of these cardio-respiratory variables. If differences could be demonstrated between the trained and untrained child, it was hoped the effects of further training during the growth period on these physiological functions could be determined and 2) the effects of training, specifically, on young adult athletes and non-athletes, each studied at several exercise loads BEFORE and again AFTER a prescribed period of physical training, each subject thus serving as his own control.

B. FUNCTIONS TO BE STUDIED

The principal features being investigated in this study, and a brief statement of the logic for their inclusion as they relate to work performance, are as follows:

1) Respiratory System.. Lung Volumes and Flow Rates

The important and obvious role of the system for external respiration is to establish appropriate pressure gradients within the lungs so that gas exchange between the lung alveoli and blood can occur. As the demands for a faster exchange are increased, such as in exercise, the volume of air ventilated per unit time rises as a consequence of both an increased frequency of breathing and increased tidal volume, and by increasing flow rate during both the inspiratory and expiratory phases of respiration. If respiration is a factor which imposes a limitation on work performance, it might be deduced that the person with the larger lungs and faster maximal flow rates would have the advantage at higher exercise intensities and perhaps these changes might be effected by regular, strenuous training during growth.

2) Pulmonary Capillary Diffusion

The effectiveness of the respiratory system in its role in gas exchange is dependant not only on the maintenance of the pressure gradients, as indicated above, but is also contingent on the physical process of diffusion which is the mechanism for gas transfer at the lungs. This topic is dealt with in some

detail below and it is adequate here in the introduction to point out its dependance on the two systems it subtends.. the respiratory and circulatory systems, as well as the characteristics of the media prevailing between the alveoli and red blood cells. In health at rest, and during exercise at sea level, this process is thought adequate, in terms of the adjacent systems, and does not impose a limitation on work performance. In certain lung diseases,and exercise where the ambient oxygen pressure is low or where restriction is placed on the breathing pattern because of the nature of the exercise (eg.swimming), the level of maximal diffusion rate may be a prime factor in limiting exercise tolerance. In a situation such as swimming, where the efficiency of work performance may be so dependant on control of the breathing pattern, a higher diffusion rate could be advantageous since this would enable a higher oxygen transfer, despite the lower mean alveolar oxygen pressure prevailing, and thus permit greater arterialization of venous blood coursing the lung capillaries.

3) Circulatory System..

The ultimate delivery of essentials to, and removal of wastes from, the exercising muscle cells is one of the prime roles of this system. It is superfluous to state that performance of work is then highly dependant on adequate delivery rate (cardiac output) of arterialized blood to the working cells. It is not surprising that, perhaps because of the

direct relation of this system to the muscle cells, many investigators (82,236,262,297) have considered cardiac output to be the major determining factor in limitation of work performance.

C. PROJECT OUTLINES:

The present study, designed to investigate the consequence of athletic training on some of the pertinent aspects of the circulatory and respiratory systems as they relate to sub-maximal exercise performance, consists of three main projects. Each is presented separately in the succeeding sections under the following headings:

Project: Controls

The purpose of this section of the study was to define pulmonary and cardiac functions in children not engaged in athletic training; they thus serve as a basis of comparison with children engaged in a swim training program.

Project: Swimmers

This is a longitudinal study involving repeat measurements on the same child who was actively engaged in competitive swim training. This permits comparison both with Controls (above) as well as observations of intraindividual differences occurring with growth and as affected by their training program. Swimmers have been chosen for this study for two reasons:

a) their training program is intense, and perhaps the most extensive of any group of athletes in that they participate in year round training.

b) the particular differences of this group, as indicated by the literature review, may make their development unique, especially since so many champions in this sport are in the young age group.

Project: Training

This study permits before and after training comparison in an individual. Young adults of college age, including athletes as well as non-athletes, have been included. The project is divided into two sub-projects in the presentation below, according to the primary function being investigated.

1. Effects of training on Cardiac Function
2. Effects of training on Diffusing Capacity.

Each project is complete in itself in that it includes topics such as experimental outline, subjects, results as well as discussion specifically pertinent to the project. An attempt has been made in the concluding discussion to integrate the findings of these projects. This 'divided' handling of the material facilitated the writing and hopefully the reading, of this thesis.

PART II

THE TOPIC IN REVIEW

Contents

INTRODUCTORY REMARKS

Changes in anthropometric measurements with age in the growing child have been clearly defined (66,336). As a consequence, normality of growth in terms of physical development may readily be determined.

By contrast, there are several areas in which the normal growth pattern is less well documented. This is particularily true of those functions which are more difficult to assess. Thus, in terms of cardio-respiratory measurements, such functions as static lung volumes, ventilation, oxygen uptake and heart rate being easier to measure have been well studied in relation to growth or age both at rest and in exercise. On the other hand, surprisingly few studies have been made describing the dynamic lung functions in children at rest (MMFR,FEV) while there is a virtual paucity of studies to determine cardiac output and diffusing capacity in normal children during exercise and with training.

The following is a summary of the more pertinent literature on lung functions at rest and cardio-respiratory adaptions to exercise in children of varying ages. For convenience,the functions have been divided in an attempt to facilitate both the writing as well as the readers comprehension of this review. Where it was felt contributory to a better understanding of the background, either in terms of appreciation of the problems that prevailed among earlier investigators or of the disparity of existing data, some attention is given to methods development.

In addition, where no data on children exists, studies on adults have been included to enable comparison of the present data on children with that of adults. A brief summary follows each section.

PART II

CHAPTER 2. The Lungs and Growth

A. Morphology

B. Lung Statics
1. subdivisions of lung volume
2. method and repeatability
3. relation to age, body size and sex
4. training
5. summary

C. Lung Dynamics
1. flow rates methods
2. studies on children
3. training
4. summary

THE LUNGS AND GROWTH:

Attempts to define the pattern and mechanisms of lung growth have followed two principal paths..indirect and direct.

The total lung volume and its sub-divisions give an indication of the size of the overall respiratory system and potential area available for the processes of gas transfer in the lung. Such measurements have made clear the pattern of growth in terms of lung size and these have been combined with measurements of total lung diffusing capacity in an attempt to deduce indirectly the rate of addition and size of avleoli.

Morphologists have employed the direct technique of measuring the lung volumes in vitro and by use of x-sectional tissue slices have employed a statistical approach to determine the number of alveoli, their size and number of generations as a function of age in man and animal.

The essential process of gas diffusion across the lung depends on the surface area available for such interchange. Thus, the significance of the pattern of lung growth (i.e. by addition of new alveoli or by simple expansion of existing alveoli) to lung function is apparent and can be clearly demonstrated mathematically. Hence, if growth of the lung is by expansion only, the area/volume ratio will be reduced, whereas growth by the addition of new alveoli will increase the effective surface area.

The literature in these related aspects dates back to 1731,

in the case of lung morphology, and 1846 saw the introduction of measurement of the sub-divisions of lung volumes. It will be appreciated that, as a consequence, the literature on these topics is extensive.

A. MORPHOLOGY

Since the advent of the spirommeter in 1846 (195) many studies have been made by physiologists to define the processes of pulmonary ventilation. As a consequence some of the changes with age, in disease, on exercise, as well as sex differences are well documented. By contrast, the changes at structural level in the growing period have not been as clearly quantitated.

Weibel in his recent monograph "Morphology of the Human Lung" (355) attributes the first attempt to quantitate at alveolar level the structure and magnitude of the lung to Rev. Stephen Hales. Hales, in 1731, concluded that the vast inner layer of the lungs (about 27 M^2), with alveolar diameters of 1/100 inch, might make it possible for particles in the air to enter the blood through the lung rather than by injestion of animal foods as had been previously beleived. His thought was based on the idea that the blood in the lungs is

> ..."by an admirable contrivance there spread into a large expanse commensurate to a very large surface of air, from which it is parted by very thin partitions; so very thin, as thereby probably to admit the blood and air particles within reach of each others attraction".

Since Hales' original observations, numerous estimates of the alveolar number, surface area and diameter have been made.

Engel in "The Childs Lung" (126) reviews the topic of lung development. He refers to the 'Old' concept of Koelliker, who held the view that the whole lung was intact at birth and future growth was by expansion only, and the 'New' concept of Broman that new elements or acini were produced after birth.

Engel divides post-natal lung growth into two periods: a) 0-4 years..during which time new acini and saccular outgrowth proceeds along with linear expansion of existing structures, and b) subsequent years...in which growth is by enlargement; his view then in effect combines both the 'Old' and 'New' concepts.

Palmer in 1936 (282) compared foetal and adult lungs of humans and noted an increase from 17 to 24 in the generations of branching airways in this period. More recently (1960), Emery and Mithal (125) reported a nine-fold increase in the number of terminal respiratory units in the first 10 years of life, with a two-fold increase in the ratio number of alveoli/ number of respiratory units between 5 and 12 years. This finding was essentially substantiated by Dunhill (120) in 1962. He observed a ten-fold increase in alveoli from birth to adulthood, with most of the increase occurring in the first 8 years. In general agreement with Palmer, he found the mean number of generations of airways rose from 21 to 23 (the full adult complement) in the period three months to 8 years. Dunhill also points out the direct linear relationship of surface area of the lungs and body size during the growth period. With reference to alveolar dimensions, recent measurements of the adult lung by Dunhill and Weibel give mean values of 250-300 microns. It is of interest to note Hales observed a mean alveolar diameter in adults of 254 microns, 231 years before Dunhill. It seems that accuracy has been little improved by sophistication of instrumentation!

Krahl (219) in "The Handbook of Physiology" reviews the anatomy of the mammalian lung. He appropriately concludes his chapter by citing a group of questions posed by the Third Aspen Conference on Research in Emphysema. One such question still not adequately resolved is "How does the lung grow postnatally?".

B. LUNG STATICS

1. Subdivisions of Lung Volume:

Probably the greatest single contribution in the area of lung volumes study was made by the inventor of the spirometer. In 1846, Mr.J.Hutchinson (195) a surgeon, described and demonstrated his invention to the members of the Royal Medical and Chirurgical Society in London, England. In his treatise, he presented his findings on vital capacity (V.C.) measurements made on 2070 adults of varying age, size, sex and groups which included firemen, pupilists, paupers, wrestlers, a giant, a dwarf and even gentlemen.

The first vital capacity measurements to be made on children are attributed to Wintrich in 1854, according to Puschel (289). Despite this early attempt to define the growth of the lungs in children, as indicated by vital capacity, it was not until the 1920's that extensive use was made of this measurement (124,362,329). Since then however, vital capacity measurements in children, and more particularily in adults, have been almost innumerable.

It had long been recognized by workers in physiology that there was a certain volume of air which remained in the lungs "independant of will" (Hutchinson's words), that being the residual volume (RV), and in order to determine the total lung capacity (i.e. VC + RV) of an individual this volume must be known. Davy in 1799 (104) made the first reported measurements

by the dilution technique using hydrogen. While the same basic technique is still in use, there has since that time been numerous variations in method. The most significant of these were made by VanSlyke and Binger in 1923 (348) and Ronald V.Christie in 1932 (86). These modifications related to two primary problems in the measurement of residual volume: a) circumvention of forced breathing and b) accurate rapid test gas analysis. As a consequence, RV is deduced presently from the functional residual capacity (FRC) thus making the measurement applicable to patients; the second problem has been alleviated by the advent of electronic gas analizers.

The earliest report encountered in which the complete elaboration of lung volumes in children was described was that by Robinson in 1938 (298). His study on 30 boys aged 6 to 15 years was followed in 1952 by Morse et al (264), a study which included 94 boys ranging in age 10 to 17 years. Both these original studies have been criticized on two counts:

1) measurements were made with the children supine, which yields lower volumes (360) and

2) the gas analizer employed was not reliable for the test gas used (294).

Since 1954, there have been many reports of normal values for lung volumes in children (45,54,107,128,147,166,171,239,270). It seems not feasible to elaborate in detail on each individually. Not all are directly comparable since the numbers and ages studied, as well as method use, almost invariably differ.

For the purpose of this resume, only the more salient common features, points of difference in findings and conclusions are presented. Results of some of these previous studies will be included along with those of the present study.

2. Method and Repeatability

The subdivisions on lung volumes as used herein follows the standardized nomenclature (132) and are defined in the glossary of terms. Details of the procedure employed in the present study are given elsewhere (Part III). The general common features of method of most investigators are here summarized in brief. The procedure consists of two phases; a) vital capacity and its components are determined by having the seated subject breath quietly from an oxygen filled spirometer. At end expiratory lung volume, the subject inspires maximally and follows this with a maximal expiration. b) Functional residual capacity is measured by having the seated subject breath quietly from a closed circuit containing some tracer gas, (usually helium) air and oxygen. From dilution of this gas, the resting end tidal lung volume (FRC) can be determined.

By combining these direct measurements, the other subdivisions can be calculated. The most extensive recent studies of lung volumes in children include those of Demuth (107), Lyons and Tanner (239), Bernstein (45), Helliesen (171) and Engstrom (128). Each of these investigators has employed the helium dilution, closed circuit technique for FRC measurements, subjects seated. All were made during quiet breathing except in one study (107) in which the subjects hyperventilated. There is

good general agreement among these workers that such measurements, requiring close subject cooperation, are more difficult to determine accurately in the child than in adults, reasons being that the young child is less capable of following instructions and is more easily distracted. Thus, double determinations are recommended by most workers. Workers are also in agreement that of the various subdivisions, the most repeatable is vital capacity. The source of error in this regard lies in the accurate determination of its components, rather than the overall measurement; of these components, the most variable is the expiratory reserve volume (ERV). Since the ERV is also used to determine RV, which in turn is employed to calculate TLC, the compounding of errors results in decreased accuracy of the derived subdivisions. Few authors indicate repeatability of these measurements. In her careful study, Engstrom (128) found agreement of duplicate measurements in children to be 2.9% for VC, ERV of 8.0% and RV of 8.5%.

An indication of the repeatability on FRC duplicates in the same child is shown in the summary table (below). This indicates an overall S.D. of about + 5.0%.

FRC REPEATABILITY

REF. No.	SUBJECTS Sex M	F	Age	SD± %
239	196	242	6-14	< 10.0
107	147		4-18	6.55
128	50	43	6-14	4.1
171	52	33	5-17	< 5.0*
45	35	35	6-15	< 5.0**

* - mean difference of 75cc

** - not > 10%, usually < 5%

3. Relationship to Age, Body Size and Sex:

The dependance of lung volumes on body size was clearly shown by Hutchinson in his original 'classical' study in 1846. He indicated at that time that the

> .." quantity of air exhaled from the lungs is affected by four circumstances - height, weight, age and disease.."(195)

and he presented tables and plaster models to illustrate the close relationship of vital capacity to height. Investigators since that time have employed many independant variables of physical dimensions, both single and multiple, to predict the subdivisions of lung volumes.

Early reports found a highest correlation of lung volumes in adults was with radiological measurements (194,200). The close dependance of these volumes to height to the cube power (Ht^3) was first pointed out by Kelly (206). This exponential relationship, or its logarithmetic equivalent, has since been extensively employed to relate lung volumes to growth in the child (96,107,128,171). Needham (270) reports sitting height and body surface area (BSA) to be the best single predictors while Bernstein (45), Cherniack (83) and Ferris (134) found the use of multiple regressions using height, weight and age to be best. The simpler linear relation to standing height has been used by others (239,240,347), in which the subjects did not exceed 14 years of age. Of the various lung volumes, TLC and VC give the highest correlation with height, while ERV and RV showed poorest correlation (239).

The sex differences in lung volumes for a given height in adults has been reported by many investigators (152,270) but the age at which these differences become apparent is uncertain. One study reports maximum volumes reached at 25 to 35 years (44). Engstrom et al (128) observed the tendancy for values to be somewhat lower in female children than in boys; however, they found no statistical difference between the sexes in their series. Likewise, Bjure (54), who studied VC only on more subjects, found no significant difference when comparing groups of boys and girls; he did observe a sex difference ($P \leq .001$) in the older children, a difference which became apparent at heights greater than 160 cms. Helliesen et al (171) found no consistent sex difference, although Cook et al (96), whose study included the data of Helliesen, as well as more and older subjects, found VC and TLC slightly greater in the males but no difference was seen in RV and FRC. Needham (270), in agreeement with Bjure (54) found little sex difference up to age 12 to 13; thereafter, the boys were found to have the larger volumes. They also showed the female child to reach adult values at an earlier age than the boys, in agreement with the earlier findings of Stewart (329) and Kelly (206). Demuth (107) found a consistent sex difference in respect to VC in their longitudinal study; they made no such analysis with respect to the other lung volumes.

4. Training

Information on this subject has been obtained in the two ways discussed above (i.e. by group comparison and longitudinal studies).

In 1924, Gordon et al (153) measured the VC of a group of Marathon runners. Comparison with average values for normals revealed no difference nor was there any correlation between the magnitude of VC and the order of finish of the runners. Their observations have been confirmed by numerous other reports for runners and other athletes (16,274), although the findings of others (214,334) were contrary. By contrast, reports on swimmers are unanimous; not only are these athletes physically larger than non-athletes, as indicated by height (266,273) (a difference which is apparent even at the age of 7 years (20)), but VC (273) and all other subdivisions of TLC except RV are significantly greater (20).

Bock et al (57) indicated in 1928 that training increased the vital capacity. Schwartz(313) found that training in adolescents and young college students increased the growth rate in this respect, and this finding was supported by others (203,299). However, such change was not found to occur with training in older subjects (299).

5. Summary

1. The static lung volumes increase with body growth. Of the various body measurements, correlation is closest with height, to which these volumes are exponentially related.

2. Distinct sex differences, though readily apparent in adults, have not been consistently observed in young children. Most studies report no significant difference in any subdivision, although VC and TLC are slightly greater in boys. The one longitudinal study reported VC significantly greater in boys.

3. Sex differences become more apparent after the onset of puberty. The age at which adult values are attained has not been extensively studied.

4. Trained and untrained do not differ in respect to FRC and RV, nor is TLC greater in athletes of comparable size, except in swimmers where TLC has been found greater as a consequence of a larger VC.

5. Earlier studies indicate training accelerates the growth rate of TLC but this occurs only in the subjects of college age or younger.

C. LUNG DYNAMICS

1. Flow Rates Methods

Flow rates are measures of the dynamic functional ability of respiration and have the units volume/time. The earliest such measurement was made by Hermannsen (173) in 1933 and consisted of measuring the maximum ventilation during hyperventilation effected voluntarily, by exercise or by inspiring CO_2. This volume he termed the Maximum Voluntary Ventilation (Atemgrenzwert). This ability to develop and sustain high flows is dependant on numerous factors as cited by Comroe et al in "The Lung" (95) which include: the available muscle force, lung and rib cage compliance, airway resistance. In addition to such intrinsic properties of the subject, these measurements are also highly dependant on the characteristics of the test equipment, such as valve and tubing resistance (369), inertia of spirometer bell (26) and water oscillations (46). As cited by Bates (33) and others (244) this maximum voluntary ventilation as an indicator of pulmonary performance has several limitations. As a consequence, many varieties of methods, designed to indicate ventilatory capacity, have evolved (95). Many such tests presently employed make use of the single, rather than multiple, forced expiration or inspiration. Two such variations include the Forced Expiratory Volume (FEV) and Maximal Mid-Expiratory Flow Rate (MMFR).

Although the concept of a single force maximal inspiration

or expiration as a means of assessing pulmonary function had been introduced earlier (Barach in 1938 (28)), it was not until 1953 that Kennedy (207) developed the EFR_{40}. Recognizing the drawbacks of the test, he argued then that it should be possible to evaluate this from a single forced spirogram. Because of the extensive and persistent use made of the MVV at that time, and to permit comparison between results of different workers, he compared the two tests (MVV and EFR_{40}) and found a correlation coefficient of .927, SE $\pm$ 5%. The high correlation, in addition to the numerous advantages of his new test, led to adoption of the EFR_{40} (later termed FEV_{40} (145)) as the more favored flow rate test.

The MMFR was introduced by Leuallen and Fowler (230) in 1955. They appreciated the usefulness of the single, maximal spirogram tracing but they also realized that investigators were not in agreement as to the method for using such tests. In general, most of the disagreement related to the mechanical limitations of the testing equipment (spirometers generally). They compared results derived simultaneously from a fast response pneumotachograph and wet spirometer,and showed the spirometer to be accurate over the range 1/4 - 3/4 of vital capacity. This value, expressed as flow rate (l/sec) they defined as the MMFR. Subsequent studies on 140 adults led them to conclude that this might be a more sensitive indicator of expiratory obstruction than the FEV.

2. Studies on Children

Early flow rate measurements of flow rates on children were

confined to the determination of maximal breathing capacity (MBC). Ferris (134) in 1951, appreciating the lack of suitable standards of normality for flow rates in children, performed the first such studies on 161 boys, aged 5 to 18 years. They observed that the increase in MBC with age accelerated at age 12 to 14, the period in which there are pronounced developments of chest size and muscle mass. Because of the variability of growth with respect to age, they recommended that multiple variables be employed as a means of predicting normality. Turner and MacLean (347) in 1951 found a linear relation of MVV to height, (age range studied 5-3/4 to 14 years) though this linearity was not as clearly marked as that for VC. No apparent sex difference was seen in their limited study.

Kennedy (208) in a study done in 1949, reported in 1957 on results obtained on 175 normal boys 8 to 14 years. They analized the single maximal expiration (EFR) and inspiration (IFR) as well as MVV. Because the EFR was less affected by the two different spirometers used in the study, (one for subjects under 10.5 years, another for older children) and presumably was less sensitive to instrument characteristics, they selected it as the preferred measurement. Stem height correlated with EFR slightly better than with height, both of which were considerably superior as predictors than weight, age and chest measurements. This is in contrast to the relationship observed in adults by Brody (65) who found flow rates to correlate best with age and weight. In recent studies numerous authors (54,83,129,144,168,171) employing

either the single forced spirogram or multiple breath techniques, report the highest correlation of flow rates with height in children. A sex difference was found only in the post-puberty age groups (54,270,332) although one study (144) observed that FEV, when expressed as % of VC, was greater in boys thoughout the age range 5 to 14 years.

Lyons (240) measured the maximal expiratory flow rate (MEFR) (the time required to expire a given volume of the maximal inspiration) in a large number of subjects (6 to 14 years). Correlation was highest with vital capacity, followed by age, which are the two independant variables presented in their regression equation. Murry and Cook (267) made measurements of peak expiratory flow (PFR). Results were similar to the earlier study of Nairn et al (269). They showed peak flow rates to be readily predictable in children by height with no advantage being gained by using an exponential description.

The only reports encountered in which the MMFR was measured in children was that of Cherniack (225). Like others, they found the correlation highest with height and the inclusion of age did not improve the predicted value by more than 10%.

3. Training

Comparison of trained and untrained groups indicate that there are no consistent group differences in respect to FEV or MBC, except in those studies in which swimmers were the trained subjects (20,273). However, the recent report of Grimby and Saltin (159) found this value higher than predicted in 32 older

adults (42 to 68 years) who had been continuously active in 'orienteering' for 20 or more years. Freedman (141) studied various cardio-respiratory functions in three college track athletes before and after a season of training. They found the only consequence of training was an increased MBC.

4. Summary

1. Growth trends in flow rates are similar to those noted above for lung volumes although the sex difference may be apparent at an earlier age.

2. The reports on flow rates in general indicate no group difference in trained or untrained, except where swimmers were compared. One study (159) reports higher values in older, continuously active athletes and a season of training had the same effect on three track athletes (141).

PART II: THE TOPIC IN REVIEW

Chapter 3. Diffusing Capacity

A. Introduction

B. Methods .. development and problems

C. D_L and Growth ..atrest

D. D_L in Exercise - 1. general
2. relation to exercise
3. plateauing
4. mechanisms for increase
5. D_L Limiting Work performance
6. training

DIFFUSING CAPACITY

A. Introduction

The term 'Diffusing Capacity' will be used to describe the rate of transfer of gas from alveoli to pulmonary capillary blood consequent on an established pressure gradient across the alveolar-capillary membrane. It has been described in terms of the normal respiratory gas (oxygen) or carbon monoxide (CO), the gas of choice used by many investigators because of its' greater ease of measurement as well as interpretation of results (33). The transfer of respiratory gases across various membranes or media..(here confined to events at the lung although the same principles must apply at the level of the skeletal muscle cell as well..) is effected by the physical process of diffusion which, as pointed out by Forster in his review of the subject (137), is essentially similar to the processes implied in Fick's Law of Diffusion. Whereas Fick's Law is concerned with describing movement of molecules of a substance in one medium however, the gas exchange at the lung becomes more complex to describe since it involves movement of gas molecules through various media. Because of this, the diffusing capacity is affected by a series of factors which influence the rate of uptake of a gas; these include: rate of intrapulmonary mixing, area and state of the functional alveolar-capillary interface, blood plasma, red cell membrane and the amount of, and rate of combination with, hemoglobin in the red blood cell.

Attempts have been made to assess the relative effects of these various components of D_L cited above, Thus, Roughton and Forster (306) and others (36,250) have shown these factors to be related to D_L in the following manner:

$$\frac{1}{D_L} = \frac{1}{D_m} + \frac{1}{\theta Vc}$$

where

$\frac{1}{D_L}$ is the reciprocal of diffusing capacity, being analogous to the resistance to diffusion.

θ is the volume of a gas which will combine with the red blood cells in 1 ml. of blood/min./mm Hg.pressure gradient between plasma and cells.

Vc is the volume (ccs) of pulmonary capillary blood

$\frac{1}{D_m}$ includes all the above mentioned factors other than θ and Vc.

From this it becomes evident that the measured diffusing capacity will be altered by manoeuvres or conditions which change any of the above factors. Thus, variations in method used (eg.single breath or steady-state methods..see below), state of the subject (rest or exercise, supine or sitting), in addition to such factors as lung growth,changes in membrane thickness, ventilation - perfusion irregularities, degree of exercise, disease, and perhaps state of athletic training as well as other conditions, can bring about changes in D_L. Because of this multiplicity of factors which affect diffusing capacity, the discussion of the literature is perforce confined to that concerned with normal healthy subjects and the consequence of growth, exercise and athletic training.

B. Methods..development and problems

Despite the relatively brief period since its' inception as a test for evaluating a physiological function (225), studies of D_L have been numerous, particularily in the last 20 years, and a complete review of the multi and varied methods employed by different investigators would require scope well beyond the confines of this thesis. A careful and detailed summary of the development, significance and mathematical justification of the measurement is contained in the review by Forster (137). In addition, Bates and Christie in their recent book (33) devote considerable attention to the various methods used in pulmonary function laboratories. They point out too that the values obtained can be different because of the method employed, making this an important point to consider when comparing results of different investigators.

A major problem which confronted early workers was that of easily and accurately determining the gas concentrations. The advent of fast response analyzers,such as the Infra-red meter, has been a major advancement in this regard and its' rapid response time has made it possible to almost instantaneously analyze the fractional concentration of CO under varying conditions (eg.steady-state or end-tidal sampling).

The principle methods presently employed may be classified into two types,each of which may include different variations:

1) Single Breath..the method originally developed by Krogh(221) in which the uptake of a gas is computed from analysis

of the collected expirate of a single held breath. The method has subsequently been modified by other workers (138,277). Because of the breath-holding required in the method, it is considered by some (31,41) less well suited for D_L measurements in exercise although it has been so used by several investigators (147,198,274,277).

2) Steady State.. in which the subject breathes normally at rest or during exercise. After having reached a metabolic equilibrium, or steady state, the subject is introduced to the test gas which he breathes until the mixed expired concentration of the gas is constant. D_L is calculated from analysis of inspired and mixed expired gas concentrations (eg.CO) and the volume respired, account being taken for the anatomical dead space of the subject (see Method below). Again, several variations of this method are used, and for the most part these differences relate to the problem of determining the best estimate of the dead space for use in the calculation of mean alveolar pressure ($\bar{P}_{A_{CO}}$).

Comparison of results using the two methods have been made (139) and it has been shown that higher values in a given individual are achieved with the single breath method, with the following relationship observed:

$$D_L CO \text{ (steady state)} = .85\ D_L\ CO \text{ (breath hold)}$$

A steady state rebreathing method, described by Lewis (233) yields intermediate values to the above methods. Because this

latter method involves rebreathing a mixture of helium and CO in air, it can often be accompanied by hyperventilation and hence is probably not the method best suited for exercise studies.

From the above it may be concluded that agreement among investigators as to the preferred method has been far from unanimous. In part, this lack of agreement is related to the varied views among workers in this field on how best to circumvent problems related to the measurement. The most perplexing and persistent problem in the measurement relates to the best means of accurately determining the mean alveolar partial pressur ($\bar{P}_A$) or mean alveolar fractional concentration ($F_{A\ CO}$) which has a critical effect on the calculated value for D_L. An estimate of the mean alveolar concentration of a gas can be made by analysis of the mixed expired gas if the anatomical dead space (V_D) is accurately known. However, since the first such determination (V_D) was made by Loewry (238) this problem more than any other has stimulated controversy among respiratory workers, chief among which was the famous A.Krogh - J.S.Haldane confrontation of 1912-1914 (118,223,163). Originally, calculation of dead space involved in one form or another the use of the famous Bohr Equation.

$$V_{D\ CO_2} = V_T \frac{(F_{A\ CO_2} - F_{E\ CO_2})}{F_{A\ CO_2}}$$

or the equation written for O_2 as the test gas. However, for

its solution, a value for mean alveolar concentration of the gas is required and this question has received critical appraisal by some of the more prominent investigators in recent years (135,138,290,294). The Nitrogen washout method of Fowler (140) provided a way around these difficulties and it has been found to give accurate measurement of the anatomical dead space which in healthy subjects is similar to the physiological dead space. It has more recently been shown (32) that the error in D_L as a consequence on incorrect estimate of V_D in the computation of F_A is minimal especially in exercise when the V_D/V_T ratio is small (366) and D_L is virtually insensitive to sizeable changes in this ratio.

From the above, it was concluded that an assumed value for V_D may be used in the calculation of $D_{L\ CO}$ in exercise; the mean alveolar concentration can be derived from the analysis of mixed expired samples according to the expression:

$$\overline{F}_{A\ CO} = \frac{(V_T \times F_{E\ CO}) - (V_D \times F_{I\ CO})}{V_T - V_D}$$

where $F_{I\ CO}$ ..inspired CO concentration

$F_{E\ CO}$ ..mixed expired CO concentration

$\overline{F}_{A\ CO}$ ..mean alveolar CO concentration

An additional point of concern among investigators has related to the significance of back pressure due to carboxy-hemoglobin (CO Hb) increase during the performance of the test.

Although Pace (281) found this effect negligible in his earlier study, Linderholm (235) later investigated this topic and showed back pressure effect to be considerable at rest, though less at exercise, when the time of exposure to CO was long and when repeat measurements on the same subject were to be made. He concluded that failure to correct for such back pressure could well have led investigators to wrongly conclude that a plateau for $D_{L\ CO}$ had been attained at modest exercise loads (32,135). This work of Linderholm was confirmed by Holmgren in 1965 (178, 179) who showed that in young adults the absolute value for diffusing capacity would be raised by 3.8 units when the correction for CO Hb was applied.

Summary

1) While agreement is not unanimous on the method of choice for determining D_L in exercise, there is good evidence to favour the use of the steady state method on the grounds that it may be more physiological, since no alteration in the normal respiratory pattern is required, and since it avoids the possible errors which may be inherent when spot sampling is employed.

2) The problem of accurately determining the mean alveolar concentration of the test gas during the measurement of D_L remains a major concern to investigators. However, it has been shown that the use of an assumed dead space value in the calculation of exercise D_L introduces no greater error than direct measurement of dead space using the Bohr equation, because during exercise the ratio V_D/V_T is small.

3) The effect of build up of back pressure due to CO Hb has been shown to be significant in adult subjects, especially when repeat determinations using long exposure are being made.

C. D_L and Growth ..at rest

The changes in D_L, as measured under resting conditions, which occurs as one grows in stature have not been extensively studied. The youngest age group studied include those by Stahlman (324) using the Filley steady state method (dead space determined by the Bohr equation from arterial CO_2 concentration). He measured the D_L CO at rest in 31 infants, age 9 to 9-96 hours, and reported values on the order of 1.65 ml/min/mm Hg*, this value varying directly with weight. It is of interest to note that Bates (33), combining this with data of others, speculates on what this value would be in an adult if it were based on the ratio D_L/FRC. These authors calculate that the D_L of a man with FRC of 3L would be 70, a value which corresponds to that found in man during maximal work. By inference, this suggests that the 'resting' infant has a cardiac output of near maximal value. This speculation is cited here only to point out that the conditions prevailing during the test under seemingly similar conditions (rest) may in fact be quite different and this, as much as the method used, may have accounted for lack in agreement among earlier workers. Indeed, it has been shown recently that the initial resting value on an individual is higher than the second determination (54) and that apprehension can alter the D_L (89). It is interest to note also that under exercise

* the units hereafter will be implied.

conditions these variables, especially those affected by psychological factors, are thought to be reduced considerably in significance.

The first measurements of D_L in children were made by Krogh (225) who studied 6 subjects, 3 of each sex age 10 to 18, and reported values from 16.7 in the youngest to 23.0 in the one 18 year-old girl. When expressed in terms of body surface area (BSA) she found no difference between the child and adult.

Strang (333) employed a modification of the steady state technique described by Bates (32) to make duplicate determinations on 133 children at rest, 79 of whom were normals, ranging in age from 5 to 14 years. The linear regression using height as the single independant variable gave a positive correlation ($r = .654$) and the mean of these values was significantly greater than those found in children with bronchiectasis or asthma, although the latter values lay within the confidence limits (coef. of variation 19.3%) of the normals. Bucci et al (70) used the single breath technique to study 59 subjects., 7 to 40 years of age, 43 of whom were under 19, and found that the children followed the regression line for adults at rest. For a total lung capacity of 4 Ls, the predicted D_LCO would be 20.8; Krogh (225) 45 years earlier using a similar method, found a mean of 19.5 in children whose mean TLC would be expected to be about the same value. Bucci observed no sex variation when difference in BSA was taken into account and they concluded that D_LCO and pulmonary capillary blood volume (Vc) both increase along normal growth lines. They found a high correlation between

$D_L CO$ and TLC. In another study (69) they showed $D_L CO$ to be greater than predicted in children having conditions in which there was an elevated Vc (septal defects, patent ductus arteriosus etc.) which was reduced to normal upon correction of the condition.

The most extensive study of D_L on children was made by Demuth (107) at the University of Michigan. They made duplicate measurements on successive years on a large number of boys and girls 4 to 18 years using the rebreathing method of Lewis (233). Their experimental design enabled them to follow the growth pattern in the same individual, thereby eliminating the effect on interindividual comparisons on the results. They found no significant difference in the regressions of the two series (year 1 and year 2). Like Bucci and others (147) they report that $D_L CO$ grows along growth lines, increasing in a very similar manner to that of lung volumes; that is to say, both lung volumes and D_L showed similar relationship to height as well as to age, weight and surface area. With respect to these physical measurements, D_L correlated best with height while the highest correlation with a single independant variable among the lung volumes was TLC. These authors showed also that the ratio D_L/TLC did not vary with physical dimensions of the subjects, nor did this ratio show any sex difference; however, when comparing the regressions for each sex, the intercept for the boys was significantly greater than for girls although the slope of the regressions were not different. From their results, they concluded that

the constancy of the ratio D_L/TLC during growth supports the hypothesis that the lung grows over the age range 5 to 18 years by the addition of new air spaces rather than by simple expansion of pre-existing ones. Englert's recent study would support this view (127).

Summary

1) All investigators agree that growth of resting D_L parallels that of physical growth.

2) When a single independant variable is selected, the correlati with physical measurements is best for height; with subdivisions of lung volume, correlation is best with TLC.

3) No clear sex difference has been observed, especially when difference in BSA are considered.

It has been suggested on the basis of the above that lung growth up to the age of 18 years occurs by the addition of new alveoli since the D_L/TLC ratio remains constant.

D. D_L in Exercise

1. General:

Christian Bohr in 1909 (58) first showed that diffusion in the lung was greater in exercise than at rest in the same individual. Similar results on the effects of exercise on diffusing capacity were reported by Krogh in 1914 (225), Bøje in 1934 (59) and the innumerable studies made since 1945 make agreement unanimous in this regard. Considering the vast number of studies of D_L in exercise in the past 20 years, it might be expected that this function in children during exercise would

have been extensively studied. However, only two reports were encountered in which children were the subjects of the study.

In 1965, Giammona and Daly (147) measured D_L on 20 children 8.2 ± 2 years of age. The test exercise was done on a treadmill at a level of work adequate to increase the oxygen consumption by only 90% above the resting level and this gave an average increase in $D_L CO$ of 3.7 units. This increase, due to greater Vc and Dm, was significant and the authors concluded from these determinations made at a single exercise load that the increase in D_L in children was comparable to that for adults. Johnson et al in 1965 (198) included in their study of maximal diffusing capacity 5 children (8 to 15 years) and remark in their summary that $D_L CO$ increased linearly with oxygen uptake. No values for $D_L CO$ were given; however from the figures given for VC and Dm, D_L was calculated and values for rest and maximal exercise only were obtained. Rest values varied from 19.8 to 37.7 and at $\dot{V}O_2$ max. from 28.4 to 42.8, ($\dot{V}O_2$ range 1.46 to 2.06). It is difficult to draw any conclusions from such few data; however, it is apparent that their resting values are high in relation to data of others while the exercise values seem to be comparable to that for adults at comparable oxygen uptakes. These authors employed the breath-holding method (197), a technique which may be difficult to apply to young children and especially so during maximal exercise (33).

Although there is no doubt that $D_L CO$ rises in exercise, considerable disagreement prevails on several other points as

regards exercise D_L, which include:

1) the relationship or magnitude of increase with increasing severity of work
2) the level of exercise at which D_L levels off or plateaus despite increments in load and $\dot{V}O_2$
3) the mechanisms responsible for increasing D_L during exercise.
4) the effects of age and sex
5) the significance of D_L as a factor limiting performance
6) the effects of athletic training

These points are considered in detail below.

2. Relation to exercise

Bøje in 1934 (59) and Lilienthal in 1946 (234) were among the earliest to make successive determinations of D_L at increasing workloads in the same subjects. Using the single breath technique of Krogh, Bøje found D_L in exercise to reach values approximately twice that at rest, although there was wide individual variation both at rest and in exercise. The highest value for $D_{L\,O_2}$ was 61 ($D_L CO$ of 48.7). Lilienthal et al employed the low O_2 method and found a linear relationship between D_L over the full range studied. Filley et al (135) found the $D_{L\,O_2}$ steady state $D_L CO$ to increase in exercise but 'in a given subject $D_L CO$ remained approximately constant at various levels of exercise'. Although there was again wide interindividual variation, (23.2 - 55.0), in general the leveling off occurred at a $\dot{V}O_2$

of approximately 2 Ls (about 4 times resting $\dot{V}O_2$ level), $D_L CO$ being about twice the resting value. Two publications appearing shortly after supported the findings of Filley (32, 296). The table following shows a summary of early results by different investigators:

Ref. No.	Author	Approximate Mean Increase in D_L Over Resting Value %	Method *
225	Krogh	36	SB
277	Ogilvie	46	SB
59	Bøje	100	SB
234	Lilienthal et al	300	Low O_2
135	Filley et al	110	SS
32	Bates et al	80	SS

The above summary illustrates clearly the great variability in results, much of which might be attributed to the method used. For example, the SB method yields high values at rest by comparison with the SS while the two methods give similar values with increasing exercise. The low O_2 method causes hypoxia and thus hyperventilation, for which a correction must be applied.

More recent studies on adults have helped clarify the relationship of D_L to varying exercise. Studies by Donevan in 1959 (117) on 20 subjects ages 24 to 49 years, with $\dot{V}O_2$ ranging from 1.09 - 3.59 showed a linear relation of D_L with $\dot{V}O_2$, a finding similar to that of Linderholm (236) in humans, and Brashear et al (62) in dogs. $D_L CO$ increased by approximately 10 units/litre 02. Newman et al (274) in many repeat determinations on one subject at $\dot{V}O_2$ .3-3.5 L found the relation of kCO **

* SB- single breath, SS - steady-state.

** kCO - Krogh's constant which take into account alveolar volume (V_A) prevailing during the test ie. $kCO = \frac{D_L CO\ (P_b - 47)}{V_A}$

to $\dot{V}O_2$ to be rectilinear throughout. When expressed as $D_L CO$ ($D_L CO = 6\ kCO$), D_L increased by 7 units/litre 02., a ratio similar to that found by Ogilvie (277). This same relationship has been observed in females (338).

In a recent study on 20 well trained young subjects, Holmgren and Astrand (182) found a hyperbolic relation between $D_L CO$ and $\dot{V}O_2$, the slope of the line describing this relationship reducing at a heart rate of ≥120/min. or $\dot{V}O_2$ of 40% of maximal.

Summary

1) There is no doubt that D_L increases in exercise in adults and children.

2) The magnitude of the increase and the slope describing the relationship D_L/Litre $\dot{V}O_2$ seems highly dependant on the method employed in measurement.

3) In more recent studies, the relationship of D_L to $\dot{V}O_2$ has been found linear up to $\dot{V}O_2 = 3.6L$, the ratio being 6-10 units/L $\dot{V}O_2$, although others (182) found a hyperbolic relationship.

4) No reports of studies on children at varying workloads were encountered, thus the effects of growth on exercise D_L and the relation D_L/TLC have not been elucidated.

3. Plateauing

Plateauing of D_L is indicated when an increase in $\dot{V}O_2$ fails to cause a further rise in D_L.

Earlier reports (32,135,296) suggested that D_L rose

precipitously on exercise to a maximum value at 1-2 L $\dot{V}O_2$ which was approximately twice that of the resting D_L value. It was subsequently shown by Linderholm (235) that build up of CO Hb in prolonged (135) or repeat (32) exposure, unless taken into account in the calculating of D_L, would lead to a false plateauing of D_L CO.

Riley (296) and Cohn (93) measured the D_L O_2 in 3 and 21 male adults respectively. They found a plateau was reached at $\dot{V}O_2$ of 1-2 ls. Shepard et al, in the same laboratory (316) found similar results and showed this leveling off to occur when the cardiac output ($\dot{Q}c$) reached 15 litres/min.

By contrast, recent studies using the steady state CO method, (117,266) and the single breath method (277) showed no plateau in D_L CO at $\dot{V}O_2$ up to 31/2 L 02. More recently, Johnson (197) employed the single breath technique to simultaneously measured D_L CO and $\dot{Q}c$ in 11 subjects, 5 of whom were 15 years or under. A high correlation (.92) between these two functions was found, the relationship of which is expressed..

$$D_L CO = 12.0 + 2.2\ \dot{Q}c \pm 6.0 \text{ (i.e. 2 SE)}$$

They concluded that maximal D_L CO is reached when $\dot{Q}c$ is maximal, both of which are lower in children than in adults. A subsequent study by Johnson et al (198) confirmed these findings and showed $\dot{V}O_2$ to plateau concurrently with D_L CO.

Holmgren in 1965 (180) presented data which showed that at heart rate (H.R.) $\geq$ 120/min., there was only a slight additional increase in D_L CO with increased $\dot{V}O_2$. Since the further rise in

D_L at heart rates over 120 was so slight, he felt justified, considering the reproducability of the method (178), to accept values at heart rate $\geq$120 "as a measure related to maximal $D_{L}CO$ of the subject". He and Astrand (182) in a recent and extensive study of 20 "healthy, well trained young" Swedes, measured the functional capacities of the various elements of the oxygen transport system. Using the above criterion, for maximal $D_{L}CO$, these authors indicate that their findings support the concept of a maximal $D_{L}CO$ which is reached prior to maximal $\dot{V}O_2$ or $\dot{Q}c$.

Summary

1) A plateauing of $D_{L}O_2$, under hypoxic conditions, occurs at a $\dot{V}O_2$ .9 - 1.2 Ls in young, and earlier in older, adults subjects.

2) There is disagreement as to whether a maximum value for $D_{L}CO$ is ever reached, some workers claiming this value continues to rise (117) till maximum cardiac output is reached (197), others (180) suggesting that there is a rapid increase on commencing effort, but that after heart rate has reached about 120 (and by inference, stroke volume has reached its maximal level), there is only minimal further increase in $D_{L}CO$.

4. Mechanisms for Increase

Forster has suggested (137) that the D_L can be considered in terms of three components which offer "resistance" to gas transfer in the lung, and are related as follows:

$$\frac{1}{D_L} = \frac{1}{D_m} + \frac{1}{\theta Vc}$$ (terms defined above)

It is convenient to analyse how these "resistances" might be reduced to enable D_L to increase on exercise.

θ represents effectively the concentration of hemoglobin as a receptor for CO (or O_2) in an individual and can be considered constant during exercise although it is appreciated that it is possible that some slight change in hematocrit, and hence θ, can occur when exercise is progressively increased (19) or of long duration (24). However, these changes, although in the right direction, cannot be of sufficient magnitude, especially in exercise of relatively short duration, to account for the rise in D_L.

The other two factors (D_m and Vc) were considered by Barcroft (1938) to be of greater importance and he wrote

> "..the two most obvious means..(for the increase in D_L on effort) are distention of the lung, which makes the cells thinner and the opening up of vascular areas, either by increasing the calibre of the vessels already open or opening up those hitherto shut" (29).

It is however important to bear in mind that these two mechanisms are interdependant in the sense that changes in one aspect almost invariably effects changes in the other. Also, it must be fully appreciated that events occurring on the 'lung' side (i.e ventilation) must be appropriately matched by events on the circulatory side if either lung distention or capillary blood volume changes are to be effective in increasing D_L in exercise.

Increase in ventilation is one of the best known adaptations occurring in exercise. This has two effects relative to diffusion:

1) the mean alveolar concentration of the gas concerned (CO or O_2) is raised, hence a greater driving pressure is established, especially since in the case of O_2 the returning mixed venous concentration is also lowered.

2) the ventilated area of the lung is greater, which, in accordance with Fick's Law of diffusion, enhances the diffusability of a gas.

It has been difficult to partition clearly the effects of a particular factor from others, in respect to their relative contribution to the increased D_L, because of the interdependance; thus, the relative effects of hyperventilation per se on D_L are not certain although this has been a concern of numerous investigations. Ross (304) in 1958 made a careful study on the relationship between D_L, $\dot{Q}c$ and minute ventilation under varying conditions. Using the Filley SS method, they found an increase in all subjects with exercise whereas when $\dot{Q}c$ alone was increased by means of drugs, no change in $\dot{V}$ or D_L were observed. On the other hand, voluntary increase in $\dot{V}$, which only increases $\dot{Q}c$ slightly (246), increased D_L to a value near that caused by exercise requiring the same $\dot{V}$. These authors concluded that D_L does not increase unless $\dot{V}$ does, a relationship supported by the findings of Turino (346). Additional support for these findings is given by MacNamara (242) who also found hyperventilation

increased D_L at rest although this value was lower than for a corresponding $\dot{V}$ during exercise (243), in agreement with an earlier finding of Bates (30) who measured the fractional uptake of CO. In contrast, during a fixed exercise, voluntarily raising the $\dot{V}$ by 25 L had no effect on D_L (36,266). Others have observed that the D_L increase with hyperventilation occurs only if the V_T is raised; that is, the increase is a function of alveolar volume and not minute alveolar ventilation, whether the steady state (211) or breath-hold (4) method is employed.

The effects of changes in Vc on D_L has been a topic of some considerable interest in recent years. To assess these effects, direct changes in Vc in a resting individual have been effected by different means. In 10 seated subjects, the venous pressure was raised by 5 - 10 mmHg by means of albumin infusion and positive pressure on the lower body by a G-suit (304); it was expected these changes would have resulted in enhanced venous return, thereby elevating both $\dot{Q}c$ and Vc. No change in D_L CO was found. Lewis (231) measured D_L and its components, Vc and Dm while applying positive pressure to the lower body; only a slight decrease in Dm was observed, with no consistant change in D_L or Vc. In a recent study, Guyatt (162) found immersion in water increased Vc by 47%, D_L rose by 16.2%. On the other hand, (387) negative pressure to the lower body caused a marked drop in the mean D_L CO (36 to 28), a direct consequence of the decreased Vc. Likewise, inversion of the body caused an increase in kCO (275); the supine D_L at rest was 20% greater than the value while

seated (35) and rising from the supine position decreased D_L and Vc (101,232,271). Increasing environmental temperature had the same effect (142). These results are compatible with the recent findings that both ventilation (260) and perfusion (68,202) distribution in the lung are gravity dependant. Thus not only is Vc greater in the supine than sitting posture but the distribution of ventilation and perfusion is more uniform throughout the lung (67). As a consequence, in resting subjects the direct relationship of Vc to D_L is not doubted.

Exercise can be regarded in many respects as an anti-gravitational force. Hence, the circulatory changes occuring in the lung at the onset of exercise are somewhat similar to those occurring when one goes from sitting to supine. These changes occurring in the lung during exercise are discussed in some detail by various authors. In respect of pulmonary capillary blood volume, Roughton (305) in 1945 ingeniously calculated this value and showed an increase from rest to hard exercise by 63% (60 cc to 95 cc) and from this modest increase he concluded there was no extensive opening of additional capillaries in heavy exercise. The corresponding mean transit time of blood through the lung capillaries he calculated to be reduced from .73 sec.(at rest) to a minimum of .34 sec. in work. (A recent report found a decrease in Vc in strenuous exercise (291)). Dollery and Co-workers (115,358) showed that exercise was associated with increased perfusion, and hence an increased Vc, to the upper lobes of the lung resulting in a rise in

$D_{L\,C\,O}$. 15 This finding was supported by Bryan (67) who showed flow to the upper regions of the lungs much greater in exercise than at rest. Johnson et al (197) found a close correlation of D_L and Vc with $\dot{Q}c$ in exercise adequate to give a three-fold rise over resting $\dot{Q}c$. Transit time varied in these conditions from .79 sec.(rest) to .5 sec. In another paper, Johnson (198) reports that the D_L increase in exercise requiring maximal $\dot{V}O_2$ is due mainly to a two-fold rise in Vc, Dm increased by only 20%. This relationship is similar to that in animals where Vc was found to increase linearily with $\dot{V}O_2$ (62).

Bates et al (34) point: out the inseparability of Vc from mean transit time, both of which have direct bearing on D_L. In a detailed study of normals and patients during exercise, they ascribe the rise in D_L to be due mainly to Vc; in addition, individual variation was found to be largely attributable to differences in this volume. Support for these findings is given by Mostyn (266) who found a higher Vc, and correspondingly higher D_L, in trained champion swimmers.

In summary, it is generally agreed that of the two main factors which affect D_L (i.e. Dm and Vc) an increase in Vc is the primary mechanism whereby D_L is increased in exercise in normal healthy subjects. This increase in Vc in exercise is a consequence of increased cardiac output and the opening of additional, or further expansion of already opened, pulmonary capillaries; this, along with increased tidal volume, markedly increases the effective area for gas transfer and also makes

ventilation and perfusion better matched throughout the lungs, thus resulting in an increased D_L in exercise.

5. Diffusing Capacity Limiting Work Perforamnce

During work, the ability to take up large quantities of oxygen is essential to enable one to perform sustained work at a high rate. Thus, a close relationship between work performance and maximal aerobic capacity has been found by many investigators (15,78,88,191,364). This high aerobic capacity is dependant on the inter-relationship, and suitable matching, of the various dimensional capacities of the O_2 transport system (182). The link of the various systems involved in exercise (i.e. respiratory, circulatory and muscular systems) is diffusion which in turn must also be suitably matched to the systems to which it is related.

It is clear that in the case of the pulmonary diffusing capacity, this function is directly affected by both respiratory and circulatory systems. It is equally true however that D_L can affect the efficiencies of the systems it subtends, a fact which is especially apparent in disease (236). As a potential factor causing limitation of work performance, workers are in good agreement that in healthy subjects D_L is not a factor at sea level (34,185,236) although this can be a 'weak link in the chain' during exercise at altitude as indicated by West (357,359) and others (288). It has also been suggested that in competitive swimmers, because of the restrictions this activity places on

respiration (i.e. immerson) a high D_L would be advantageous in enhancing their performance and, it is argued, would be essential for maintaining the high work rates necessary in champion swim performance. (266)

6. Training

In the few studies on the effects of athletic training on exercise D_L, most have compared the trained athlete with the untrained non-athlete. Earlier reports (32,135) showed that by comparison with other non-athletic types the single athlete in each study had a higher D_L in exercise than others although this difference was not present at rest. Group comparison was made by Bannister et al (27) who found that the changes in D_L with increasing exercise were comparable in athletes and non-athletes but the values in the athletes were higher throughout the work range studied. Newman (272,274) in a similarily designed study involving group comparison supported these findings. In a study relating resting $D_L CO$ with exercise pulse rate, Heinonen et al (170) found a significant negative correlation between these parameters and postulated that D_L increases with improved fitness. In support of this postulate, Newman (274) made many repeat measurements of D_L on one non-athleti subject followed over a 16 week period of training. These authors reported that kCO increased in relation to $\dot{V}O_2$, $\dot{V}_A$ and pulse rate, since the latter variables decreased for a given work load. In this regard, the non-athlete moved, by virtue of training, from the non-athlete to athlete regression line

describing the relationship of kCO and $\dot{V}O_2$. In a recent study of resting D_L, Rosenberg (303) found similar results with training in water poloists though not in rugger or soccer players.

By contrast, Mostyn (266), comparing different groups of athletes and non-athletes, was unable to show any group differences in respect of D_L except in three Olympic swimmers; they had D_L values significantly higher for a given $\dot{V}O_2$ than all others including other trained intercollegiate swimmers in the group. In our preliminary study, (3) in a group of 21 college athletes and 26 non-athletes studied at one exercise load before and again after training, a significant decrease was found with the moderate training in the group comprised of the four older subjects while no change was seen in the athletes and younger non-athletic group; no group difference was found. These findings were in agreement with Coates and Meade (91) who found no change in 11 volunteer service men studied during exercise before and after 12 weeks of basic training.

Lack of agreement thus persists as regards the effects of athletic training on D_L. A high correlation has been shown between maximal D_L and maximal aerobic capacity (182), presumably a function of the athletes' larger cardio-respiratory dimensions (20). However, a recent presentation by Reddan (291) in which training decreased the $D_L CO$, is markedly divergent from these above findings in that they show the decrease is a consequence of reduced Vc and total blood volume, both of which have been reported higher than normal in some trained athletes (266, 212).

Summary

1) The effects of training on exercise D_L have not been extensively studied.

2) Reports in which group comparison was made are inconsistent. Some observed higher values in athletes (27,170,274), others found no difference (266) except in champion swimmers.

3) Similar controversy prevails when pre and post-training comparison was made (91, 204).

4) No longitudinal studies on exercise D_L in children undergoing regular athletic training have been reported.

PART II: THE TOPIC IN REVIEW

Chapter 4. Cardiac Function in Exercise

A. Introduction

B. Oxygen Consumption and Ventilation

1. general
2. adaptation to exercise
3. studies on children
4. training
5. summary

C. Cardiac Output - history of methodology

- in exercise
1. relation to oxygen consumption
2. effects of posture and sex
3. studies on children
4. training ..at rest
..in exercise
5. summary

- mechanisms for increase
1. heart rate
2. stroke volume
3. training
4. summary

D. Arterio-Venous Oxygen Difference

Concluding Remarks

CARDIO-RESPIRATORY FUNCTION IN EXERCISE

A. Introduction

The 1920's, which saw the advent of the Harvard Fatigue Laboratory in Boston, is regarded as one of the most significant periods in terms of the awakening of an interest among physiologists on this continent in the area of exercise study. At that time, it was stated by Bock et al, investigators at that laboratory, that:

> "..the superiority of the athlete lies in his ability to meet the demands for oxygen, enabling him to maintain an internal environment varying within narrow limits only from the resting state"(57).

In 1952, in his review, Astrand (16) concludes:

> "..the individuals' capacity for oxygen intake should be decisive in determing his ability to sustain heavy prolonged exercise".

In performance of aerobic work, as during prolonged exercise when the oxygen uptake balances the oxygen demands, the respiratory and circulatory systems, or "the oxygen conduction line" (181), play a dominant role. These systems have been clearly displayed in analog form by Holmgren (181) and the dimensions of the various components carefully considered in the detailed study by Holmgren and Astrand (182). As indicated above, it is the principal purpose of this thesis to study the training effects on the "O_2 transport" system during sub-maximal exercise. A brief summary of the adaptations to exercise, as well as the effects of various factors such as age, sex, posture, temperature etc., are included along with the following summary of the literature on the effects of training.

Probably the most concise review of events involved in the process of exercise is given in the well known Fick equation which states that the minute oxygen uptake ($\dot{V}_{O_2}$) is the product of the minute cardiac output ($\dot{Q}_c$) and the arterio-venous oxygen difference (or O_2 extraction). This is thus written:

$$\dot{V}_{O_2} = \dot{Q}_c \times (A\text{-}V)_{O_2} \text{ Difference}$$

Each part of this equation is considered separately in the following summary.

B. Oxygen Consumption and Ventilation : 1. General

Physiologists have clearly shown that work performance requires energy, that there is a linear relationship between the rate of energy production and work rate, and that this relationship holds in interindividual comparison, provided efficiency is not different. In this respect a human is like any other mechanical work-performing device.

The body has 2 available mechanisms for supplying this necessary energy..1) aerobic - which requires the utilization of O_2 during the work period and 2) anaerobic - a mechanism which is associated with the accumulation of lactic acid (lactate) in circulating blood. Ultimately, removal of lactate requires O_2 utilization and the amount of accumulated lactate can thus be expressed as an "O_2 debt", a term first introduced by A.V.Hill (176). During work performance of maximal intensity for short durations (eg. 100 M sprint) almost all energy results from the anaerobic processes (252), but in more extended work periods it must be the aerobic system that is the major contributor since there is a maximal tolerable level of lactate

beyond which performance ceases, and fatigue occurs.

2. Adaptation to Exercise

On commencement of exercise of light to moderate severity the rate of O_2 consumption rises rapidly to reach a constant level..or "steady state" in about 1 to 3 minutes (52,79,114, 116,192,341,344). Attainment of this state is related exponentially with time (252) and may (201,354) or may not (22) require longer at higher work intensities (201,354) or in those with heart disease (133). During moderate exercise, the lactate rise is negligible (217) and all the needed energy is provided by the aerobic means solely (217,252); there is thus a linear relation of $\dot{V}O_2$ to work rate (341). This relationship is not affected by body position (245,292), age (39,117) altitude (287) and sex (13,39), although there is not unanimity on this latter point (90, 174). For a given work load $\dot{V}_{O_2}$ may be decreased slightly with increased environmental temperature (5). As the work rate is raised, a point is reached in man, but not in dogs apparently (77,286), where oxygen uptake does not rise, or may even decrease (259) despite higher work loads. This is defined as the maximal $\dot{V}_{O_2}$ ($\dot{V}_{O_2\ max}$) or maximal aerobic capacity (259, 365). The energy needed for this extra work after the aerobic limit is reached is provided totally by anaerobic means (176). The level of exercise at which $\dot{V}_{O_2\ max.}$ is reached is variable, depending on the type of exercise (148,276) and muscle mass employed (21,23,88,102,341). It is also dependant on body size (223) and age, increasing in children to about age 19 (16,218),

or 16 years in female (218), and decreasing in adults (10,109, 111,331), possibly after age 24 years (298). This maximal value is lower also in altitude (112,113,288), in the supine position (23), but is greater with 'physical fitness' (159,203, 258) and athletic ability (15,78,191,272). Decreasing plasma volume (103) or dehydration (71,97) lowers this peak value while the addition of an O_2 rich inspiratory gas mixture (253, 255) or raised environmental temperatue (5) may increase this value. Females cannot reach as high $\dot{V}_{O_2}$ levels as males, nor can children of comparable size reach adult levels (13). The relation of work done to energy produced to do this work is defined as efficiency.* This has been shown to be 22.4 in females, 23.4 in males (13) and this is not affected by age (265,298) or other individual differences, provided the test exercise does not require special skill (16,131,343).

The increase in O_2 demands with the onset of exercise is associated with an almost instantaneous rise in minute ventilation ($\dot{V}$) as a consequence both of a greater tidal volume (V_T) and increased respiratory rate (f), each of which is related to $\dot{V}$ in a linear fashion (122,156). Ventilation is related to work rate in a linear manner (18,57,247) in moderate exercise and under such exercise conditions is hence linearly related to $\dot{V}_{O_2}$. Like oxygen consumption, it is precisely adjusted to the metabolic requirements of the organism. Because of this linear relation, the ventilatory equivalent

*. $\frac{\text{work done (calories)} \times 100}{\text{total calories used}}$

($\dot{V}/\dot{V}_{O_2}$) remains constant through moderate work levels up to about 70% of $\dot{V}_{O_2\ max.}$ (174,247) after which the increase in $\dot{V}$ is more marked than is the rise in O_2 consumption. This increase in ventilatory equivalent is associated with a sharp rise in the O_2 cost of breathing (i.e. ml O_2/l $\dot{V}$) (73,248,26) until a point is reached at which it is probable that all further increase in oxygen uptake is used by the respiratory muscles; thus no additional O_2 is made available for working muscles (84,279) as a result of the added ventilation.

The topic of ventilation control mechanisms in adapting to exercise has been the subject of many reports (7,105,106, 190,356); of particular interest is the instantaneous rise (7,224) with exercise commencement. In those conditioned to exercise commencement by count-down, this increase proceeds the onset of exercise (345) in moderate exercise of short duration, "steady state" is quickly attained (79) although with prolonged exercise there is a continuous increase (122,185). Holmgren found that under these conditions (185) and as workload was gradually increased, arterial pH and pCO_2 fell, pO_2 was unchanged, while body temperature increased. The exact relationship of these factors to ventilation control is still not certain (16).

3. Studies on Children

Robinson in 1938, in a detailed report compared treadmill exercise performance in groups of male subjects of age 5.7 to 91 years. No difference in efficiency at moderate work was found after maturity (i.e. about age 15), though younger boys were

less efficient. The respiratory quotient under these exercise conditions rose with age. Maximal oxygen consumption, expressed a cc/mm/Kg., showed a wide scatter and was not different in boys to age 20. In absolute values, the range was from 0.98 in the youngest boys to 3.61 in boys of 17.4 years.

Morse et al (265) also used a moderate and exhaustive treadmill exercise on boys 10 to 17 years to make comparisons during the growth period. Under these conditions, as in Robinson's study, the workload is a function of body zie. Nonetheless, for comparable moderate levels of exercise, respiratory frequency and minute ventilation decreased with age from 14 to 17 years and the oxygen requirement and respiratory quotient increased from ages 10 to 13 years. Maximal $\dot{V}_{O_2}$ was lowest in the 13 year-old boys but increased with age in the older subjects. This was accompanied by a progressive rise in blood lactate levels with age.

Astrand (13) in 1952 reported an extensive study of the physical working capacity as related to age and sex..Over 200 persons.. 4 to 33 years..were studied. Comparisons of maximal values in respect to work, $\dot{V}O_2$, heart rate and lactate levels were made. Maximal aerobic capacity and maximal work rate showed a linear relation to age in each sex to age 13 years, and sex differences were slight, though consistently less in females. Sex differences became more marked at age 14 to 16 and adult values were reached at age 20. Peak values for $\dot{V}_{O2}$ ranged through 1.01 (4 to 6 years), 2.04 (10 to 11 years), and

3.53 (14 to 15 years) for males; corresponding values for females were .88, 1.7 and 2.58 l/min. Males had higher maximal values for ventilation, due to greater f and V_T while the ventilatory equivalent was consistently greater in females.

The results of the limited study of maximal $\dot{V}_{O_2}$ on five children 8 to 15 years by Johnson (198) are similar to those of Astrand although when expressed as $\dot{V}_{O_2}$/kg body weight no sex difference was seen by Johnson whereas Astrand indicates this value was 10% lower in females at ages above 12 years.

Work capacity measurements in children have been made by numerous workers (1,2,14,42,47,98,99,150,151). Methods employed in these studies often vary and determinations of oxygen consumption were not always made. Furthermore, age, rather than body size was generally the common factor, and this could account for marked variations in children who may differ in rate of development. Thus, Bengtsson (42) found wide interindividual variation in work performance in children, especially in the younger age ranges. From the sub-maximal bicycle exercise tests, he found the relation of $\dot{V}_{O_2}$ and $\dot{V}$ to be similar in children of different ages and this relationship was similar to that found in adults. Mean mechanical efficiency was 20.6± .5%.

4. Training

In 1915 Lindhard (237) compared athletes with non-athletes and reported the "stoffwechsel" (metabolism) though higher in the athlete at rest, is lower during exercise in the trained person, a finding supported by early reports by Briggs (63,64)

and others (25,146). These earlier studies are further supported by numerous more recent reports where greater efficiency was observed in athletes (27,90,203,216) and with training (91,274). By contrast, a number of workers found no difference in this respect (123,141,165,198,268) while Hermansen and Andersen (174) found a greater O_2 requirement in Norwegian athletes during submaximal exercise,a difference they attribute to the higher basal metabolic rate of these trained persons.

The difference in findings seemingly is related to the acquisition of skill (114) and according to Steinhaus,

> "..the improvements in mechanical efficiency which comes with practice are really a measure of the effects of training on the central nervous system and not a measure of improved metabolism in the sense of more economical intracellular activity". (326).

Astrand makes a similar conclusion in his review (16). No marked change in efficiency is seen (131) unless the test and training exercises are similar, as was the case in several of the above studies reporting improvement (90,216,274). Perhaps, as Karpovich suggests (203),differences among findings in respect to efficiency and training might be resolved if the elevation in post-exercise O_2 consumption was included in the total O_2 cost of work.

Of far greater significance than any slight changes in O_2 requirement at submaximal exercise are those which are evident at maximal exercise. There is no doubt that the trained person has the higher maximal aerobic capacity (20,71,78,186,274) and

that in the individual prolonged strenuous training has a similar effect on $\dot{V}_{O_2\ max}$.

Because of the relationship of maximal $\dot{V}_{O_2}$ to body size (72,341) interindividual comparisons in this regard are better made by expressing the measurement as $ml O_2$/min/kg body weight. When this is done, values for normal young males, including the Bantu and Bushman (364), are of the order of 50 (78,81,262, 298) whereas those for trained older children (14,220) and trained adults (78,174) average about 60 to 70. This difference becomes even more apparent in elite Olympic athletes (15) where reported values reach as high as 82 ml/min/kg in a champion cross-country skier; slightly lower values are reported for distance runners (299). Females athletes, with values of 64.5 (88) and 68 (16) are likewise higher than normals. Older trained subjects (159) also have higher values when compared with normals of comparable age.

Ventilation drops with training (63,146,291) and this has the consequence of reducing the ventilatory equivalent (21,91,149,251,340). This in turn is responsible for a lower cost of breathing, at any given exercise level, in the trained subject (258). By contrast, the reverse is true in detraining (274) or for a period of bed rest (342). The decrease in ventilation is a consequence principally of a reduced respiratory rate (63,146). There is no doubt the trained athlete is capable of achieving higher levels of ventilation during maximal exercise (23).

An additional distinguishing feature reflecting superiority of the trained athlete is the faster return to normal of both $\dot{V}_{O_2}$ and $\dot{V}$ for any given submaximal exercise load, a change clearly shown by earlier workers (199,319) as well as more recent studies (91,130,257). This implies that the O_2 debt, a topic discussed in some detail by many workers (74,110, 254,301), is lower in the trained for a given work level although this was not found by some (123,141).

5. Summary

1) The adaptations to exercise in respect to $\dot{V}_{O_2}$ and $\dot{V}$ are similar in adults and children.

2) Maximal aerobic capacity increases linearily with age until puberty, at which age the increase becomes more notable, especially in boys.

3) Maximal $\dot{V}_{O_2}$ is lower in children than in adults, though when related to body weight this difference disappears.

4) Training alters the relation of $\dot{V}_{O_2}$ to work intensity little, if at all, except where the acquisition of skill with training relates to the test exercise. Maximal values are greater in the trained, and recovery time is shorter.

5) $\dot{V}$ decreases with training, for a given exercise load, and this results in a lower ventilatory equivalent.

C. Cardiac Output

Our knowledge of $\dot{Q}c$, particularly during exercise, has developed as appropriate methods have been developed for its measurements under specified conditions. The methods employed and a brief historical background are presented by Assmussen and Nielsen in their 1956 review (8). There are three principal techniques..the principle of Fick, the Bornstein technique using foreign gas (60) and the dye dilution method developed by Stewart (330).

Although Fick first proposed his direct technique for $\dot{Q}c$ measurement in 1870 (which he personally never did apply), it was not until 1898 that the method was actually first employed at which time Zuntz and Hagemann (368) made measurements of exercise cardiac output on a horse. They showed an almost 1:1 relationship between $\dot{V}_{O_2}$ and $\dot{Q}c$ and found only a slight change in O_2 extraction. The first record of its use in humans is 1929 when Forssmann "volunteered" to be his own subject (136). The record shows that he survived the ordeal which then was considered a dangerous procedure. Nineteen years later this technique was first used in exercising humans (295).

The intervening years, between 1890 and 1929, saw the development of the other techniques. In particular, the foreign gas method, because it did not require the use of needles, gained in popularity, and it was applied in various forms under exercise

conditions by Krogh and Lindhard (222), Christensen (87), Bock (56,57) and Grollman (161) using different gases.

The method is based on the Bornstein Principle whereby a plasma soluble but otherwise inert foreign gas is taken up by blood as it passes through the pulmonary capillary bed. By measuring the volume of the gas taken up, and by knowing the partition coefficient (λ)* of the gas in blood, the pulmonary capillary blood flow can be accurately determined, provided such measurements are performed at a time of constant alveolar levels of the test gas. Early investigators who used this method for measuring cardiac output were confronted with the major problem of test gas analysis. Chemical methods for analysis were slow, tedious and rather prone to error. As a consequence, the method rapidly fell into disuse in favor of the then more accurate dye dilution method and, more recently the Direct Fick technique. The later development of fast response gas analysers enabled circumvention of these early problems. Gas analysis became not only accurate but easy and investigators were readily able to assess the completeness of equilibration and the time of onset of recirculation, points which earlier had given rise to doubts as to the validity of the method.

The dye dilution method gained prominence in the 1930's, especially following the method improvement of Hamilton (164) in 1932. More recently, the direct Fick became more applied

*...mls of dry nitrous oxide which will dissolve in one ml. of blood when equilibrated at 760 mmHg. at 37°C.

in research on humans at rest (226) and exercise (108,175, 325). These results, as well as comparative studies of the dye and indirect methods on the same subjects (6) have confirmed the reliability of each technique as a means for accurate cardiac output determination.

Cardiac Output in Exercise

The circulatory system, its adaptation to and control in exercise has been reviewed earlier in detail by several authors (8,309,310,350) and more recently in the extensive and excellent reviews by Bevegard and Shepherd (52) and others (80) in 1967.

1. Relation to Oxygen Consumption

The original finding of Zuntz and Hagemann that there is a direct relationship between $\dot{Q}c$ and $\dot{V}_{O_2}$ in the horse has been found to be true in man (10,11,161,237,293). In adult males, $\dot{Q}c$ (226) rises from a resting value of about 6.6 L/min (3.7 l/min/M) to 8.2 at 1L O_2 consumption in submaximal exercise (19). Thus the rise in $\dot{Q}c$ per litre rise in $\dot{V}_{O_2}$ is 6.01 and this relationship prevails until cardiac output reaches about 16 ls/min.(49). This linearity and its constancy are however doubted by some workers (193,339). "Steady state" in such moderate exercise is reached in about 1 minute (48,116). As the intensity of the exercise (or $\dot{V}_{O_2}$) is increased the rise in $\dot{Q}c$ per litre rise in $\dot{V}_{O_2}$ decreases to 4.35 (19).

At maximal work levels cardiac output reaches values of 20 to 25 L/min.(19,81,352), a value which is maintained even under prolonged severe exercise (92,122,311) and in heat (361),

though not at altitude (287). Once maximal cardiac output is reached, $\dot{V}_{O_2}$ is further increased with greater work loads (280) because of increased O_2 extraction. For this reason, the cardiac output has been regarded by many investigators as being the major limiting factor of work performance (82,236,261,297).

2. Effects of Posture and Sex

For a given level of $\dot{V}_{O_2}$, $\dot{Q}c$ is greater in the supine than sitting or standing positions (49,154,245,292,327,352). At rest, Bevegard (48) reports a difference of 2.2L and this difference was maintained even during exercise requiring a $\dot{V}_{O_2}$ of 2.5 l. The lower value in the upright position is attributed to a decrease in central blood volume due to a hydrostatic shift increasing the blood volume in the lower extremities (352), and to a reduced heart volume (187).

In females, the adaptations of cardiac output to exercise is similar although the increase in $\dot{Q}c/l\ \dot{V}_{O_2}$ is greater in the females (19) (rise in $\dot{Q}c$ per litre rise in $\dot{V}_{O_2}$ is 6.81) and maximal values attainable (18.5 L/min) are lower.

3. Studies on Children

Reports on resting supine cardiac output indicate the cardiac index in children is comparable to adults (196). However, there are few reports of exercise cardiac output measurements in normal children. Cayler (75) studied 8 patients (mean age 10 years) "with no demonstrable or only minor heart lesions" in mild supine leg exercise. The mean increase of $\dot{V}_{O_2}$ over rest was .214 ls and the corresponding

rise in $\dot{Q}c$ in the children was .846 liters/100 ml O_2. This is higher than the adult value of Donald (116), though comparable to that reported by Astrand (19), in adults. Johnson (198) made simultaneous determinations of D_L and $\dot{Q}c$ at rest and maximal exercise on five children (4 females) age 8 to 15 years. Cardiac output was determined by the indirect Fick, foreign gas method during breath-holding. Values measured at maximal $\dot{V}_{O_2}$ were 11.1 l in the 8 year old while the range for other subjects was 10.3 - 12.9 litres/min. Maximal oxygen consumption ranged from 1.46 to 2.06 l/min. This would indicate that the maximal cardiac output of these children was about half that of adult females (19) and that the ratio $\dot{Q}c/\dot{V}_{O_2}$ at maximal exercise might be greater in children than in adults.

4. Training

There have been numerous studies reported in which the effects of training on $\dot{Q}c$ have been deduced from comparison of trained athletes with non-athletes. This experimental approach of group comparison assumes that any differences observed may be ascribed solely to athletic training. In general, this method of study has been used to avoid repeat measurements before and after training on any one individual and so minimize subject discomfort, especially when intravascular intrusion is required. High interindividual variation in $\dot{Q}c$ perhaps accounts for divergent findings among workers.

Resting studies in the trained subject

In an older review, Steinhaus made a comprehensive

summary of the "Chronic Effects of Exercise" (326). He suggested that

> "..the trained individual ..(at rest)..may be said to have a relatively uneconomical circulatory adjustment.."

His statement was based on the early work of Lindhard (237) who found the resting minute output ($\dot{Q}c$) higher in athletes and since $\dot{V}_{O_2}$ was not different in the groups, O_2 extraction was lower. This finding of Lindhard is supported by the recent studies of Frick (143), on 14 soldiers studied before and after two months basic training, and that of Wang (353) in which comparison of athletes and non-athletes was made. A high cardiac index was found in the trained subject. In contrast with these reports is the study by Musshoff (268) in which $\dot{Q}c$ was measured, using the direct Fick technique, at rest and in exercise in the recumbent position. They reported a lower resting cardiac output (in agreement with Heinecker (169)) in the nine highly trained male athletes by comparison with the thirteen normal men and four women. Since no difference was seen in metabolic rate, the greater resting O_2 extraction enabled the lower resting minute output. The comparative study of runners and normals by Hanson (165) and their "before and after" training study of runners (340) support these findings, although the differences found by Hanson were not significant. Bevegard was unable to find any difference between the small group of eight well trained subjects and non-athletes (50), nor was any effect of training seen in resting cardiac output as measured by ballistocardiogram (262).

Exercise studies in the trained subject

Similar conflict of findings on the effects of training are found in the literature when exercise studies are compared. Early studies of group comparison by Lindhard (237) and Collet (94) found cardiac output in relation to $\dot{V}_{O_2}$ lower in the trained person. Assmussen (8) compared results of four different workers in his review and attributed the higher $\dot{Q}c$ in two of the groups to be due to their greater level of training. Bock in 1928 (57) made a similar conclusion from his very limited study of four men. The marathon runner in the group (DeMar) had a higher ratio $\dot{Q}c/\dot{V}_{O_2}$ than two of the other non-athletes. However, he did not differ from the fourth subject (D.B.Dill).

More recent exercise studies have been no more unanimous in agreement than the above reports. Thus Frick (143), Freedman (141) and others (50,92,155,312) report no difference, either in the trained and untrained states (141,143,155) nor between groups (50,92,312). Likewise Musshoff (268) found no difference in his male groups nor did the males differ from the four females in the study. However, the athletes were able to reach higher levels of work and $\dot{V}_{O_2}$ and thus attained higher exercise cardiac output levels. Maximal work levels were not attempted however. Similar results were found when before and after training comparisons were made in seven males (155). Hanson and Tabakin (165, 340) found no significant differences between groups; however, when the same subject was compared before and after training, significant decreases in $\dot{Q}c$ were found at the exercise levels

which corresponded to those regularly employed in their training program. No differences were found at the lowest and highest test loads. Varnauskas (349) showed a consistent decrease with training in coronary patients.

Grimby (158) found the relationship of cardiac output to oxygen consumption to be similar in older well trained 'orienteers' and normals of the same age though this relationship was slightly higher than that of younger, highly trained persons (19,50,165). Maximal values averaged 26.8 l/min in these older men, values which are similar (19) or even greater (50) than those found in trained younger men.

5. Summary

1) Reports on adults of exercise cardiac output indicate its close relationship to O_2 consumption in submaximal exercise. Variations in this relationship are effected by posture and sex. $\dot{Q}c/\dot{V}_{O_2}$ being higher in the supine and in females in submaximal exercise.

2) Few studies of maximal $\dot{Q}c$ are reported. These indicate a decreased ratio $\dot{Q}c/\dot{V}_{O_2}$ at higher loads which has led investigators to conclude $\dot{Q}c$ may be a major factor in limiting work performance.

3) From the few encountered reports on exercise cardiac output in children, the relationship $\dot{Q}c/\dot{V}_{O_2}$ at mild exercise is similar, possibly slightly higher, in young children (75) and this may be so at maximal $\dot{V}_{O_2}$ (198).

4) The training effects are uncertain. Higher, lower and

similar values for $\dot{Q}c$ for a given $\dot{V}_{O_2}$ have been reported, for rest as well as exercise.

Mechanisms for increasing $\dot{Q}c$

1. Heart Rate

Probably the best known adaptation to exercise is the change occurring in heart rate as work is commenced. Its linear rise with increasing work intensity is not doubted and this relationship is highly repeatable in the same person and correlates closely with cardiac output (19) and oxygen uptake (11,22,43,99) as well as total hemoglobin (213). Because of this, heart rate has been often used as an index to work tolerance and fitness (1,2,151,205,229,321,328,337,351) and been employed in nomograms to predict maximal $\dot{V}_{O_2}$ from submaximal exercise levels (21).

For a given $\dot{V}_{O_2}$, or exercise load, heart rate is greater in females (13,256) and in the younger than older child (13, 265,298). It is higher too, at altitude for a given task (288) though maximal values are less (76,112,288). Because the relationship to work is markedly affected by environmental temperature (43,109,229,361) as well as numerous other factors (23,71,85,315,320,356) caution on its use alone as an indciator of either fitness or work capacity is essential (363). Maximal values attainable are greatest in the young child (13) and this value decreases with age (10,12,318).

2. Stroke Volume

Until recently, the contribution of stroke volume in

effecting cardiac output has been a topic of considerable controversy (8,49,81,268,309). This controversy is a reflection of the exercise cardiac output disagreement, since the adaptation of heart rate to exercise has been clearly defined. Because of the many recent studies of cardiac output, differences in opinion are being resolved and evidence for this can be found in the clear and concise summary of Bevegard and Shepherd (52).

At rest, stroke volume is lower by about 40% in the erect than supine position (19,49,50,158,245,353) because of blood volume distribution (8). In the supine posture, the rise during increasing work is approximately 10% over resting value; with the start of upright exercise a marked rise (by 40%) occurs to reach values close to, but still less than in supine exercise and thereafter with increasing work the change in SV is similar to that in supine exercise. Near maximal values are reached at $\dot{V}_{O_2}$ of 1 l/min (61,361) or 40% of maximal aerobic capacity (19). Stroke volume has been found to decrease in severe, prolonged exercise (122,311) and at near maximal work levels of short duration it has been reported to rise significantly (81,352) or fall (141,183). Tabakin indicates however that interindividual differences are significant and that a common pattern of response in graded exercise is often not found (339).

Stroke volume in exercise is a function of heart volume (182,269) and hence it is lower for a given $\dot{V}_{O_2}$ in females (268),

although this was not apparent in adults until the 4th decade (39). Similarily, it bears a high correlation to blood volume (50,213). Older adults have lower values at rest (154,331) while in exercise the effects of aging on SV are not definite (39,154,331).

3.Training

The lower resting heart rate in the trained athlete has long been clearly documented (189,205,312) and the training effect becomes apparent after short periods of strenuous regular exercise (143,146,184,237,321,368). This difference is even more apparent in exercise when lower values are found at any given exercise intensity in both trained adults (228) and children (192,228); maximal values are not affected by training. These differences at rest and submaximal exercise have been attributed to increased vagal tone in the athletes (204) as cited by Steinhaus (326). Recovery is faster in the trained (257,283) for any given submaximal load although this rate is not different after maximal exercise (216).

The athlete is characterized by a greater stroke volume at rest (16,109) and in exercise (20,57,109,310,312). No change was found in a season of athletic training in two studies (141, 340) though Frick (143) reports a rise with training. Stroke volume is thought to be a more important mechanism for increasing cardiac output in the athlete than non-athlete (158) and it has been suggested that it is the reserve of stroke volume which characterizes athletes from non-athletes (309).

4. Summary

1) The linear relationship of heart rate to exercise, even of maximal intensity, has been well established. For corresponding $\dot{V}_{02}$, values are greater in the young child and in female than male adults. Maximal values decrease with age.

2) Stroke volume is related to body size, thus it is larger in male than female adults, and by inference, is presumably greater in the larger child, though this has not been studied.

3) The trained have lower heart rates at rest and in exercise and seasonal training likewise reduces heart rate for a given $\dot{V}_{O_2}$.

4) Stroke volume is larger in the trained athlete than in non-athletes. The changes with seasonal training are not certain; one study (143) reports a rise while others (141, 340) found no change with training.

D. Arterio-Venous Oxygen Difference

As shown by the Fick equation, the increase in oxygen uptake can be effected by either an increase in blood flow or by greater removal of O_2 from the systemic capillary network. In practice, the demands for a higher level of metabolism are met by both mechanisms and on this point agreement among workers (80,350) is unanimous. Less unanimity exists when consideration is given to the relative significance of these two mechanisms. Since these arguments are direct reflections of those discussed in some detail above (i.e. the relation of $\dot{Q}c$ to $\dot{V}O_2$) further consideration here is not warranted.

Whether the relationship of A-V_{O_2} difference to $\dot{V}O_2$ is linear (61,141,158,268) or hyperbolic (116,293) seems relatively unimportant in the present context. Of great importance, however, is the limit to which such extraction can occur in exercise. Theoretical maximal values in normals is about 20 ml/100 ml of blood, which value represents the O_2 content of fully saturated normal arterial blood. However, since the metabolic activity of many tissues is low, as cited by Wade and Bishop (350), complete extraction from systemic blood cannot occur, although this may be possible in blood supplying exercising muscle. There is good and increasing evidence that in exercise regional redistribution of blood away from non-essential tissues (82, 121,307,350), even from non-exercising muscle (51) to working muscle, occurs and because of this high flow to such muscle (214) values for O_2 extraction of about 17 (268) or higher (19) are not

uncommon. In addition, exercise has been shown to (263) effect an increase in hematocrit making the O_2 carrying capacity of blood even greater than 20 and thus making higher extraction in vigorous exercise quite feasible.

Assmussen and Nielsen(8) discuss the topic of A-V_{O_2} difference of blood in working muscle and conclude:

> "The steadily increasing muscular A-VO_2 difference in the untrained subjects must be looked upon as a sign of a relative inefficiency of the circulation in heavy exercise".

Their conclusion is drawn from the findings of a higher exercise cardiac output for a given exercise level in the trained. Alternatively, earlier (94,237) and more recent studies (340) would lead one to the opposite conclusion while the reports of still others(141,143,268) would indicate no difference between the trained and untrained.

The excellent recent study by Grimby (158) leaves little doubt that the ability to extract O_2 in maximal exercise imposes a limitation on work performance in the older man and training seems not to have altered this ability. However, the findings of Holmgren (184,188) in studies of 'Vasoregulatory asthenia' where O_2 extraction was unduly low, suggest that training does improve the ability of muscles to extract O_2 in exercise.

Concluding Remarks:

In this review of the literature, consideration has been given to heart and lung functions in exercise and to the consequences of athletic training. This is because the cardio-

vascular and respiratory systems are the primary systems actively involved in 'delivery' of O_2 to the muscle tissues. However, it is essential to bear in mind that these are by no means the only important systems involved in exercise adaptation and affected by training. For example, no attention has been given to the "unloading" or "receiving" processes at the muscle which perhaps are as significant in exercise as is delivery of oxygen to them.

The changes in blood with exercise and with training have not been discussed, nor has any attention been given to such aspects as heart volume, temperature and muscle alterations. Each bears directly on the total process of exercise adaptation and many are affected by training. As examples, the trained individual has a larger (268) heart volume, greater total hemoglobin (212) improved heat tolerance (233,334) greater muscle mass (326) and muscle capillarity (285).

A complete review of these topics, pertinent though they be, would be unwieldy. However, where these topics bear directly on the primary objectives of this thesis, they will be included in the brief discussions following each section (below) or in the general integrated discussion at the conclusion.

PART III

METHODS, INSTRUMENTATION AND CALCULATIONS

Contents

PART III

METHODS, INSTRUMENTATION AND CALCULATIONS

Contents

A. LUNG VOLUMES:

All lung volumes measurements were made with the child seated, at rest in a straight back chair suitably adjusted to enable the subject to breath comfortably from the testing apparatus.

Instrumentation:

The circuit used for measuring the subdivisions of lung volume, described in detail (37), consisted of a 9 L spirometer* fitted with flexible tubing of 1 inch internal diameter and connected to a mouth piece by a 3-way manual valve which enabled rapid switching of the subject from breathing room air to breathing from the circuit. Attached to the spirometer was an adjustable speed, electrically driven kymograph with ink recording on the kymograph drum.

Greater accuracy on the FRC determination is achieved if the volume of the circuit gas is kept small in relation to the FRC volume to be measured, especially when studying children. Toward this end, the dead space of the circuit was reduced by placing a CO_2 absorption cannister externally on the expired line and sealing off the central core completely. Proximal to the CO_2 cannister was a blower, circulating gas at approximately 60 l/minute. Distal to the cannister a 5/16" rubber tube sampled CO_2 - free gas to the helium catharometer. This gas was returned to the main stream at a point proximal to the CO_2 absorber. O_2 was added to the circuit during the FRC measurement;

*Warren E. Collins (Boston, Mass).

it was controlled by means of a fine control valve on the O_2 supply tank and was set to match as nearly as possible the O_2 consumption of the subject as indicated on the tracing. In this way, the volume of gas in the circuit was kept virtually constant during the test.

The catharometer*, which consisted basically of a wheatstone bridge, makes use of the thermal conductivity property of helium. One arm of the bridge is enclosed in air while the gas mixture containing helium is passed through the other side of the bridge and altered the current drawn by this portion of the bridge. This change is a linear function of gas concentration and was recorded on an indicator scale attached to the catharometer, calibrated to read from 0-15% helium.

The kymograph speed was calibrated and found accurate at 25 seconds/cm. The spirometer was calibrated by means of air displacement with water and the bell factor found to be 46.1 mm/litre. The dead space of the circuit, with spirometer bell down and pen indicator reading zero, was calculated using a dilution technique. An accurately measured volume of O_2 was added to the circuit which contained room air. Analysis of the resulting gas mixture for O_2 by the Scholander technique enabled calculation of the dead space. This procedure was repeated using helium as the indicator gas to check the results.

* Cambridge

Operational Procedure:

Prior to subject testing, the spirometer was checked for leaks and the bell balanced by use of counter weights such that, with the pump on, and respiratory lines open to room air, it remained stationary over the full range. The water level in the spirometer was also checked.

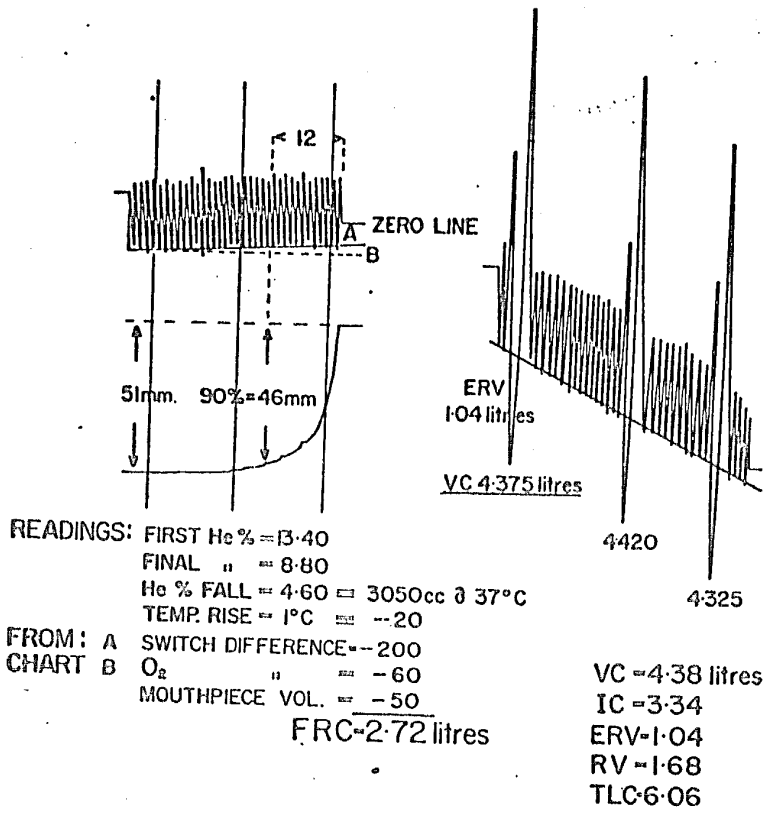
The tests were performed in the following sequence and manner.

Test 1. Vital Capacity (Fig.I_1)

About 4-6 litres O_2 were added to the circuit and the subject with nose clip in place, connected by means of the mouthpiece to the circuit. The subject was allowed to breathe quietly until he had assumed his normal respiratory pattern (see tracing). Three vital capacity manoeuvres were then performed, with adequate time being allowed between each for return to normal respiratory pattern.

Test 2. Functional Residual Capacity

The spirometer was prepared for the test by flushing with air, and then the requisite amount of helium was added to give an indicator reading (Initial Helium Concentration) in the range of 12.5 - 13.0%. The initial temperature of this gas mixture was noted. The subject was then reconnected to the mouthpiece and turned into the circuit at the end of a normal quiet expiration (FRC level). At the same time, addition of O_2 to the circuit was commenced. The fall in helium concentration was observed and when this reading stabilized the subject was disconnected and O_2 supply



READINGS: FIRST He % = 13·40
FINAL " = 8·80
He % FALL = 4·60 = 3050cc @ 37°C
TEMP. RISE = 1°C = ·20
FROM: A SWITCH DIFFERENCE = ·200
CHART B O_2 " = ·60
MOUTHPIECE VOL. = ·50
FRC = 2·72 litres

VC = 4·38 litres
IC = 3·34
ERV = 1·04
RV = 1·68
TLC 6·06

Fig. I_1 Sample tracing for lung volumes determination.

to the circuit stopped simultaneously. The final helium concentration and temperature were then recorded.

Calculations:

VC was calculated from the height of the tracing and the bell factor as follows:

$$VC(BTPS) = \frac{\text{mm. deflection}}{46.1} \text{ ls.} \times \text{correction factor for temperature and pressure.}$$

The middle value of the 3 VC measurements was analyzed.

FRC was calculated from the helium dilution as follows:

$$FRC = \frac{V (F_{He\,1} - F_{He\,2}) + O_2 \text{ Difference } (F_{He\,2})}{F_{He\,2}} \ldots$$

$$\ldots \pm \text{Switch Difference} - V_D \text{ Apparatus}$$

where

V	Initial volume of circuit, which includes the volume with the bell flat, together with the volumes of helium, O_2 and air added before the subject is switched in.
F_{He}	1 and 2 are the fractional concentrations of helium in the circuit before, and at the end of equilibration by the subject respectively.
O_2 Difference	Volume by which the final volume of the circuit differs from V, and is the consequence of a discrepancy between the O_2 addition rate and the rate of O_2 consumption by the subject (see B Fig. I_1)
Switch Difference	Volume above or below the resting end tidal level at which the subject is switched in the circuit (see Fig. I_1)

Subsequently, RV was calculated as FRC-ERV, and TLC as RV + VC.

B. LUNG FLOW RATES

Instrumentation:

The spirometer used to make these measurements (37) was built to incorporate features desirable but not available in many commercially made spirometers, namely a light weight bell and wide bore tubing. Dimensions of the water column were 12" x 16", having an inter-pipe of 2" diameter. The plastic bell measured 8" in diameter and 13½" in depth, with a weight of only 9 oz. as compared with 15 oz. for commercially produced metal bells. The tubing from subject to spirometer was reinforced with wire and had an internal diameter of 1¼". The spirometer bell was connected to a variable speed kymograph which enabled ink write out of the spirometer tracing.

Operational Procedure:

With the spirometer running at the appropriate speed, the standing subject breathed in to TLC, and held this lung volume while the mouth piece of the tubing was positioned. The subject then expired at maximal rate and depth into the spirometer. Three such measurements were made, and the largest was analyzed.

Calculations:

A smaple tracing is shown in Fig. I_2. The FEV was calculated by measuring the height of the tracing reached in the first .75 seconds of expirations. This was converted to volume using the bell factor. Multiplying this value by 40 gave the volume

$$\frac{FEV}{.75 \text{ seconds}} \times 40. \text{ (litres/min.)}$$

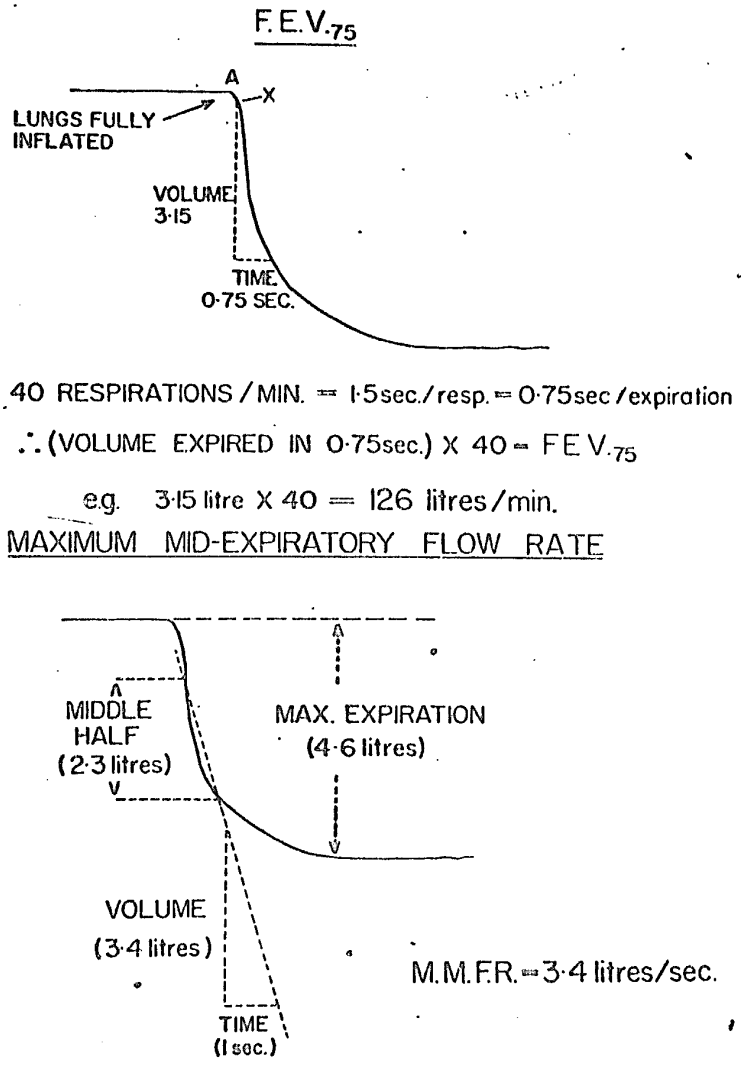


Fig. I_2 Sample tracing showing record and calculations for flow rate measurements.

The MMFR was calculated by measuring the total volume of the expirate and dividing this volume into quarters (see Fig. I_2) The points on the tracing corresponding to 1/4 and 3/4 of the total expirate (ie. the middle half of this volume) were joined and this line extended to intercept the Y axis. (volume axis). The slope of this line indicates the ratio of volume (Y axis) to time (X axis) during the middle half of a forced expiration, hence Maximal Mid-Expiratory Flow Rate and is expressed as litres/second.

By use of the plastic mask, which was designed from the calibrations of the spirometer and kymograph, both of these values could be determined by superimposing the mask of the tracing. Both the FEV and MMFR were then converted to express volume at BTPS.

C. OXYGEN UPTAKE

The volume of O_2 taken up is the difference of the amount breathed in and the quantity expired.

To measure oxygen uptake ($\dot{V}O_2$) measurements are needed of total minute volume of air breathed, either inspired or expired, and concentrations in the mixed expired gas of CO_2 ($F_{E\,CO_2}$) and O_2 ($F_{E\,O_2}$). Because the expired volume is altered in accordance with the respiratory quotient, it is necessary to make a correction for this small difference between inspiratory and expiratory volume in the calculations.

Instrumentation:

The apparatus used in measuring $\dot{V}O_2$ is described diagramatically by Fig (I_3) which also includes the circuitry used in measuring diffusing capacity (described below).

The mouth piece was connected to a high flow Hans Rudolph 2-way valve to which was attached an inspiratory and expiratory line. These lines were 1-1/16" flexible wire-supported, non-collapsible tubing, The expiratory line led to the atmosphere. Arranged in series with it was a small plexiglass mixing box containing an electrically operated fan which served to ensure mixing of the expired gas. Distal to the mixing box was a small tube through which side sampling of the expirate could be effected.

A dry bellows gas meter*, with potentiometer mounted on the indicator needle, was attached to the inspiratory line and enabled

* Parkinson-Cowan Type C

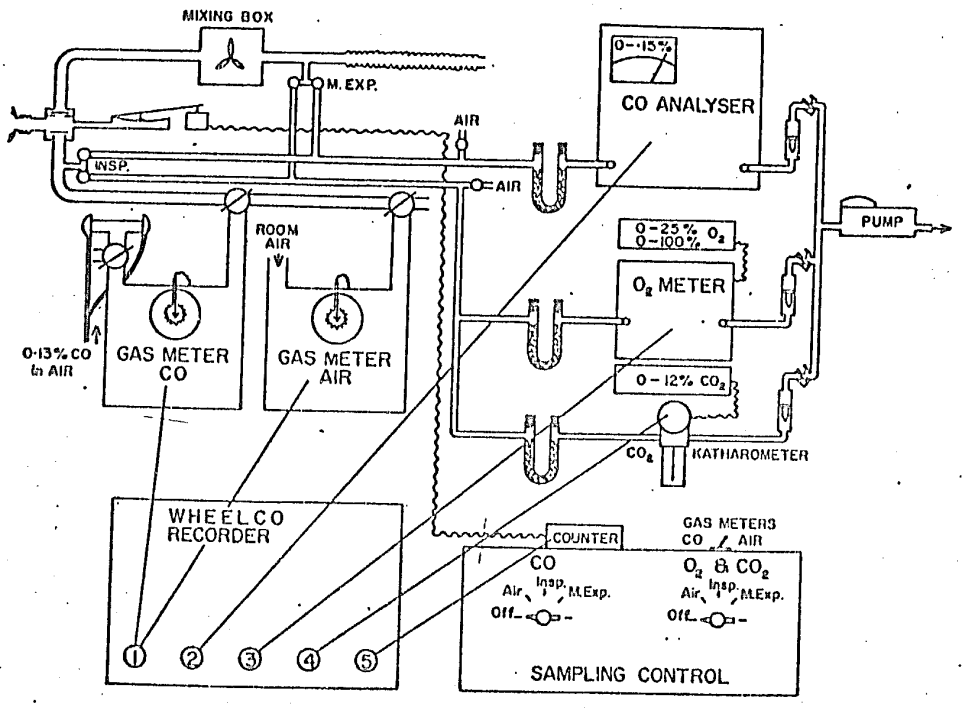


Fig. I_3 Circuit diagram for determination of oxygen consumption and diffusing capacity measurements.

measurement of the volume of air inspired.

By means of a vaccum pump*, a continuous sample of mixed expired gas was drawn from the mix box, through a $CaCl_2$ filled 'U' tube which dried the gas, to the O_2** and CO_2*** analyzers. Respiratory frequency was monitored by a pressure-activated switch placed across the two-way valve.

A permanent record for volume, concentrations and frequency was made by means of an industrial, constant speed recorder**** to which each of the measuring devices was attached. This record eliminated the need for making rapid readings of the various meters. The recorder contained 4 channels, each with its own characteristic number, operating on a 2.7 sec.cycle. Thus, a record of each observation was made every 10.8 sec.

Calculations:

The minute oxygen uptake ($\dot{V}_{O_2}$) was calculated from data recorded on the Wheelco tracing, a sample of which is shown by Fig. I4. Volume and concentrations were determined as indicated, the appropriate factors in each case being incorporated into the design of the apparatus.

Calculations were as follows:

$$\underset{l/min.}{\dot{V}_{O_2}} = \dot{V}_I F_{I O_2} - \dot{V}_E F_{E O_2}$$

* Collins P553
** Beckman paramagnetic F3
*** Cambridge differential catharometer
**** Wheelco

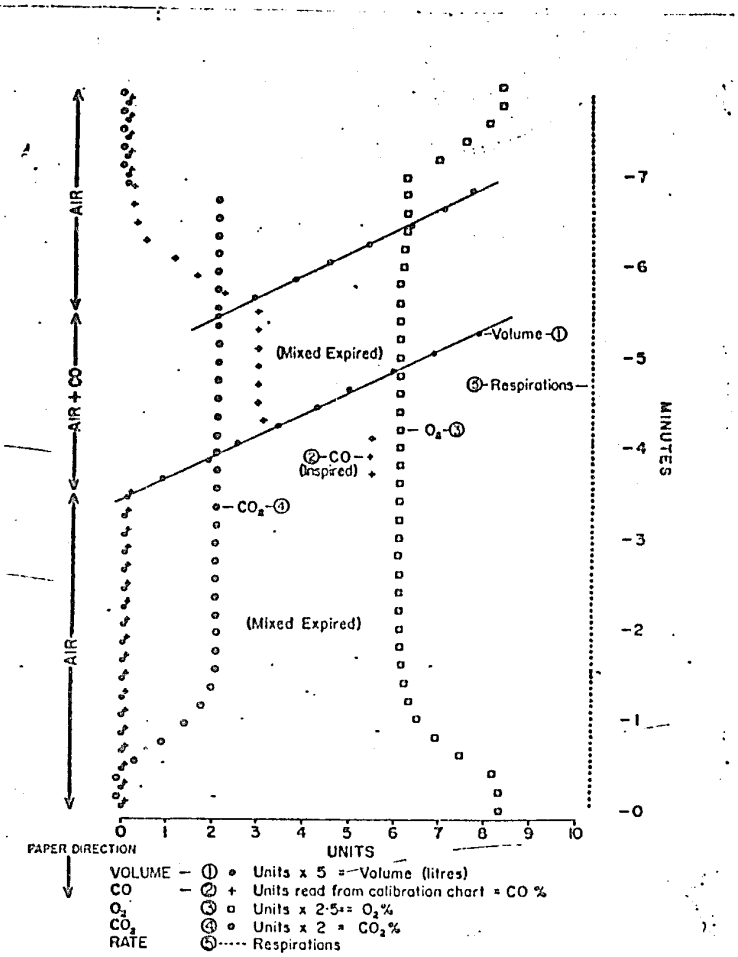


Fig. I$_4$ Sample tracing from which oxygen consumption and diffusing capacity were calculated.

where

$\dot{V}_I$ - inspired minute volume expressed in litres at Standard temperature and pressure dry (STPD)

$\dot{V}_E$ - expired minute volume (STPD) calculated form the relationship

$$\dot{V}_E = \dot{V}_I \times \frac{79.1}{100 - (F_{E\,O_2} + F_{E\,CO_2})}$$

and

$F_{I\,O_2}$ - fractional inspired oxygen concentration (20.9%)

$F_{E\,CO_2}$ - fractional expired CO_2 concentration

$F_{E\,O_2}$ - fractional expired O_2 concentration

Respiratory frequency was counted directly from the tracing.

D. DIFFUSING CAPACITY

The total diffusing capacity of the lungs for carbon monoxide ($D_L CO$) was measured during exercise (steady-state) using a gas mixture of room air containing about .125% CO. $D_L CO$ has the units mlCO/minute/mm Hg. i.e. the diffusion rate with respect to the driving pressure.

Instrumentation:

The apparatus was similar to that described initially by Donevan et al (117) and Mostyn et al (266), with only minor modification. This circuit was integrated with the $\dot{V}O_2$ circuit described above but had a separate dry gas meter, connected by demand valves to the test gas storage tank. In this way, the dry gas meter could be thoroughly rinsed with test gas and closed to the atmosphere before the test. This enabled the exposure time of the subject to the test gas to be kept to a minimum, an essential feature if the build up of significant back pressure of CO during the test is to be avoided.

Fractional concentration of CO was measured by an infra-red analyzer.* By means of a sampling control switch box, solenoid operated valves enabled sampling from the inspired line ($F_{I\ CO}$) from the mouth piece, and from the mixed expired box ($F_{E\ CO}$). Manually operated valves allowed the subject to breath from the storage tank through the demand valves, as was the case during a diffusing capacity test, or room air for determination of oxygen consumption.

*Infra-red Development Corporation

In practice, since the exercise diffusing capacity is related to the level of exercise (and hence to $\dot{V}O_2$) the $D_L CO$ measurement was made after a suitable warm-up period to enable attainment of steady-state (about 4 mins. of exercise) and the $\dot{V}O_2$ was measured during the following minute.

Calculations:

As for $\dot{V}O_2$, the measuring devices for the test were connected to the Wheelco recorder and the data derived from this permanent record (Fig. I_4) was used to calculate $D_L CO$ by the method suggested by Donevan (117) but using a predicted dead space based on the data of Hart (166) which can be used in children

$$D_L CO \text{ ml/min/mmHg} = \frac{\dot{V}_{CO}}{P_{A_{CO}}}$$

where

$$\dot{V}_{CO} = \dot{V}\,(F_{ICO} - F_{ECO} + F_{E'CO})$$

and

$$P_{ACO} = \frac{(V_T \times F_{ECO}) - (V_D \times F_{ICO})}{V_T - V_D} \times Pb - W$$

where

$\dot{V}$ - volume of test gas inspired in litres/min. STPD

V_T - $\dot{V}$ l/BTPS / respiratory rate/min.

V_D - anatomical dead space in litres, BTPS as predicted.

F_{ICO}, F_{ECO} and $F_{E'CO}$ - fractional concentrations of CO in inspired air, in mixed expired air and in end tidal air on air breathing before the $D_L CO$ measurement The latter is a correction for the slight sensitivity of the meter to watervapor and to CO_2.

E. CARDIAC OUTPUT

Measurement of the cardiac output during exercise was made utilizing the Indirect Fick foreign gas technique.

In 1962, Becklake et al (40) described in detail one foreign gas method. In their study, they compared exercise $\dot{Q}c$ values measured almost simultaneously using the foreign gas and dye dilution techniques and found a close relationship in results of the two methods. In addition, they showed the repeatability of the foreign gas method to be comparable to that of the direct Fick technique. The method is impractical for measurements made at rest, and in patients with conditions causing poor mixing in the lungs (e.g. emphysema) since equilibration time would be too long and thus recirculation might occur before the measurements could be made. However, it reaches its' greatest accuracy in moderate to heavy exercise when the equilibration time is shortened. Its' greater accuray during heavy workloads is in contrast with some other methods which may become less accurate in heavy exercise (dye method) because of fast recirculation). The method has the obvious advantage of requiring no needles and has thus neither the discomfort nor occasional hazard associated with direct Fick measurement which involves cardiac catheterization. Furthermore, the test exercise can be performed in the upright position, a factor it can be argued, which makes the technique more physiological.

Principles of the Method:

There have been various inert foreign gases used in the past, examples of which are acetylene (C_2H_2), ethyl iodide (C_2H_5I) and, as in the present study, nitrous oxide. Furthermore, single breath and equilibration methods have been used analagous to the two general methods used for this measurement of diffusing capacity. The present study was based on a steady-state method. The test gas mixture* was introduced to the exercising subject and after a short period of equilibration mixed expired gas was collected for a known time period. During this period (t secs) the concentration of N_2O in the respirate sampled at the mouth was monitored continuously. The mixed expired sample was subsequently analyzed for N_2O ($F_{E\,N_2O}$). The volume respired ($\dot{V}$) during the time period was also determined; hence, the total volume of N_2O which has been taken up from the lungs could be determined. By assuming the mean of the end-tidal concentration (i.e.alveolar) to be representative of the arterialized lung capillary blood, the blood flow through the lungs during the timed interval can be calculated using the Fick principle (see below).

The application of the foreign gas method for measuring pulmonary capillary blood flow, depends on three important essentials:

1) A complete, rapid equilibration of the lungs with the test gas.

2) Constant alveolar levels of the test gas.

* 7.5% N_2O, 20% O_2, 72.5% He.

3) The need to make measurements before significant recirculation occurs.

As regards the degree of equilibration, this can be readily determined by monitoring the wash out of nitrogen ($F_{E\,N2}$) from the lungs which is the reciprocal of the wash in of the carrier gas in the test gas mixture (this was He in the present study). By virtue of the fast response of the N_2O meter,* the level of the end-tidal concentration can be observed directly and hence the constancy of alveolar gas concentration ($F_{A\,N_2O}$) ascertained. A rising $F_{A\,N_2O}$, and simultaneous lowering of $F_{E\,N2}$, thus would indicate incomplete equilibration while a rising $F_{A\,N_2O}$ alone would indicate recirculation of blood containing some test gas.

The use of a soluble inert gas such as N_2O offers the advantage of a prolonged effective recirculation time, by comparison with the dye technique. This period is greater for two reasons:

1) the blood first exposed the test gas in the lung (and thefore first to recirculate) has the lowest concentration of the gas, since equilibration initially is not complete.

2) N_2O is highly soluble, particularily in exercising muscle. Thus, much of the dissolved N_2O diffuses out of the blood during transit through the muscle capillaries. This is in contrast with tracers or dyes, in which case the initial concentration is maximal and the tracers, attached to plasma protein, remain in the blood stream.

* 0.24 sec. to 90% of full deflection

In the present technique, it was assumed that recirculation of test gas did not become significant in 35 seconds, a conclusion based on the findings of Becklake et al (40) that computed cardiac output did not fall significantly from 10 to 35 seconds at moderate work loads, and therefore by implication, recirculation was insignificant up to 35 seconds.

Instrumentation: (Fig. I 5)

The circuitory used in the present series of studies was essentially similar to that originally described in detail by Becklake et al (40).

The test gas was transferred from a storage tank to a neoprene bag contained within an air tight plexiglass box. The changes in volume with the respiratory cycle were monitored by means of a spirometer in the first year of study, and a dry gas meter thereafter, connected to the box. Thus, as the subject inspired from the bag the volume of gas removed from the bag created a small negative pressure in the box containing the bag. As a consequence, air entered the box from either the spirometer or gas meter, to restore the original volume of gas in the bag-box system. By means of a low-torque potentiometer attached to the spirometer wheel (or dial needle of the gas meter) these volumes were directly written by the Sanborn polygraph recorder.

The inspired line, comprised of 1-1/16" I.D. copper tubing, led from the neoprene bag to the low-resistance box valve which in turn was attached to the fast response breath-through N_2O meter.*

* Infra-Red Development Corporation

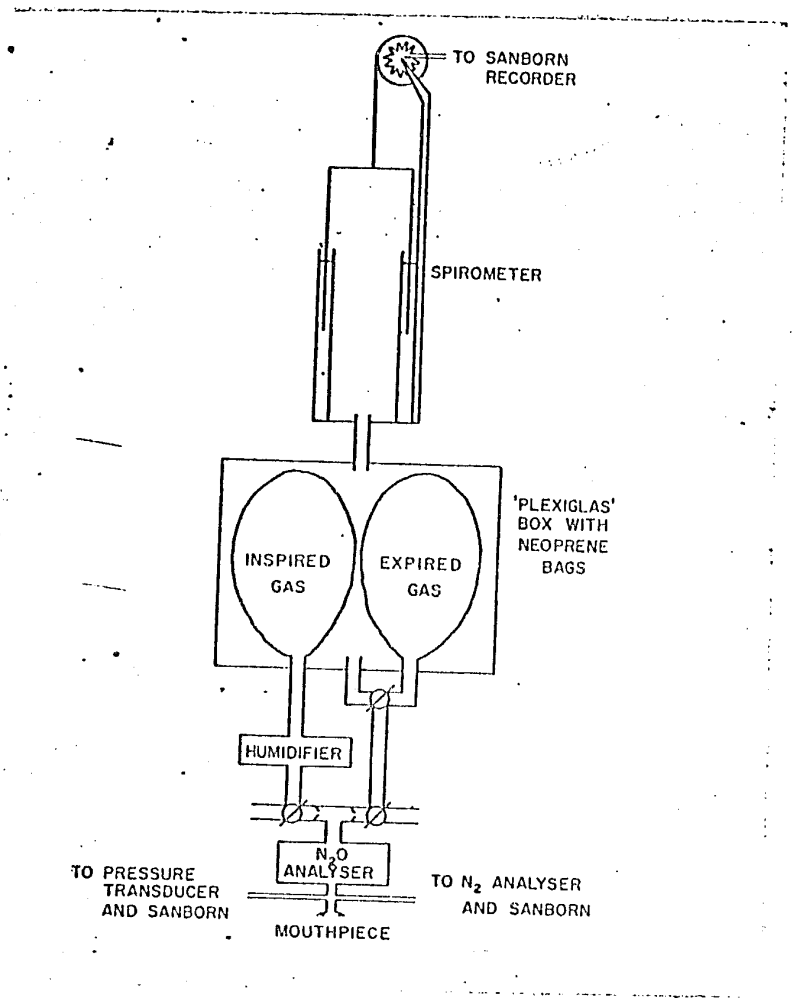


Fig. I_5 Circuit diagram of Nitrous Oxide apparatus used in measuring cardiac output.

In series with this line was an Engstrom humidifier which enabled humidification of the test gas as it entered the inspired line. This line and humidifier were maintained at a constant temperature of 37°C. by means of water circulating in the jacket heater which surrounded the inspiratory line and box valve.

The expiratory line from the box valve consisting of 1 1/16" I.D. wire supported flexible tubing was fitted with a solenoid operated valve which permitted a rapid change from expiring to the atmosphere through a mixing box to expiring into a second neoprene bag (expiratory bag), also contained within the plexiglass box. Thus, the expirate could be passed through the mix box from which continuous sampling of O_2 and CO_2 concentrations could be made, permitting the determination of oxygen consumption just prior to the cardiac output measurement. Alternately, during a $\dot{Q}c$ measurement a sample of the expired gas could be collected and passed through the N_2O analyzer at the conclusion of the test.

Attached to the mouthpiece was a nitrogen analyzer* and pressure transducer**. A vacuum pump effected continuous sampling from the mouthpiece through a needlevale to the N_2 analyzer. In this manner, the wash out of N_2 from the lungs was monitored and recorded. The pressure transducer responded to changes in directional flow at the mouthpiece. This record was used to accurately determine the onset of each inspiration and expiration and this, together with the time base of the Sanborn recorder,

* Waters-Conley Model 46
** Sanborn

enabled accurate determination of the duration of the test in seconds.

Heart rate was monitored either by means of an ear counter (284), operating on the principle of varying light transmission with pulsatile flow, or by electrocardiogram using two chest leads. In a few cases, hand count of either the carotid or radial pulse had to be made.

These various parameters were thus directly recorded on 6 channel Sanborn recorder, a sample tracing of which is shown by Fig (I_7).

Calibration and Preliminary Circuit Studies:

The nitrous oxide analyzer was calibrated using known % N_2O mixtures in dry Helium gas, concentrations ranging from 0-10%. The analyzer of the meter was then calibrated against the Sanborn recorder. These two curves were then combined to give the curve shown in Fig.(I_6) which describes the relationship of N_2O concentration to Sanborn reading. The intercept on the X axis from this resultant curve was calculated over the straight portion of the curve, which was the range of concentrations encountered during the measurement of cardiac output. This enabled the direct use of the Sanborn reading, in mm deflection and thus eliminated the necessity of reading fractional concentrations values from the original calibration curve.

Further calibrations were made using air, rather than helium as the carrier gas. The resulting curve fell directly on the

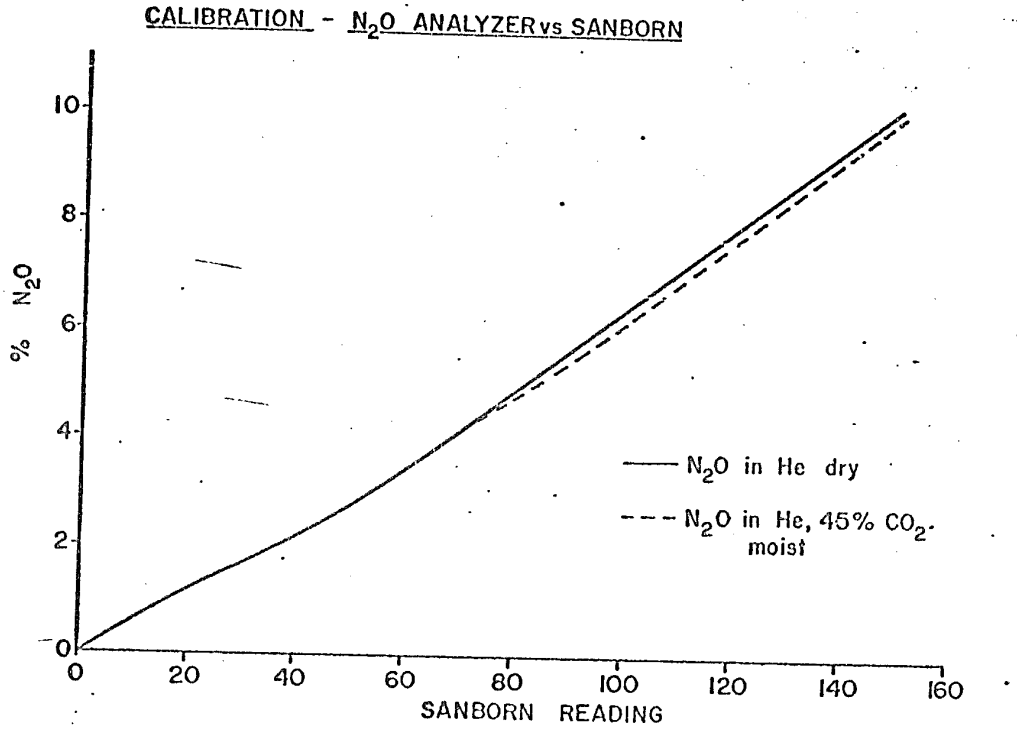


Fig. I_6 Calibration curve of nitrous oxide analyxer.

above curve; this permitted the use of room air in subsequent calibration curve checks and in zeroing the analyzer during daily meter balancing.

From preliminary investigations, it was found that the meter was sensitive to moisture and CO_2 in the gas mixture. Since the expired breaths differ from the inspired during a test in these two respects..saturation and CO_2 content, these factors tended to make the expired gas read higher on the meter than the inspired gas, for a given N_2O concentration. The effect was minimized by heating the inspired gas to body temperature and by saturating the inspired gas as completely as possible. The effect of CO_2 was taken into account by subtracting the meter response on air breathing just prior to the commencement of the measurement from the mixed expired reading. This also corrected for any residual N_2O in the body as a consequence of an earlier test.

It was also observed in preliminary observations that the meter was slightly sensitive to direction and rate of flow of gas through the analyzer. This effect was eliminated by passing the collected expirate through the analyzer in the same direction and flow rate as the inspired gas. Thus both the inspired and expired gas would be affected to the same degree and this artefact of the meter overcome.

As indicated above (instrumentation and Fig.I_5) volume was recorded by either a dry gas meter or spirometer. The spirometer,

comprising a light weight plastic bell to minimize inertia effects, was calibrated in the usual manner by adding known volumes of gas to the spirometer bell and reading deflection (in mm) on the Sanborn record. In this way, the sensitivity of the recorder amplifier was set so that 10 mm deflection on the Sanborn corresponded to 1 litre change of volume in the spirometer. This volume-deflection relationship was found to be linear over the operating range and periodic checks showed this to be constant. No difference in this relationship was noted when volume was removed from the spirometer. The dry gas meter was calibrated against the Tissot spirometer and Sanborn recorder at varying steady flow rates as well as intermittent flows such as encountered during the respiratory cycle. Under these varying conditions, the volume response was similar.

Calculations:

Fig.(I_7) shows a sample tracing of a record from which cardiac output was calculated. The parameter recorded on the various channels of the tracing was as follows:

Channel 1: Heart Rate. The paper speed was preset and rate in general counted over a 15 second period during the test. It is expressed as beats/minute.

Channel 2: Pressure. In conjunction with the time base of the recorder, this enabled exact determination of time of the measurement and permitted calculations to be made for single

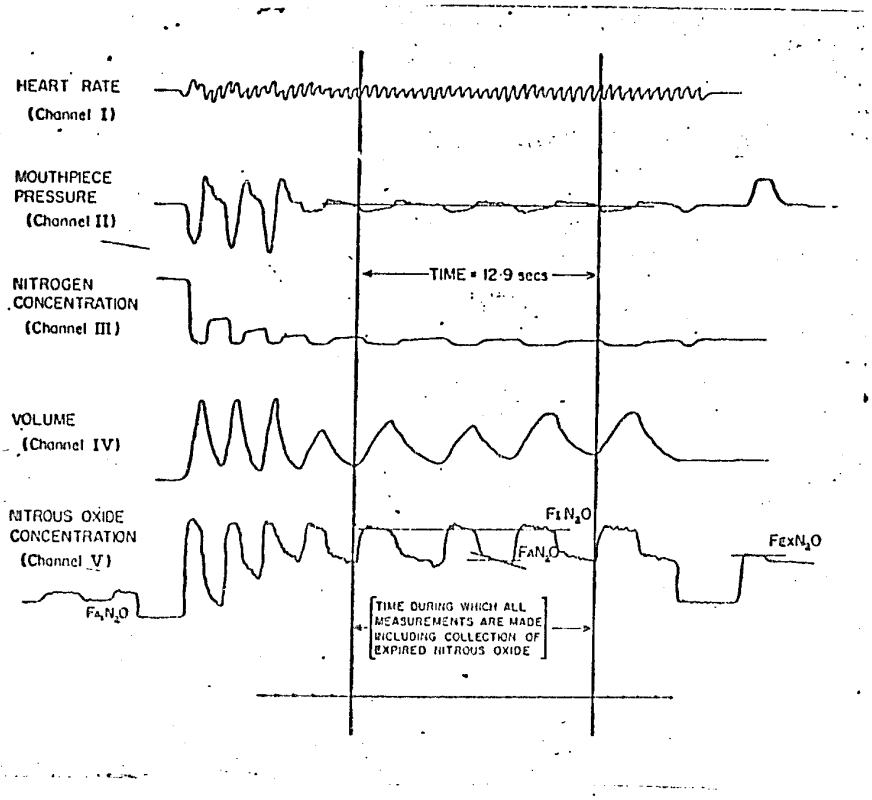


Fig. I$_7$ Sample tracing from the Sanborn Recorder from which Pulmonary Capillary Blood Flow was calculated.

breath or several consecutive breaths, the latter method being used for the most part throughout this study.

Channel 3: N_2 Concentration. This is seen to drop rapidly during the hyperventilation manoeuvre when the test gas was first presented to the subject (it will be recalled that the test gas contained helium rather than nitrogen as the carrier gas) and after 3-4 breaths remains constant. This indicates the rapidity and completeness of equilibration by the subject with the test gas. Measurement of cardiac output was made during regular breathing following attainment of this 'steady-state'.

Channel 4:. Volume. The record of tidal volume using the spirometer is shown on the tracing. When the spirometer was used, the expirate was returned to bag-box systems, so that the volume changes were recorded throughout the respiratory cycle. In the experiments in which volume was measured using the dry gas meter, a measurement of only the inspired volume was made.

Channel 5: Fractional concentration of N_2O. As shown by the sample tracing, these consist of:

i) Fractional Inspired Concentration ($F_{I\ N_2O}$)

ii) Fractional Mixed Expired Concentration ($F_{E\ N_2O}$). This is comprised of a mixture of the expired gas sample collected during the selected time (t), duration of which is indicated by the time scale on the bottom of the tracing. The expired sample contains both gas from the dead space of the respiratory system of the subject and machine as well as gas from the alveoli. Consequently,

this value must always be higher than $F_{A\,N_2O}$, a point which served as an additional check on the acceptability of the measurement.

iii) Fractional Alveolar Concentration: ($F_{A\,N_2O}$). The correct value for this would be the concentration integrated with respect to time throughout the respiratory cycle. Unfortunately, this value during inspiration cannot be measured practicably. However, it is assumed that this value would not rise greatly above that observed just after dead space wash out during an expiration, and similarly that it would not fall much below the end-expiratory level recorded just before a new breath started. The assumption that the mean of the end-tidal level is a close approximation of alveolar concentration is probably not unreasonable.

iv) Initial Meter Reading ($F_{A'N_2O}$). The end-tidal concentration of N_2O on air breathing immediately prior to the start of the experiment.

From these readings the cardiac output was calculated according to the Fick Principle utilizing the equation

I. $$\underset{\text{l/min.}}{\dot{Q}c} = \frac{\dot{V}_{N_2O}}{(A - V)_{N_2O}\ \text{Difference} \times \lambda}$$

Providing the measurement is made before 35 seconds, the venous concentration is negligible, in which case the equation may be rewritten.

$$\text{II.}\quad \dot{Q}c \text{ liters} = \frac{\dot{V}\,(F_{I\,N_2O} - F_{E\,N_2O})}{(F_{A\,N_2O} - F_{A'N_2O} - I) \times \lambda \times \frac{Pb - w}{760}}$$

where.

$\dot{V}$ = ($V_I \times \frac{60}{t}$ x BTPS correction factor) and V_I is the sum of the tidal volumes inspired during time t secs.), the period of collection of the expired gas.

λ = 0.474, the partition coefficent of N_2O between air and whole blood (210, 278) at 760 mmHg, 37 °C.

I = intercept as calculated from the calibration curve showing the relationship % N_2O and Sanborn deflection (mm)

Pb-w - barometric pressure in mmHg, less water vapour pressure at 37 °C.

The above data may also be used in single, rather than multiple, breath calculation in which case the formula was modified as follows:

$$\text{III.}\quad \dot{Q}c \text{ liters} = \frac{(V_I - n(V_d + V_{dm}))\, \times\, (F_{I\,N_2O} - F_{A\,N_2O} - F_{A'N_2O}) \times \frac{60}{t}}{\lambda \times (F_{A\,N_2O} - F_{A'N_2O}) \times \frac{Pb - w}{760}}$$

where

n - number of breaths in time t

V_d - anatomical dead space as predicted from the magnitude

of the tidal volume by Assmussen and Nielsen (9)

V_{dm} - 100cc, the dead space volume of the mouthpiece, meter and box valve.

For most subjects in the present study, calculations were made using Equation II and the mixed expired reading. In some cases where through technical error the mixed expired reading was unacceptable, such as with incomplete rinsing of the expired bag prior to the test, Equation III was used. In these few cases, all results for an individual were calculated using the same formula for each exercise test.

PART IV

RESULTS AND DISCUSSION

Contents

PART IV

Chapter 6. Project Controls

....subjects
....testing procedure
....data processing

1.A. Physical characteristics - results

B. Lung Volumes - results

C. Lung Flow Rates - results
...Dicsussion

2. Diffusing Capacity
...results
...discussion

3. Cardio-Respiratory Functions
...results..oxygen consumption and ventilation
...cardiac output and related parameters
...arterio-venous oxygen difference
...discussion..ventilatory functions
..circulatory functions.

PROJECT CONTROLS:

The purpose of this study was to define cardio-respiratory functions in exercise in normal children and thus permit comparison with children engaged in swim training.

Subjects:

The subjects who served as normals (Controls) for this study were for the most part drawn from the Parks and Playgrounds of the City of Montreal. Contact was made directly with the Park Monitor in different regions of the city, who in turn advised the children of the general nature and purpose of the tests. Those children who expressed an interest in being a subject were given a 'letter to parents' which described briefly the tests. Attached to the letter was a parental consent form. From the signed and returned forms, subjects were selected in accordance with the distribution of age and sex desired. Because of difficulty in obtaining adequate subjects in the older age groups (15-17 years) the remainder of the subjects were drawn from volunteer workers at the hospital and children of hospital staff members.

Table CI summarizes the age and physical characteristics of this group. Eighty seven (87) children were studied; results on four (4) of these were rejected, one on the basis of a systolic murmur, the others because of technical reasons. Of the 83 included in the study, 40 were boys, 43 girls. Forty-two (42)

TABLE (C 1)

PHYSICAL CHARACTERISTICS - CONTROLS

SEX	AGE GROUPING YEARS	NUMBER	MEAN AGE (years)	MEAN HEIGHT (centimeters)	MEAN WEIGHT (Kilograms)
Boys	10-11.9	14	11.21	143.07	35.61
	S.D.±		0.47	5.91	6.04
	12-13.9	13	13.46	150.85	43.00
	S.D.±		0.53	9.74	8.88
	14-15.9	9	15.16	165.22	58.22
	S.D.±		0.53	8.75	11.22
	16-17.9	4	16.75	173.86	63.00
	S.D.±		0.50	4.13	3.63
Girls	8-9.9	1	9.6	140.00	34.5
	10-11.9	12	11.17	148.00	39.29
	S.D.±		0.49	5.38	5.38
	12-13.9	13	13.04	150.54	45.04
	S.D.±		0.52	3.71	10.67
	14-15.9	10	15.10	156.00	49.35
	S.D.±		0.52	5.23	7.42
	16-17.9	7	16.64	161.00	55.07
	S.D.±		0.38	6.11	8.56

of the group were French Canadian. No attempt was made to randomize the selection of subjects, nor was any consideration given to the socio-economic level of the families of the subjects. In terms of geographical representation, these children can be considered to represent three general areas of the city, these being a West and Central region which probably are representative of families in the middle-income bracket, and a Northern region comprised mainly of a lower income group.

Testing Procedure:

All subjects were studied during the month of July, 1965. The testing was done either in the morning (9:30 - 12:30) or afternoon (1:30 - 4:30). They were brought to the Royal Victoria Hospital in groups of 3 - 4 by authorized transport and upon arrival height (with shoes removed) and weight (while wearing light summer weight clothing) measurements were made. A brief medical history was taken. In addition to the information supplied by the parents (see Appendix #1), a medical examiner listened to heart and chest sounds, counted the sitting pulse and established that in so far as such a cursory examination could reveal, the subjects were in good health.

The following series of tests were then made:

Test 1: Dynamic Lung Function Tests (Flows)...

These included measurement of Forced Expiratory Volume (F.E.V.) and Maximal Mid-Expiratory Flow Rate (M.M.F.R.). Test procedure was described above.

These tests were performed in the routine Pulmonary Function Laboratory at the hospital. It was felt that each child was motivated to do his best; means of motivation were: 1) encouragement by the experienced technician, 2) presence of other children of the group and 3) by the subject observing the tracing as it was being made.

Test 2. Lung Volumes:

Tests to measure the subdivisions of lung volumes were performed on the closed-circuit Helium dilution apparatus described in detail elsewhere (Part III). Since close attention and cooperation on the part of the subject are essential in these tests, they were performed in a separate laboratory with only the child and technician present, thus minimizing interference and distraction of the subject.

Single determinations of the FRC measurement were made, except for the occasional spot repeat test.

Test 3: Total Lung Diffusing Capacity and Oxygen Uptake:

The performance of this test consisted of 2 phases, done in succession during continuous exercise of about 6 minutes duration. Phase i..Diffusing Capacity for Carbon Monoxide..(D_{L} CO)

A suitable mild exercise load was selected on the bicycle ergometer* using as criteria for load selection the child's age and size. The majority of subjects performed the test at a load of 150 KgM/min. (see Table C5).

* Elema-Schonander, Stockholm.

The subject was seated in the normal cycling position with the seat height appropriately adjusted to match the leg length of the child. The mouthpiece of the circuit was inserted and the exercise commenced. After 3 minutes of exercise, the time normally required to reach steady-state (57,192,201), the subject was switched from breathing room air to breathing test gas (room air plus approximately .125% CO). After sampling gas from the inspired line to determine the inspired CO concentration ($F_{I\ CO}$), the sampling line from the circuit to the CO meter was connected to the expired line at a point just distal to a mixing box. This enabled determination of the mixed expired concentration of CO ($F_{E\ CO}$). Once this concentration became steady, as indicated by the vertical linearity of the CO recording (Fig.I_4), the subject was then switched to breathing room air. This portion of the test required approximately 4-1/2 minutes from onset of exercise.

Phase ii..Measurement of Oxygen Uptake ($\dot{V}_{O_2}$)

While the subject exercised continuously, the mean mixed expired concentrations of CO_2 and O_2 ($F_{E\ CO_2}$ and $F_{E\ O_2}$) were determined by continuous sampling from the expired line (as above). When these values became steady, exercise was ceased. The total duration of the exercise was not more than 6 minutes.

Two additional measurements of $\dot{V}O_2$ were made on each subject at loads which, in most cases, were 100 KgM higher than the previous workload. At least 10 minutes of rest was allowed between each test exercise.

From the data obtained above, which also included continuous records of inspired volume and respiratory frequency, total lung Diffusing Capacity at one level of exercise, and oxygen consumption at 3 workloads were determined.

Test 4: Exercise Pulmonary Capillary Blood Flow ($\dot{Q}c$)

Three test loads, similar to those employed above, were completed by each subject. The subject was connected by mouthpiece to the breathe-through N_2O meter and exercised for 3 minutes to reach steady-state. During this period, room air was being breathed. After the warm up exercise, the subject was switched to breathe test gas and hyperventilated for 3-4 breaths, as instructed prior to commencement of the test. After this hyperventilation, which enabled rapid equilibration of lung gas with the test gas, the subject resumed his regular respiratory pattern. The cardiac output measurement was then made over the following 10-20 second period after which the exercise was stopped. During this test then, measurements were made of heart rate, inspired and alveolar N_2O concentrations ($F_{I\,N_2O}$ and $F_{A\,N_2O}$ respectively), N_2 concentration (which gave indication of completeness of equilibration), volume inspired (V_I) and pressure swings (with respiration) at the mouth (used to determine exactly the onset of an inspiration and thus to enable accurate determination of time). The mixed expired sample, collected during the 10-20 second period of $\dot{Q}c$ measurement, was then passed through the N_2O meter for analysis ($F_{E\,N_2O}$).

Following a procedure similar to that for $\dot{V}O_2$ (i.e. after about 10 minutes rest), two additional measurements of $\dot{Q}c$ were made at the higher loads.

To expedite the testing procedure, the prescribed Test Schedule (App.2) was followed as far as was possible. This ensured that each subject had time to recover from a previous exercise before having lung volumes measured or commencing the next exercise.

Data Processing:

One of the major concerns in a study involving the collection of data on many individuals, such as in the present project, is the efficient handling of the data such that computations are correct and human errors minimized. In this study, permanent records for all tests were made. This not only helped reduce the chance of technician error, caused by hurried reading and writing of values during the test, but also enabled a subsequent recheck of data on any individual subject. The permanent recording also offered the advantage that extraction of the pertinent values from the tracings could be done at a more leisurely and careful pace. From these tracings, the values were read and recorded on 'raw data' sheet (App.3).

Because of the nature of the tracing, calculations for all lung volumes and flow rates were done manually. (See Fig.I_2)

Calculations for oxygen consumption, diffusing capacity and cardiac output were done on a digital computer,* using Fortran IV language. A print-out of all raw data, as well as individual results, permitted an additional check on 'rogue' values to be made, after which all final results were transcribed on magnetic tape. Use of the magnetic tape was made necessary because of the large volume of data collected. This provided ready assessability of all the data for statistical analysis. In addition, this automation of data handling allowed a far more extensive data anlaysis than would have otherwise been possible.

The statistical and regression analysis was done by computer using both Fortran IV and IBM 7044 MAP programs. Tables of mean values, including range and standard deviations, were printed for each parameter with subjects divided in various ways which included age, height, sex, group and exercise load. 't' tests and significance levels (F and P) for age, height, weight, sex and group differences for each function were also calculated. Various regression analysis were attempted for each parameter using single and multiple independant variables. In addition to linear regression equations, other equations were derived using logarithmetic as well as other transformations in order to determine the best relationship to accurately describe the data.

* IBM #7044, McGill Computor Centre.

Results:

When a comparison of groups is to be made, as in this study where swimmers are being compared not only to themselves on a longitudinal basis but also with normal children, it is essential to establish the 'normality' of our control normals. This is necessary to ensure that the subjects serving as normals have values which are within the range of published data and that values of functional measurements have not been significantly biased by subject selection.

1A. Physical Characteristics:

The age, height and weight features, divided by age, of our normals are presented in Table C1. Mean values for height are plotted as a function of age in Fig.C1 A & B for boys and girls respectively. For comparative purposes, the percentile lines (90,50 & 10%) of Stuart and Meredith (336)(a study on Boston children) are shown (dashed lines) as well as mean values for Swedish children (66). The boys of the present series are seen to fall on, or, in the age range 13-15 years, slightly below the 50 percentile line (336), while the girls show the same, but more marked, trend. In each case, both our younger and older children lie on or above this line. No statistics were done to compare the present data with these two studies.

Although our subjects tend to be shorter at age 13-15 years,

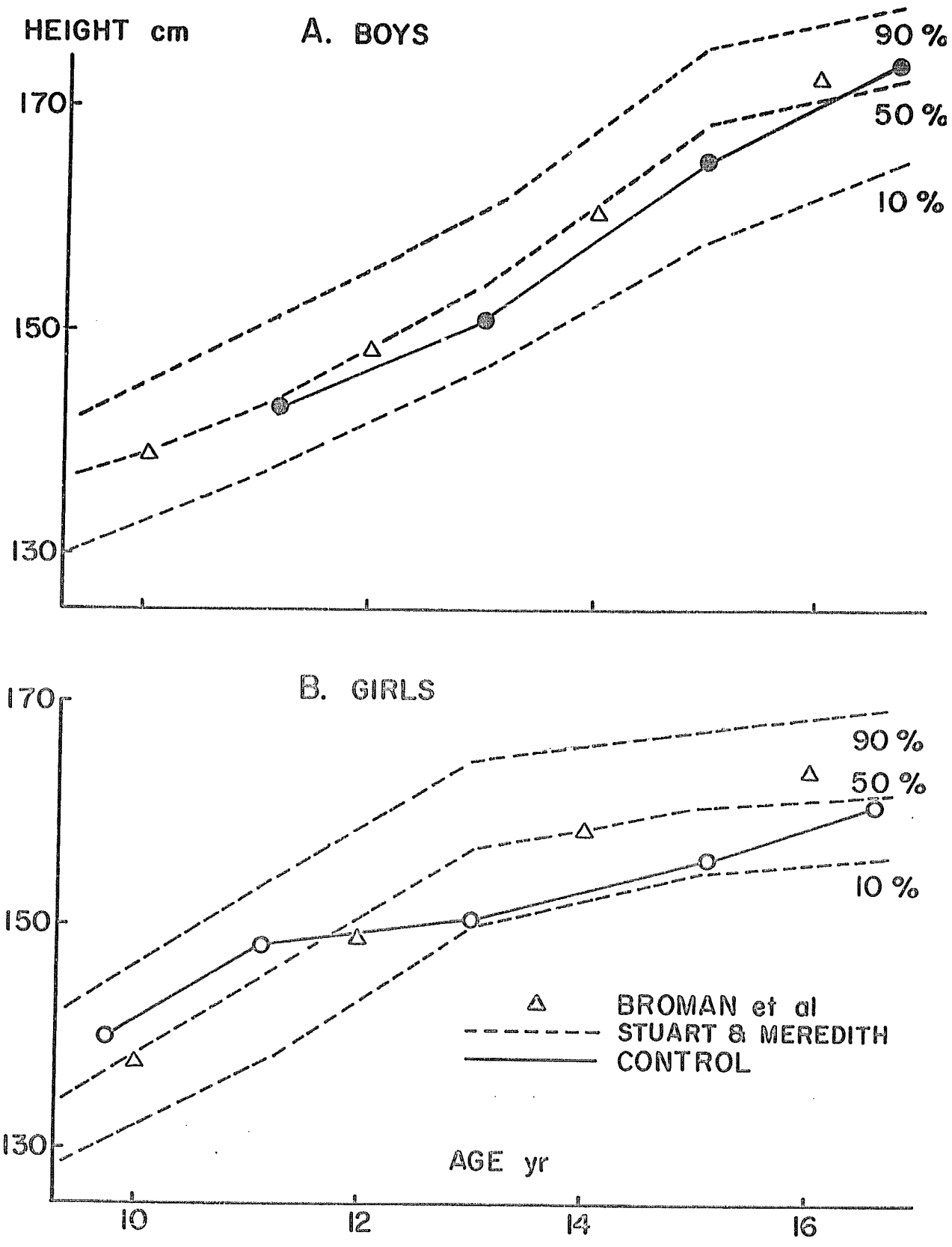


FIG. C_1 - Relationship of height to age in Control group.

this smallness of stature is not evident when weight is considered. Fig.C2 shows this relationship to age and in contrast with that expected, since weight is a function of height, our data for girls falls virtually on the 50 percentile line while our older boys are heavier than those of comparable age in the Boston and Swedish groups.

Fig.C3 shows the comparison of sexes on the basis of height (Fig.C3A) and weight (Fig.C3B). Such a plot enables the determination of the growth pattern of boys in relation to girls. These mean values are again compared with the 50 percentile lines to Stuart and Meredith (366).

In terms of height, the girls of the present series are taller (P .047) than boys until age 13 years where the lines are seen to cross, after which age the boys are taller. In general, this shows the same results as that of Stuart whose lines cross at the age of 13.5 years.

As would be expected, the crossing of the sex line relating weight to age occurs at about the same age (13.3 years) while those of Stuart cross at age 14.5 years.

1B. Lung Volumes.

Since published data indicates that height is the best single independant variable against which to compare lung volumes, the present data were analyzed in respect to height. Fig.C4 shows the plots of linear regressions (Table C3) for TLC, VC, FRC and RV for boys (solid lines) and girls (dashed lines) as a function of height. Mean values for the subjects divided by

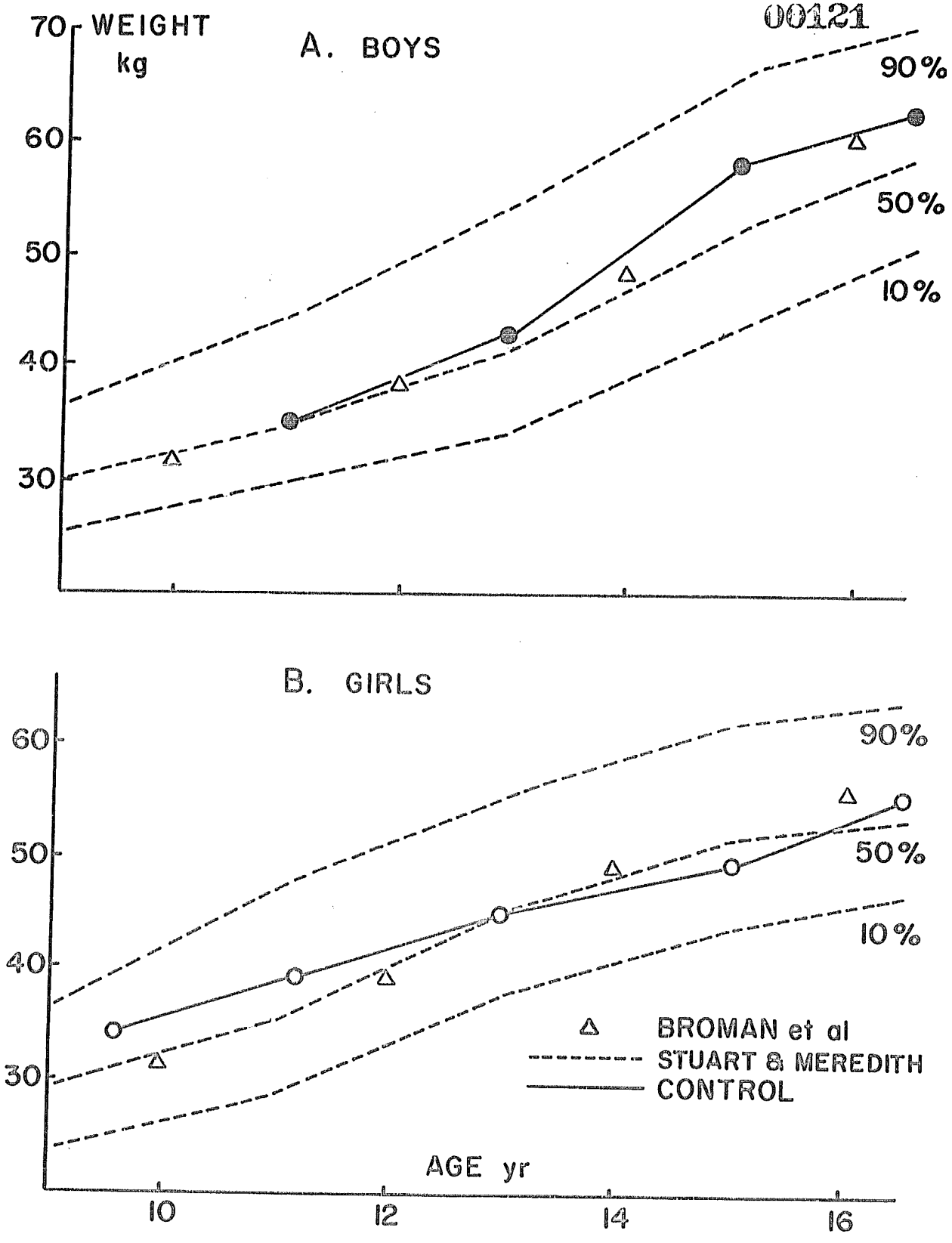


FIG. C_2 - Relationship of weight to age in Control group.

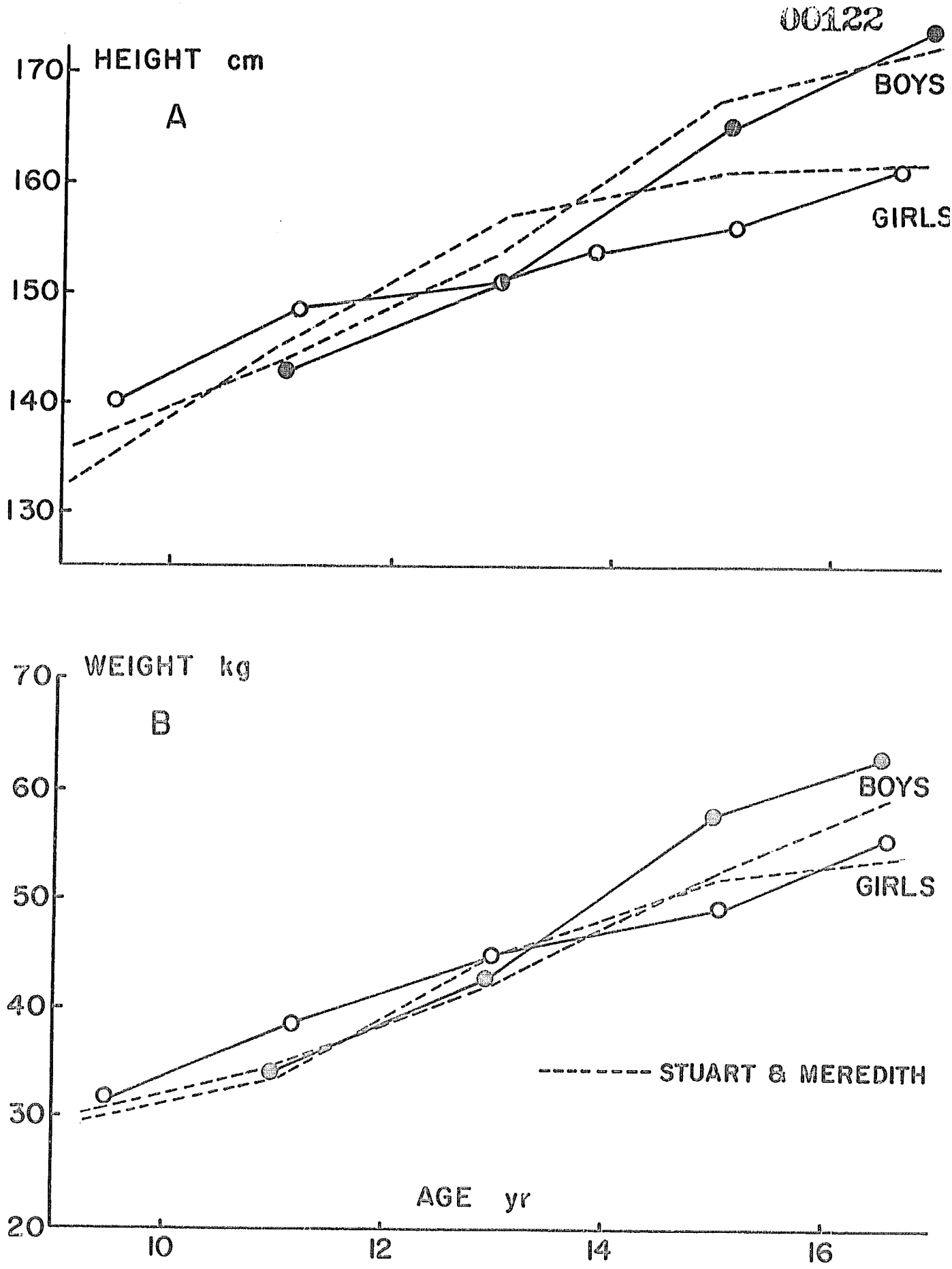


FIG. C_3 - Sex comparison of Controls for height and weight in relation to age

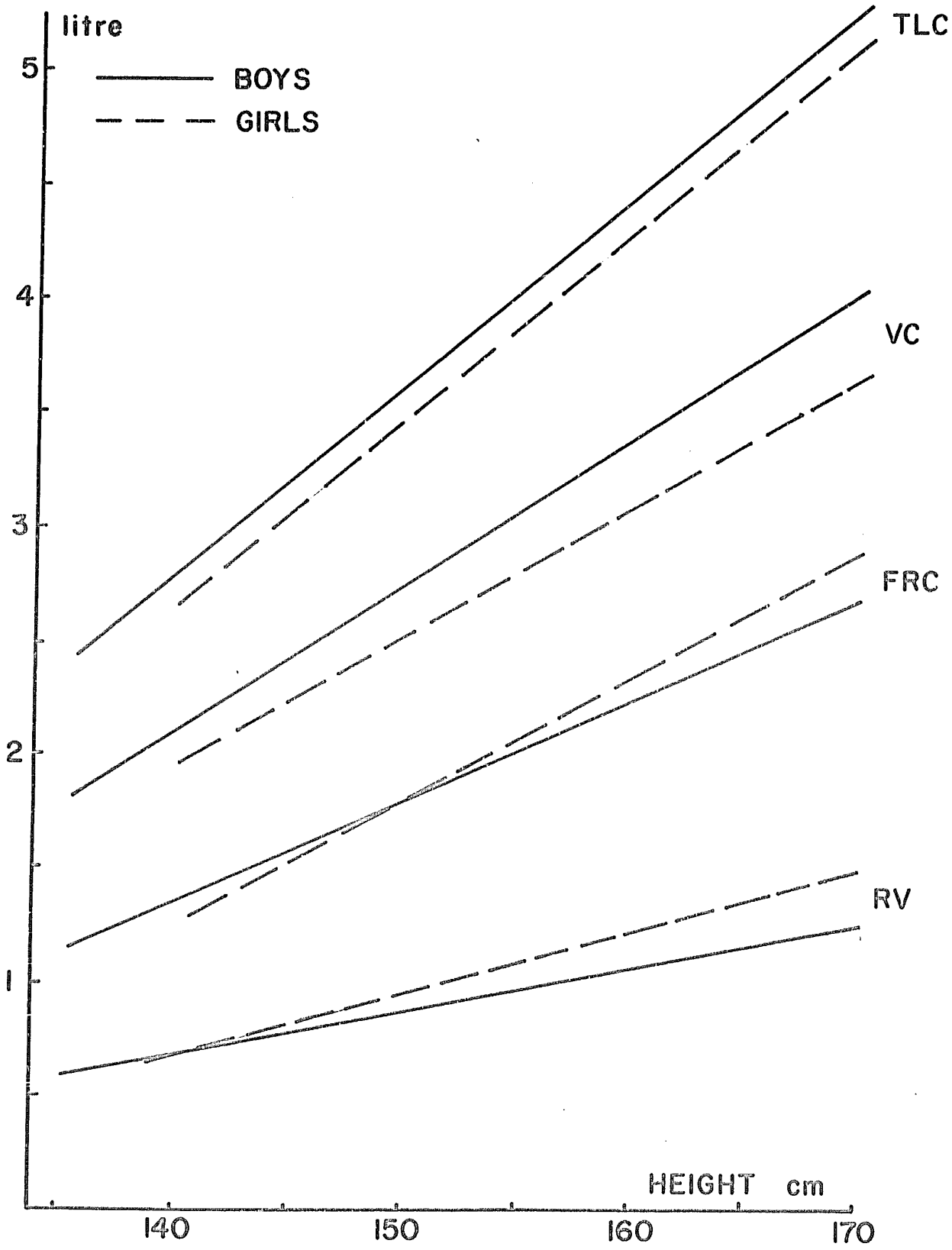


FIG. C_4 - Relation of subdivisions of lung volumes to height in Control group.

height, are presented in Table C2; the standard deviation is shown below the mean values.

Results show no ~~sex~~ significant sex difference, for corresponding height, in any of these functions over the age range studied (Table C7). The regression lines of each sex for FRC and RV cross, the girls having higher values at the taller heights. VC in boys was greater over the whole height range resulting in a larger TLC. The comparison of the coefficients of the regressions (betas-b) indicated no statistical difference in the slopes of the lines for any of the subdivisions of lung volume. Likewise, a statistical comparison of the mean values, using the Student's t-test, showed no significant sex difference at the 5% level; however, vital capacity, which was consistently greater in boys, was found significant at the 6% level (P .006). When the sexes were divided into groups by height, using intervals of 10 cms., FRC and RV in females, at height when numbers were adequate for such comparison, were greater and this difference was consistent, occasionally significant (P .05).

The comparison of our data with others has been made both with the sexes separated and combined. This approach has enabled a wider comparison with findings of other investigators.

Figures C5 and C6 show, respectively, boys and girls compared with previously published results. In each figure, the present series (solid line) are plotted using the linear regression, ((Table C3) as above) for which the general equation of the line is

TABLE (C 2) MEAN LUNG VOLUMES AND FLOW RATES - CONTROLS

	AGE YRS.	NO.	HT. (cms.)	WT. (Kgs)	V.C. (ls)	E.R.V. (ls)	F.R.C. (ls)	R.V. (ls)	T.L.C. (ls)	MMFR (l/sec)	FEV (l/min.)
Boys											
	11.00	6	136.4	32.17	2.18	0.67	1.33	0.66	2.84	1.88	60.83
S.D.±	1.27		2.75	1.97	0.31	0.18	0.10	0.16	0.20	0.58	8.93
	11.36	11	144.8	35.96	2.37	0.84	1.61	0.78	3.14	2.19	64.54
S.D.±	0.67		2.56	4.29	0.36	0.26	0.29	0.27	0.42	0.69	8.65
	12.30	10	152.2	45.55	2.74	0.86	1.80	0.94	3.68	2.34	68.70
S.D.±	1.25		2.25	7.56	0.48	0.28	0.48	0.24	0.65	0.22	8.83
	14.00	3	163.2	57.17	3.41	1.04	1.87	0.83	4.24	3.68	97.50
S.D.±	1.00		5.49	15.43	0.40	0.08	0.23	0.31	0.46	0.25	12.97
	15.00	9	171.60	61.11	4.23	1.53	2.90	1.37	5.60	4.56	128.57
S.D.±	1.00		1.39	5.27	0.48	0.19	0.23	0.26	0.58	0.94	29.88
	17.00	1	180.00	68.00	5.41	2.01	3.67	1.66	7.07	5.23	168.70
Girls											
	11.31	13	144.92	31.19	2.33	0.70	1.50	0.80	3.13	2.75	68.60
S.D.±	1.44		3.22	4.19	0.28	0.19	0.22	0.15	0.37	0.550	12.63
	13.29	24	153.71	47.77	2.69	0.94	2.03	1.10	3.79	2.70	75.68
S.D.±	1.90		2.93	8.78	0.37	0.24	0.42	0.30	0.48	0.65	12.74
	15.50	6	164.50	56.75	3.45	1.23	2.58	1.35	4.80	3.84	103.00
S.D.±	0.84		3.54	8.50	0.39	0.21	0.44	0.29	0.53	0.96	13.34

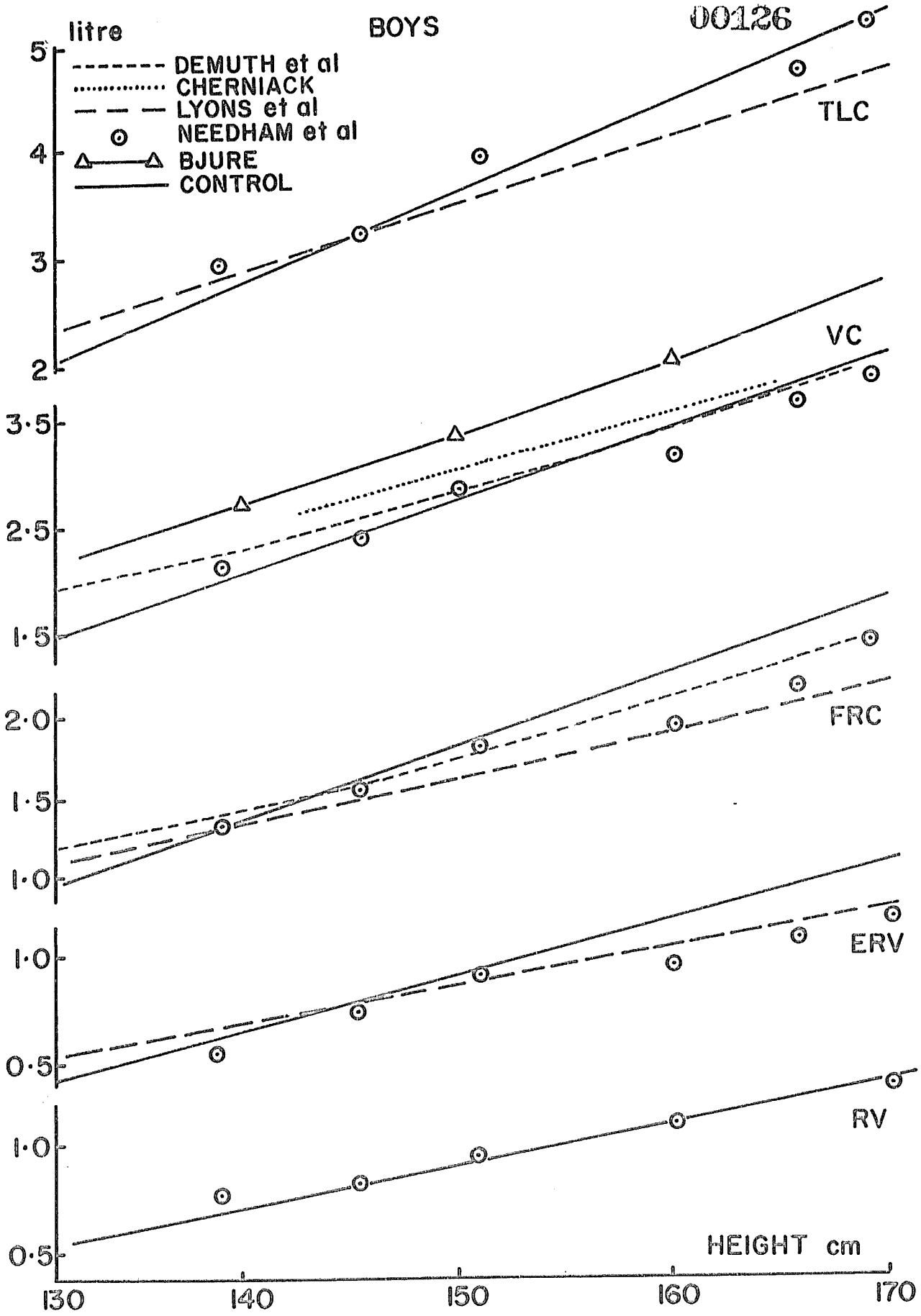


FIG. C_5 - Comparison of lung volumes, in relation to height, of Control boys with results of others.

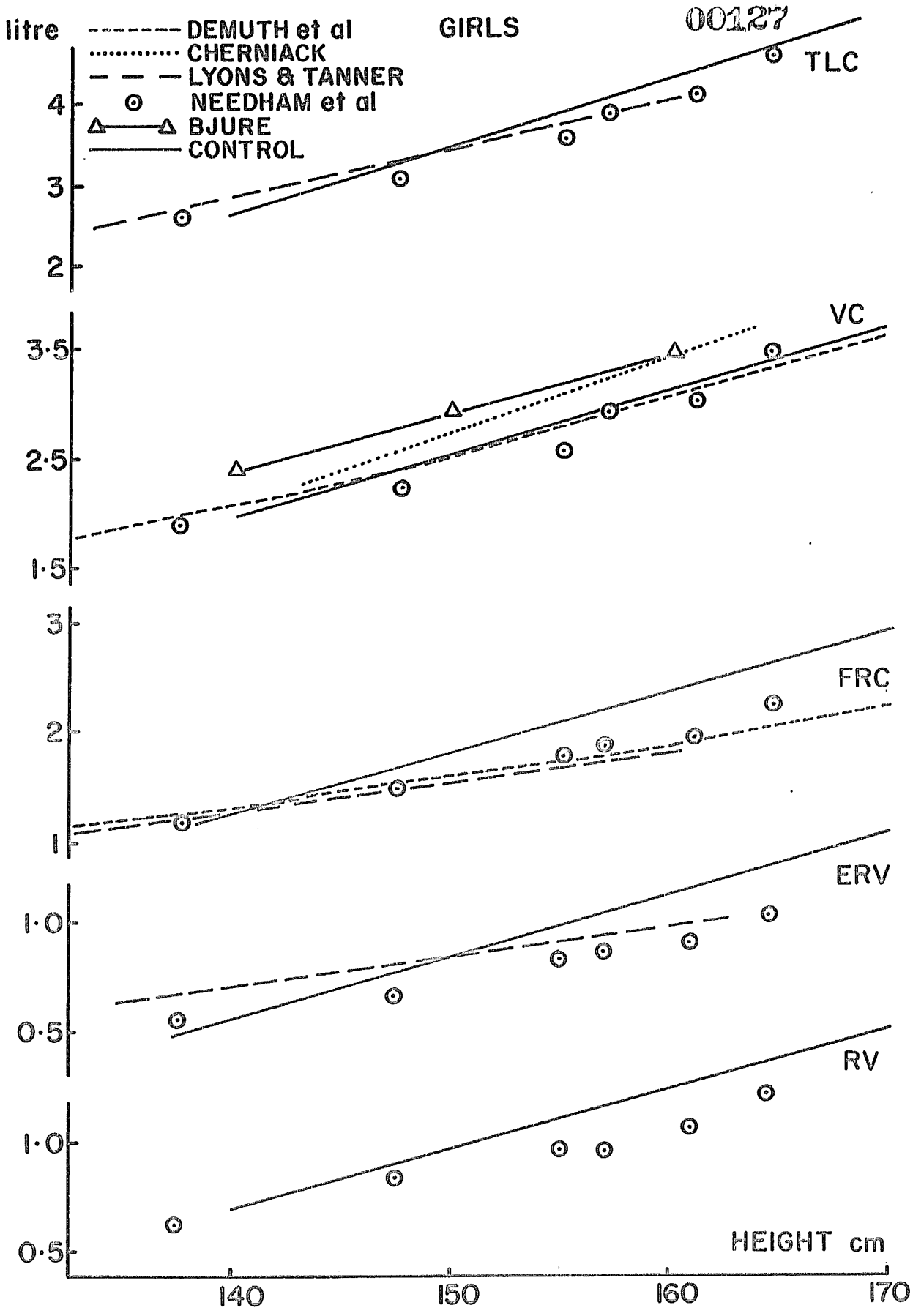


FIG. C_6 - Comparison of lung volumes, in relation to height, of Control girls with results of others.

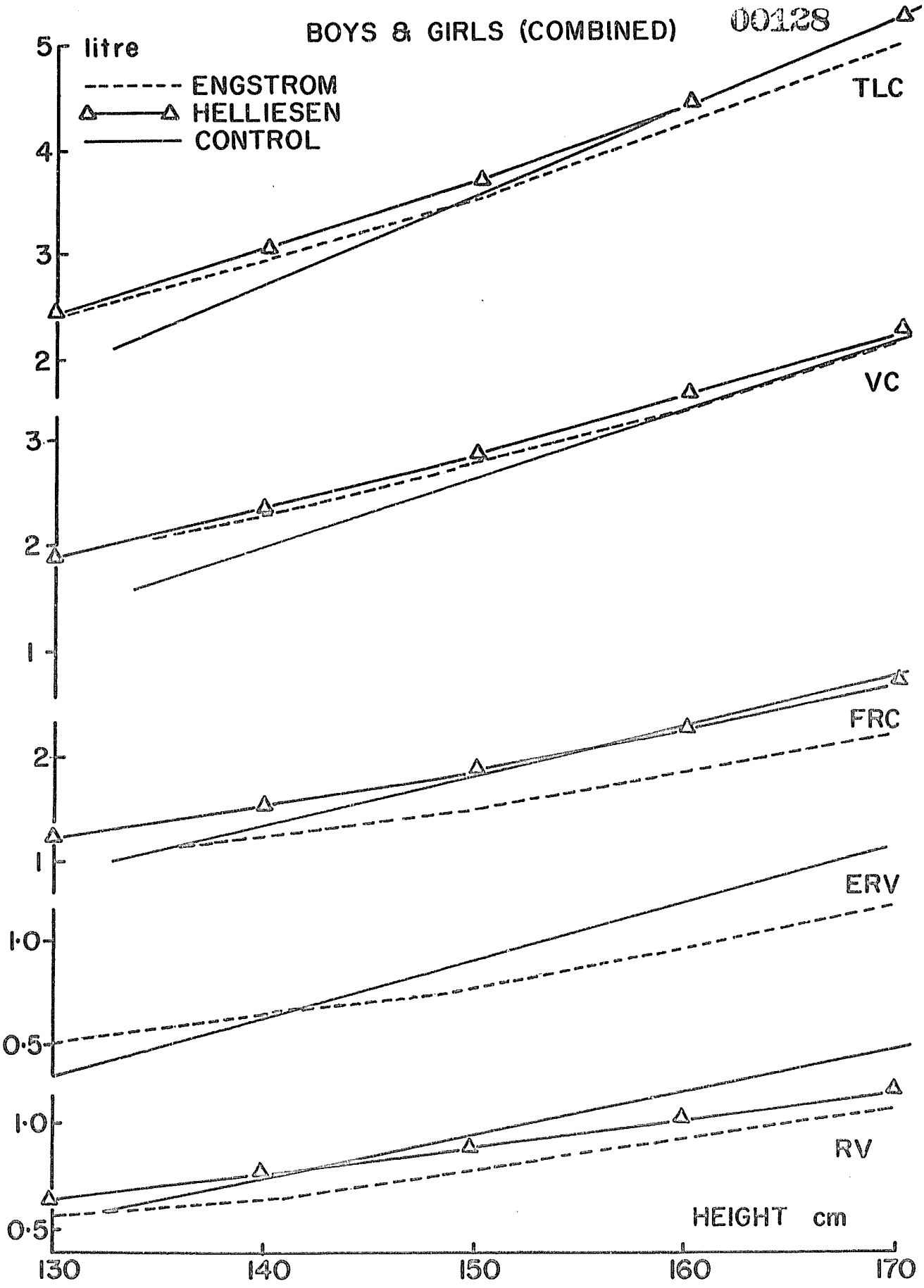


FIG. C_7 - Regression lines showing subdivision of lung volume, in relation to height, with sexes combined.

TABLE (C 3) LUNG VOLUMES AND FLOW RATES REGRESSIONS - CONTROLS

SEX	Dependant Variable (Y)	Constant		Coef. of Indep. Var. (b) (X)		Corr'n (r)	S.D. of (b)	S.E. of (Y)
		Ht	$(Ht)^3$	Ht	$(Ht)^3$			
Boys	FRC	-4.93		.0450		.865	.0042	.348
			-.317		.619	.877	.0551	.334
	VC	-6.95		.0648		.899	.0051	.419
			-.292		.889	.910	.0660	.399
	TLC	-8.97		.0842		.901	.0065	.538
			-.328		1.158	.913	.0837	.507
	RV	-2.02		.0194		.709	.0031	.257
			-.035		.268	.723	.0416	.252
	ERV	-2.91		.0255		.820	.0029	.238
			-.282		.351	.830	.0385	.233
	MMFR	-9.17		.0786		.826	.0087	.717
			-1.118		1.084	.839	.1142	.692
	FEV	-245.13		2.1452		.835	.2293	18.860
			-25.65		29.71	.852	2.968	17.97
Girls	FRC	-6.45		.0051		.757	.0074	.334
			-.826		.777	.759	.1040	.333
	VC	-5.98		.0568		.809	.0064	.290
			-.183		.803	.813	.0897	.287
	TLC	-9.08		.0839		.845	.0083	.374
			-.493		1.183	.847	.1160	.372
	RV	-3.09		.0271		.597	.0057	.256
			-.314		.380	.595	.0801	.257
	ERV	-3.36		.0280		.707	.0044	.197
			-.512		.397	.712	.0610	.196
	MMFR	-5.85		.0572		.518	.0147	.664
			-.092		.830	.535	.2048	.656
	FEV	- 195.60		1.790		.750	.2462	11.09
			-13.48		25.43	.758	3.414	10.94

$$Y = a + bX$$

where Y - dependant variable (volume)

X - independant variable (height)

a - constant

b - coefficient of X
(i.e. slope of the line)

The linear regressions derived from the extensive data of Lyons and Tanner (239) are shown by the dashed lines. Methods employed in their study and in the present one were essentially the same. It is seen (Fig.5-6) that where comparisons can be made (TLC, FRC and ERV), our regressions have the greater slope and thus our subjects had larger volumes at the taller heights. The greatest difference between the data is in respect to FRC which is more marked in the girls (Fig.C6) It is noted that the lines cross at a height of 145-150 cms which represents the height range that includes the greatest number of subjects in the two studies (Fig.C21).

A comparison with the extensive data of Demuth et al (107) shows our results virtually identical for VC and FRC for boys (Fig.C.5) at heights greater than 145 cms. In analizing their data, log transformations were done and their regressions follow the general equation $y = ax^b$. This gives a curvilinear description of the data and could account for the slight divergence in results for FRC in boys at the extremes of the height range.

FRC values for girls show our results are identical with Demuth (and Lyons and Tanner) at height 140 cms.,but at height 165 cms., our subjects had FRC values .65L greater than both Demuth et al and Lyons' study.

Needham et al(270) tested 150 males and females, ages 11-19 years (Fig.C21) and they present multiple regression equations for prediction of the various subdivisions of lung volume. Unfortunately, this does not enable us to plot our data using their formulae; however, a comparison of their mean values (cross circles) indicates that our results tend to be slightly higher, particularly as height increases.

Results of Cherniack (83) for VC on 521 Winnipeg children are shown (dotted line) to be in close agreement with the present series. Although his values, as well as those of Bjure (54) for Swedish children, lie slightly above our predicted values.

In Fig.C7 the sexes are combined and results are compared with data of Helliesen et al (171) and Engstrom et al (128). Close agreement is seen with Helliesen for all subdivisions and with Engstrom for VC and TLC. However, our values for FRC, ERV and RV were higher than those found in the Swedish study (128).

1 C. Dynamic Lung Function Results (Table C2 and Fig.C8)

Fig.C8 compares the linear regression equations of MMFR and FEV on height in boys and girls. The girls have higher flow rates at the shorter heights but lower values than boys

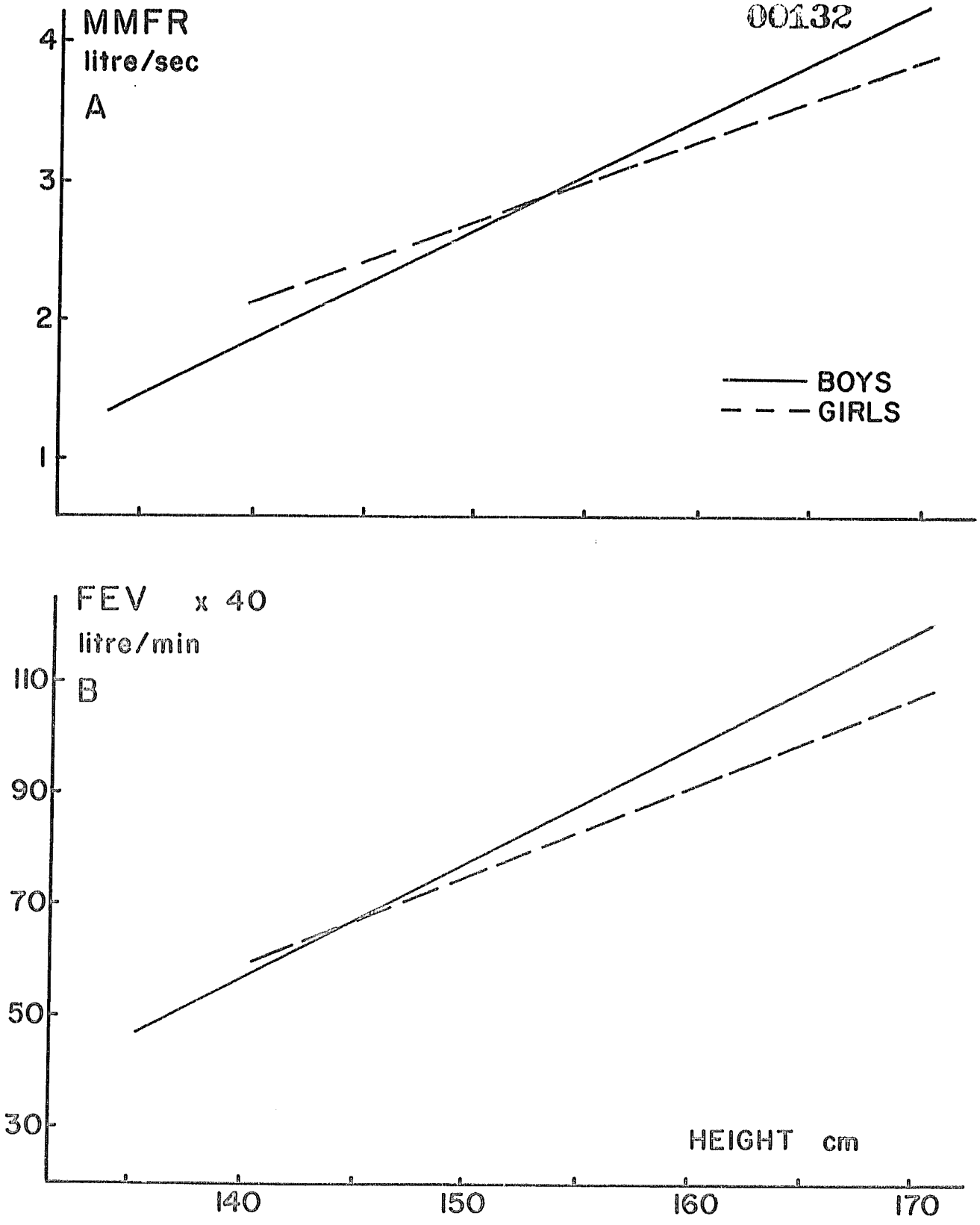


FIG. C_8 - Regressions for Controls showing flow rates (MMFR & $FEV_{.75}$ X 40) in relation to height - sexes separate.

as height increases beyond 152 cms. This same sex relationship is shown for FEV (Fig.8B) with the lines crossing at 145 cms. No significant difference in slopes of the regressions was found ($P < .3$), nor was there any overall statistical difference between sexes when means were compared.

Few data are available in the literature for comparison of MMFR. Cherniack (83) found values which differed markedly from those of the taller boys of the present series but otherwise values for the two studies are virtually identical. (Fig.C9)

Fig.C10 shows our data with sexes combined, compared with the unpublished data of Beaudry (38). Here, our results are described both by a linear regression and logarithmetically such as employed by Beaudry. As can be seen (Table C4) the log transformation has not improved the correlation of our data with height, nor has it affected the relationship of the present series with the data of Beaudry. The two sets of data show a wide difference in flow rate (1 l/min.) at shorter heights, although agreement is good at taller heights (.25 l/min difference). His study includes data on 270 children, many of whom were in the younger age groups.

Fig.C11 shows the present data in relation to others who have measured $FEV_{.75\ sec}$ (168) and $FEV_{1.0\ sec}$ (54). To permit comparison their values were expressed as l/min.by multiplying by 40 and 30 respectively. Close agreement is found with

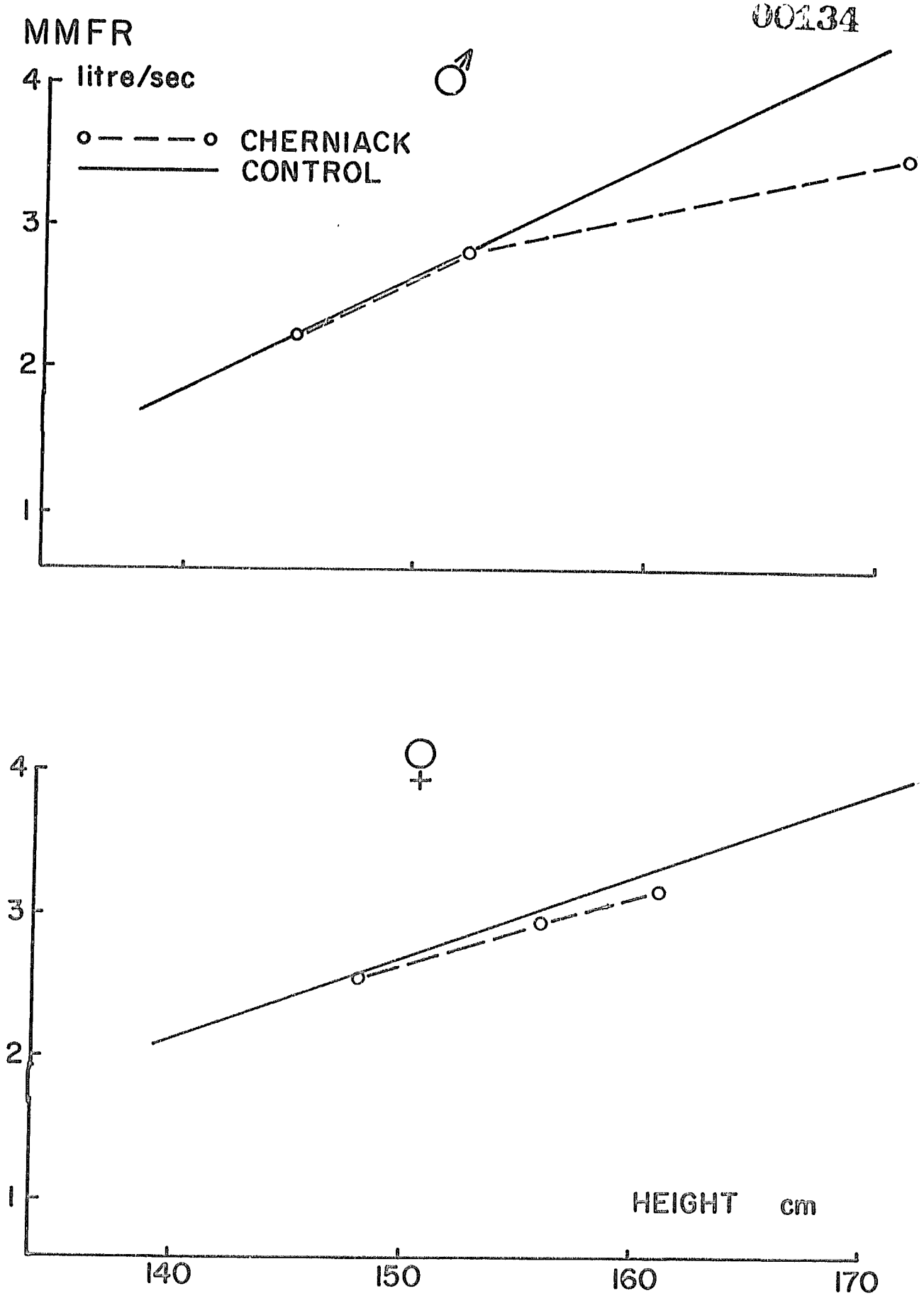


FIG. C_9 - Comparison of MMFR values predicted on height for present study on Controls with mean values of others.

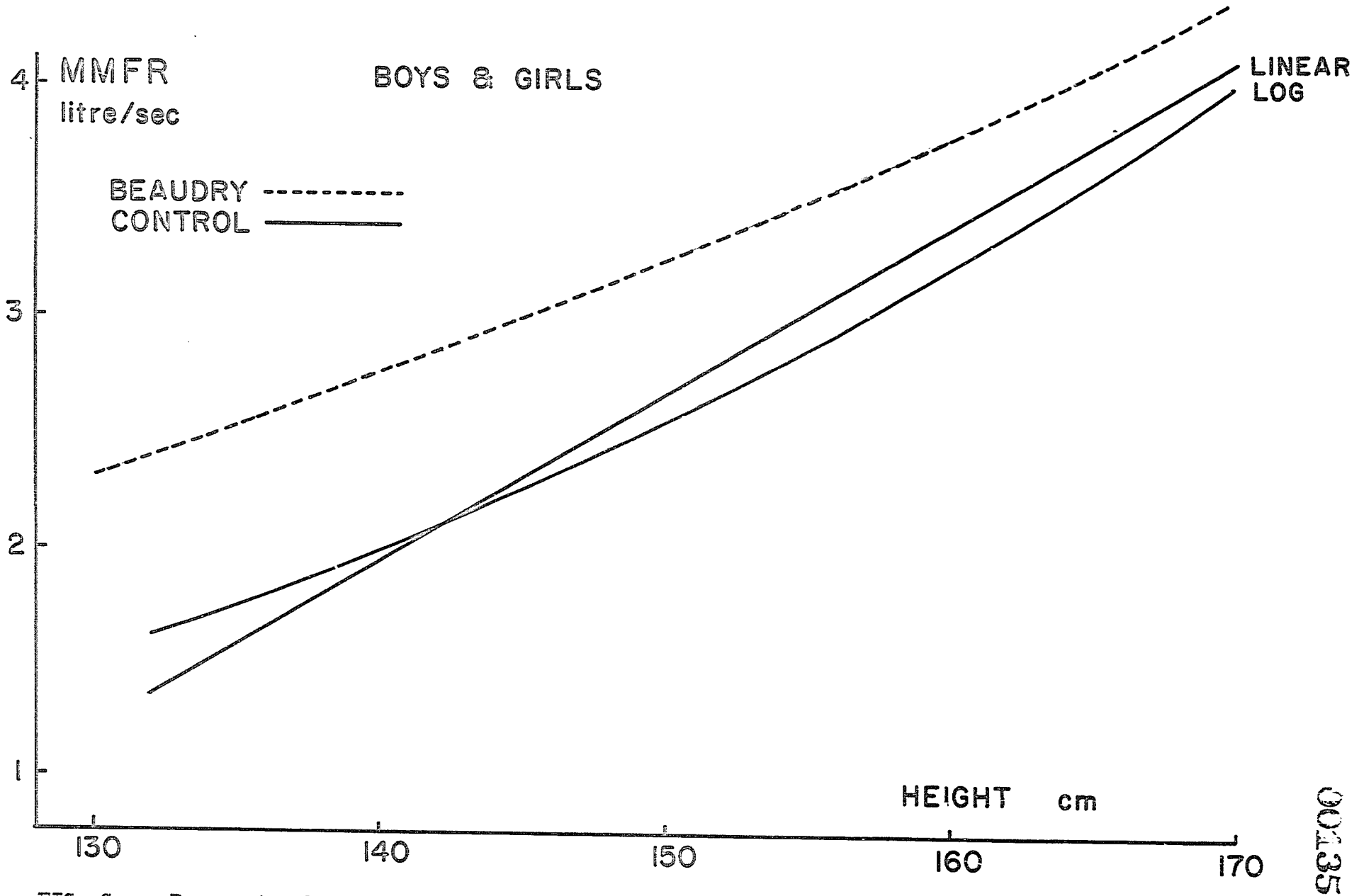


FIG. C_{10} - Regression lines showing the relation of MMFR to Height. Present data (solid lines) for Controls are shown as a linear and exponental function of height and compared with results of Beaudry.

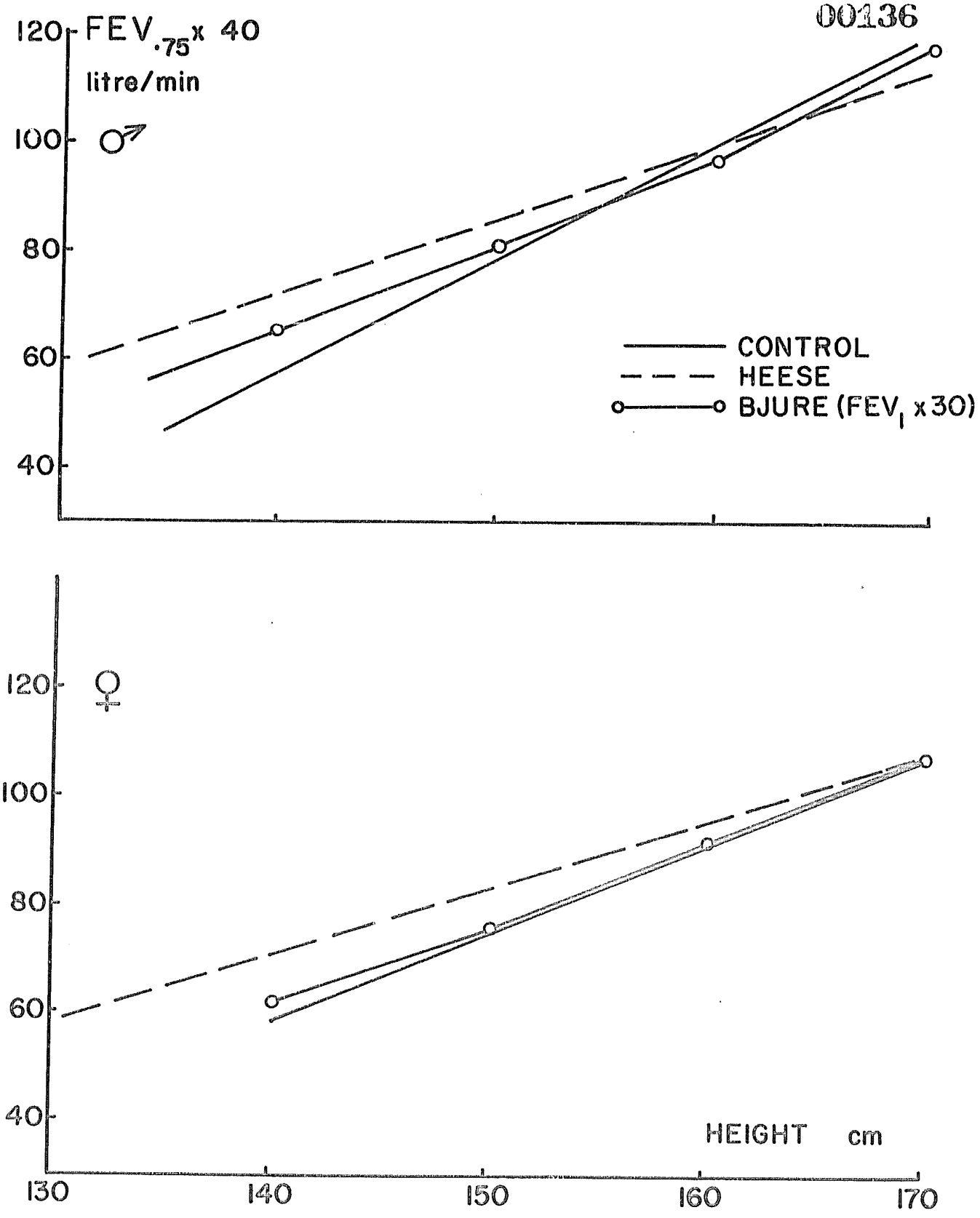


FIG. C_{11} - Relation of $FEV_{.75}$ X40 regression on height in Controls with sexes separate. Present data is compared with results of others.

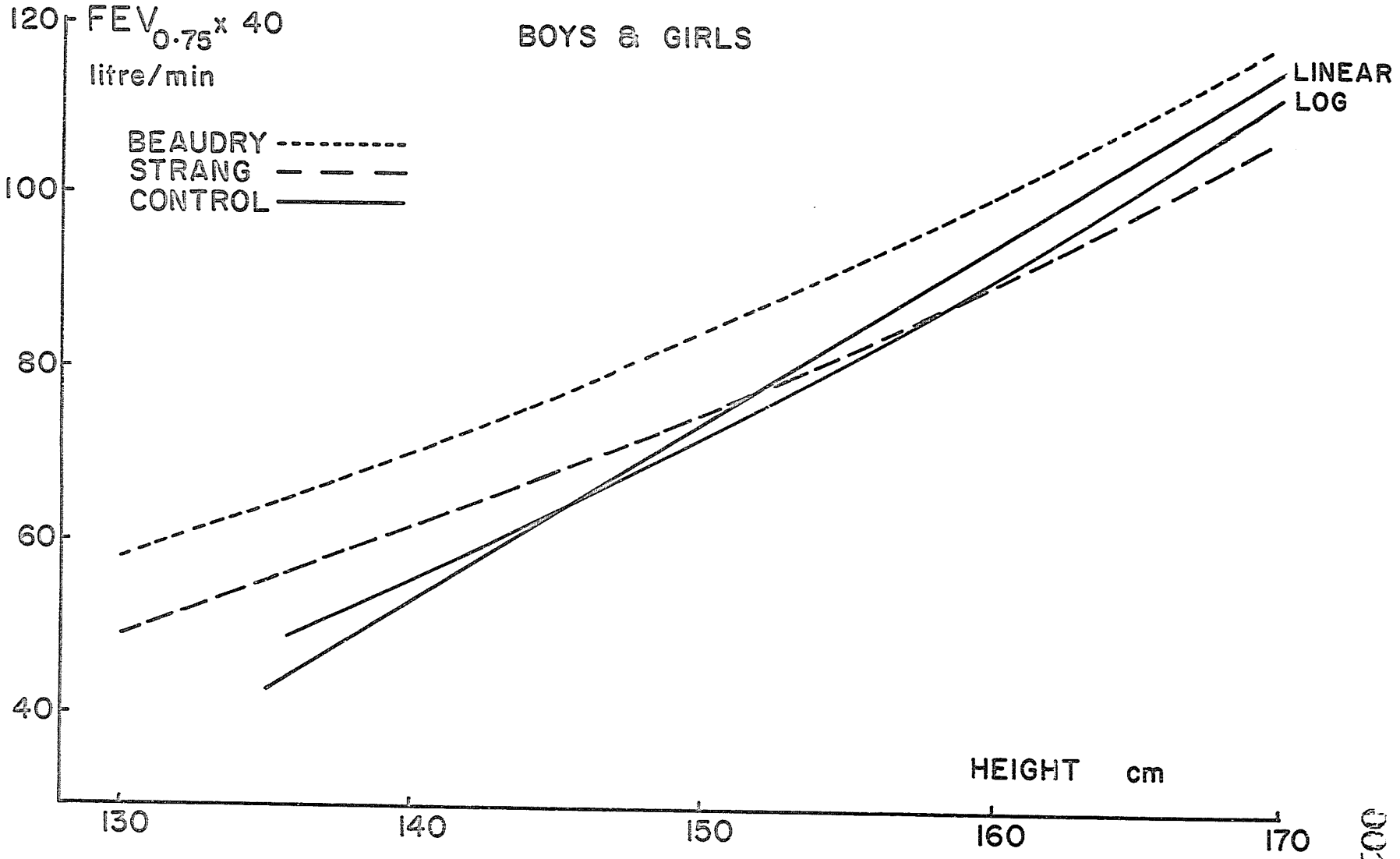


FIG. C_{12} - $FEV_{.75}$X40 results for Controls with sexes combined. Present results (solid lines) plotted as linear & exponental function of height and compared with others.

Bjure's results (54) over the whole range studied, but only with Heese's data on taller children (168). At shorter heights, Heese's values considerably exceeded the present values, and those of Bjure (54). Furthermore, Heese's data were expressed at ambient pressure and temperature (ATP) and conversion to BTPS would exaggerate the differences.

In Fig.12C, data from both sexes are combined, and FEV is plotted as an exponential function of height. Our results are compared with those of Strang (332) and Beaudry (38). Although results of both these workers show a parallel increase with age, Strang's values are lower at all ages than Beaudry's. Our values at heights greater than 150 cms. lie between these two groups.

Individual Results:

Fig.C13 - C20 show individual results for VC, FRC, MMFR and FEV for each sex and in relation to the calculated regression line on height.

Discussion

It has already been mentioned that certain authors in describing growth of lung volumes in children have treated the sexes separately (54,83,107), others have choosen to combine the sexes (38,128,171). There is general agreement that 1) the sex differences up to the age of puberty are not significant and 2) that sex differences in the adult are significant. The age, or stage of development at which these sex differences become apparent is not certain but must lie between puberty and

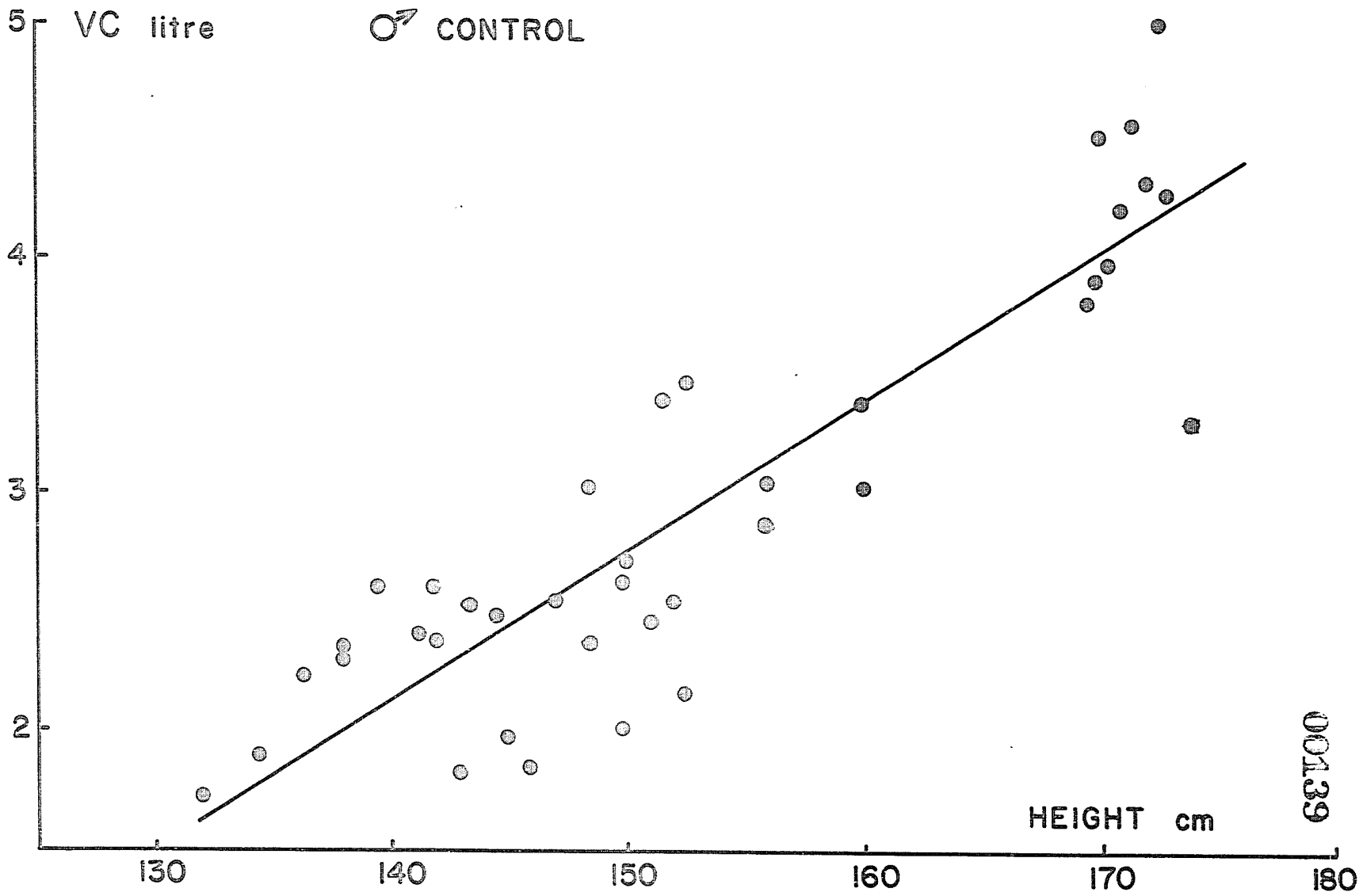


FIG. C_{15}- Individual results for VC in Control boys.

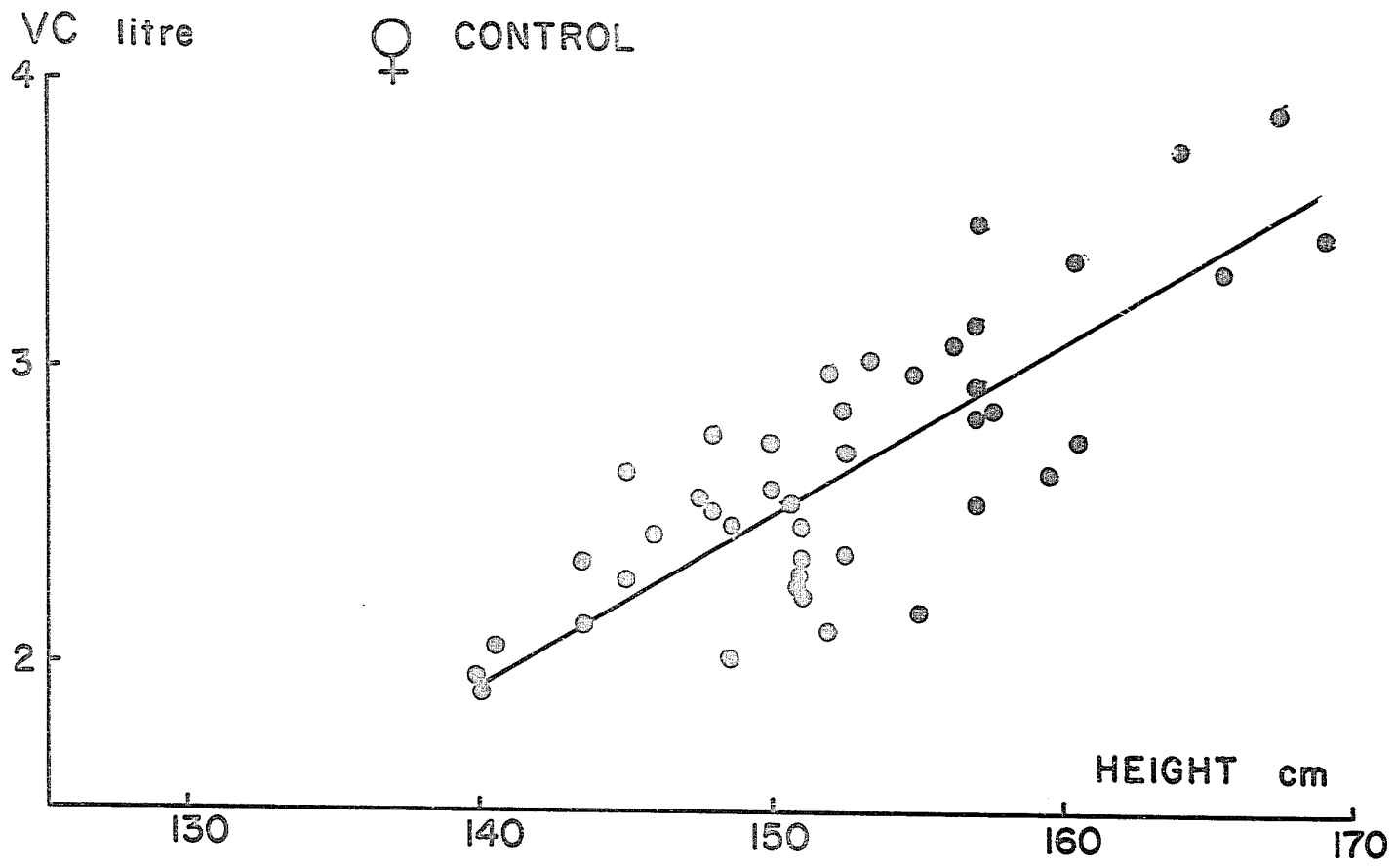


FIG. C_{14}. Individual results for VC in Control girls.

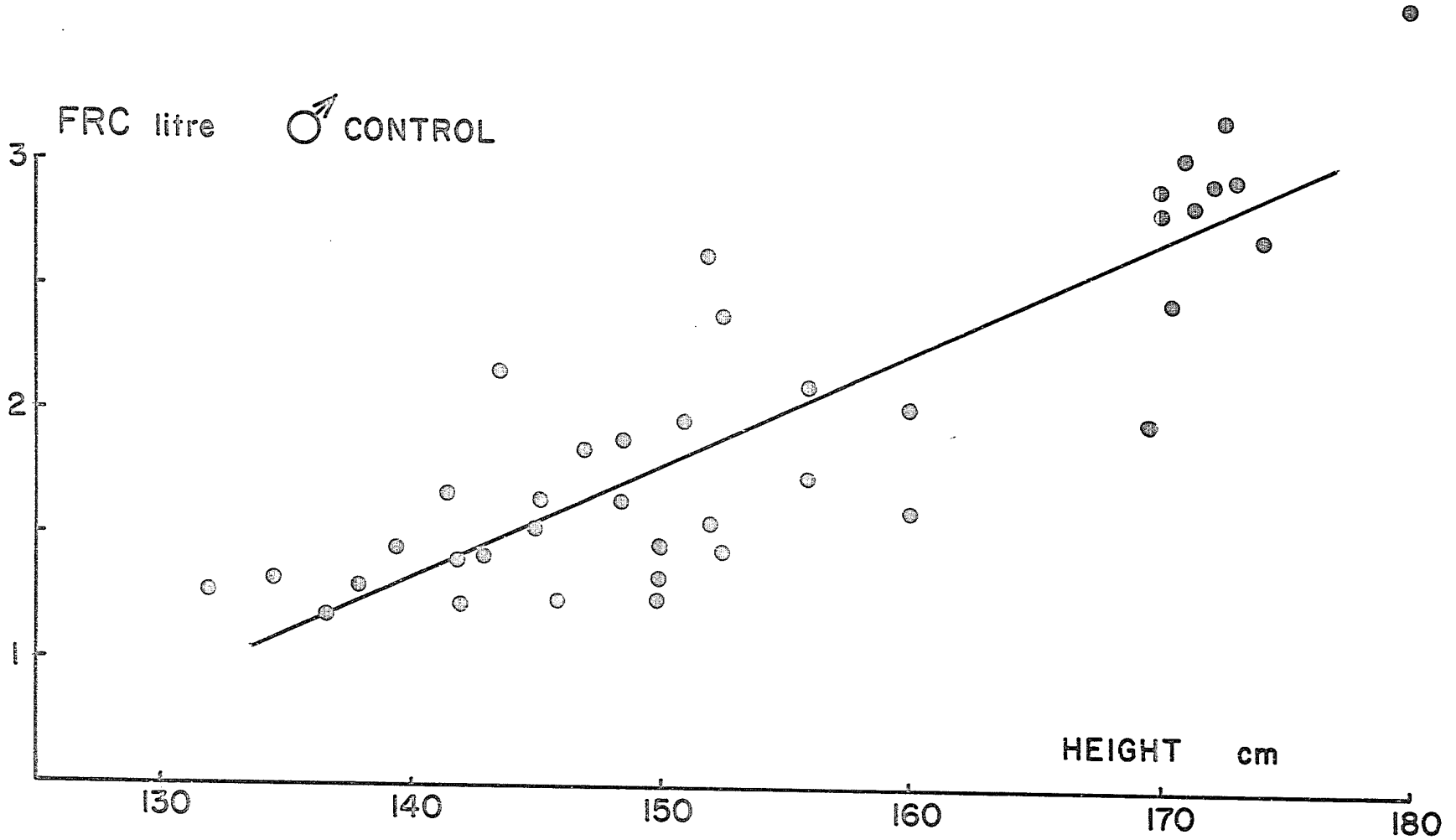


FIG. C_{15} - Individual results for FRC in Control boys.

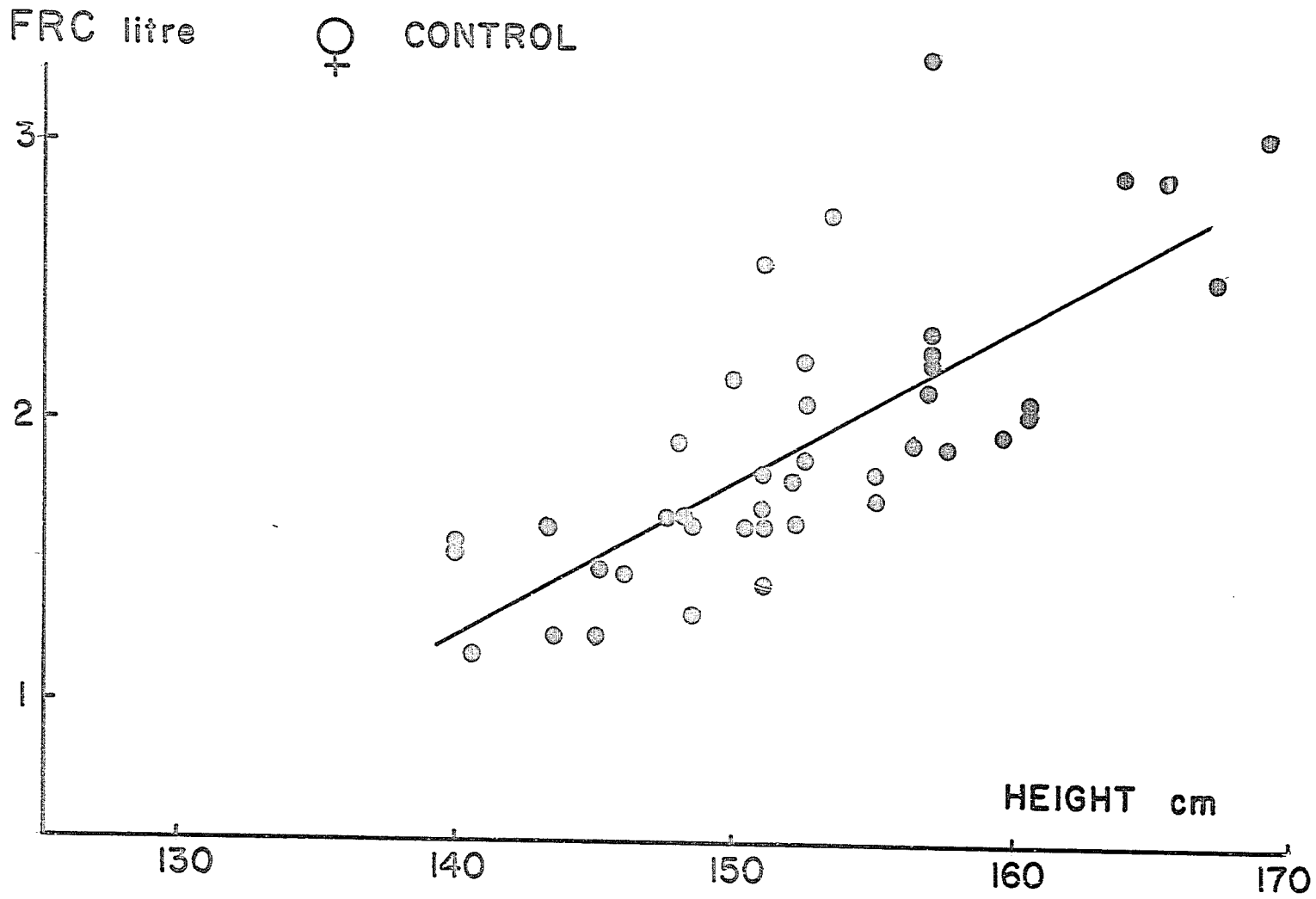


FIG. C_{16} - Indivudual results for FRC in Control girls.

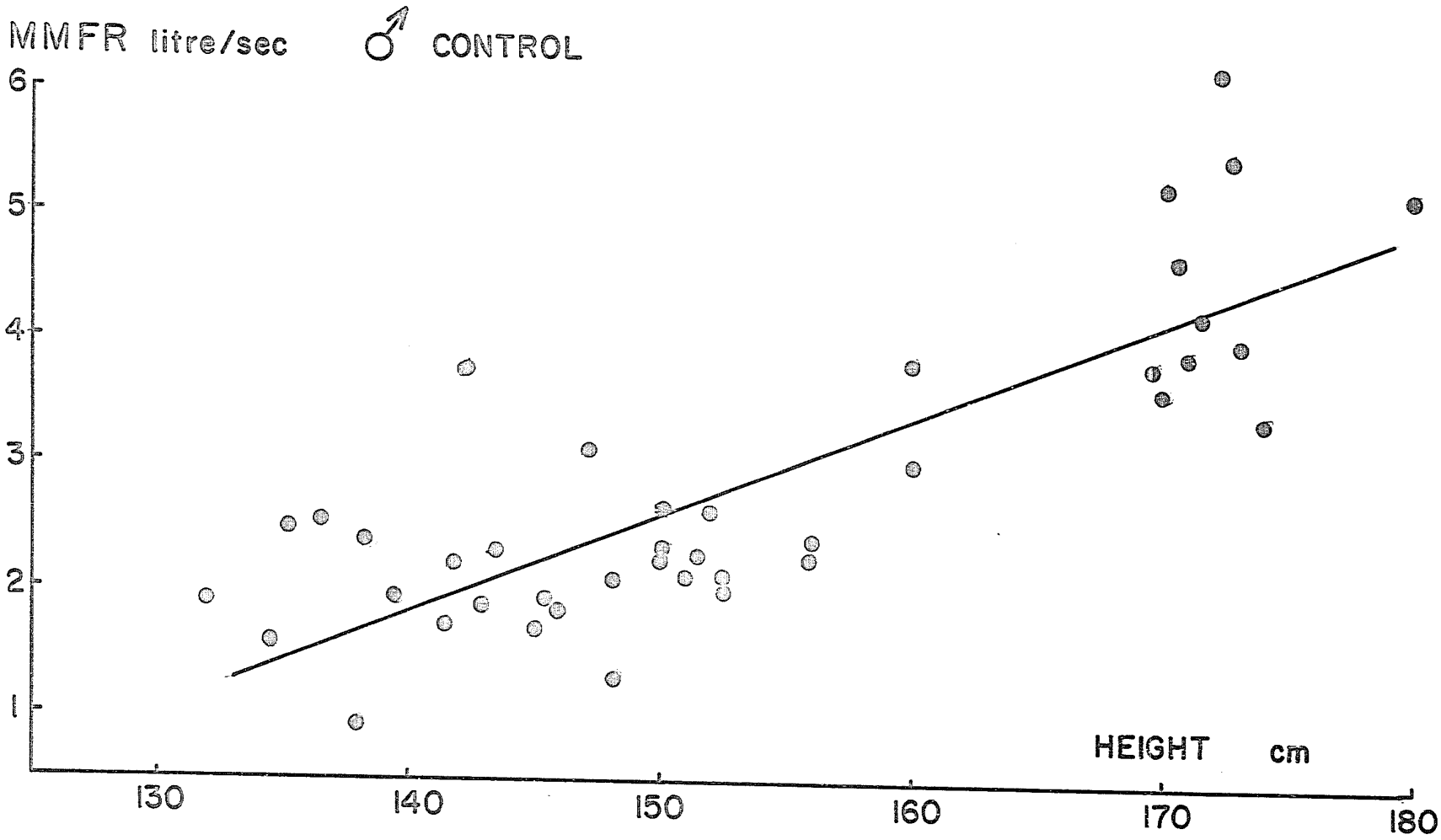


FIG. C_{17} - Individual results for MMFR in Control boys.

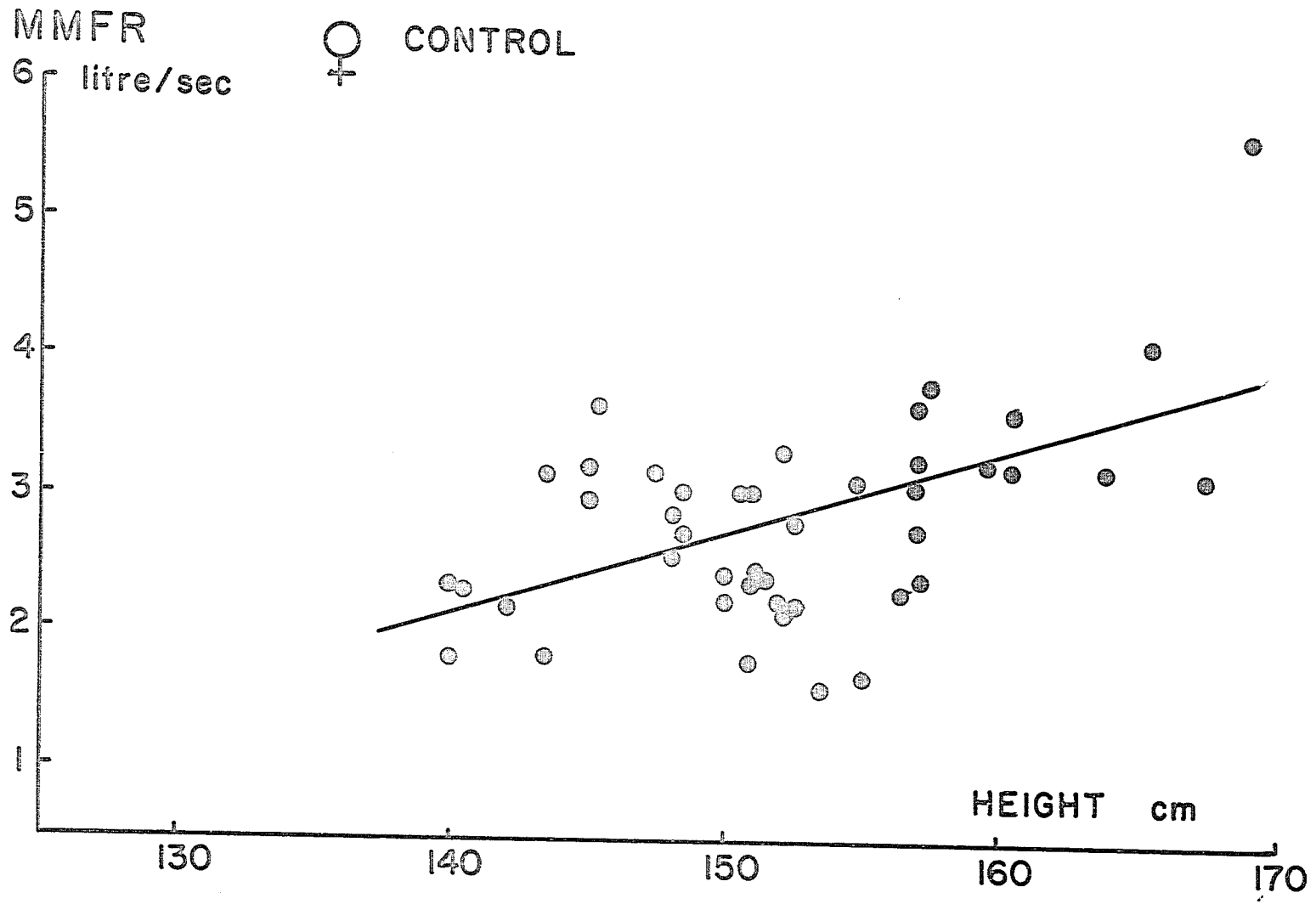


FIG. C_{18} - Individual results for MMFR in Control girls.

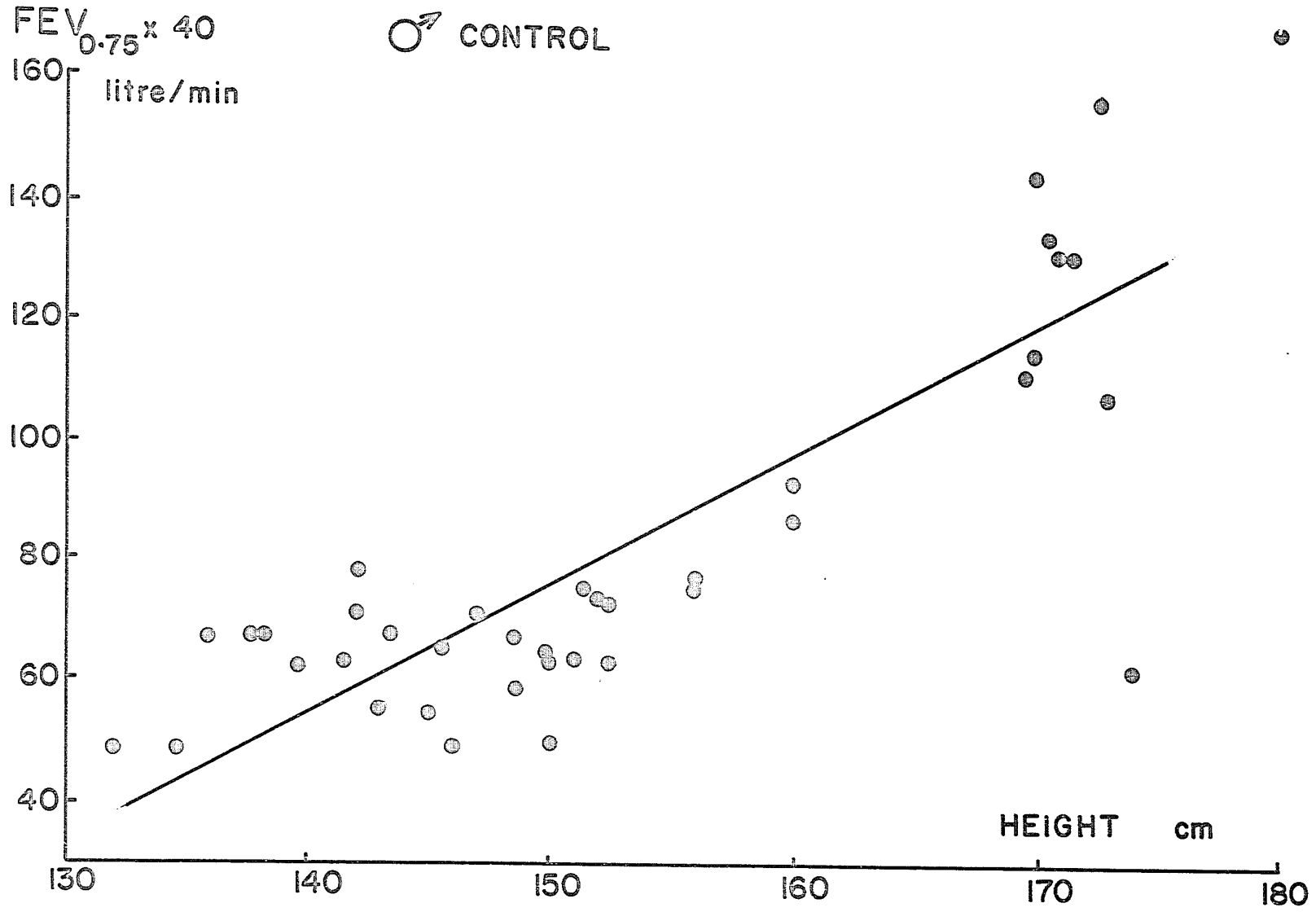


FIG. C_{19} - Individual results for $FEV_{.75}$X40 for Control boys.

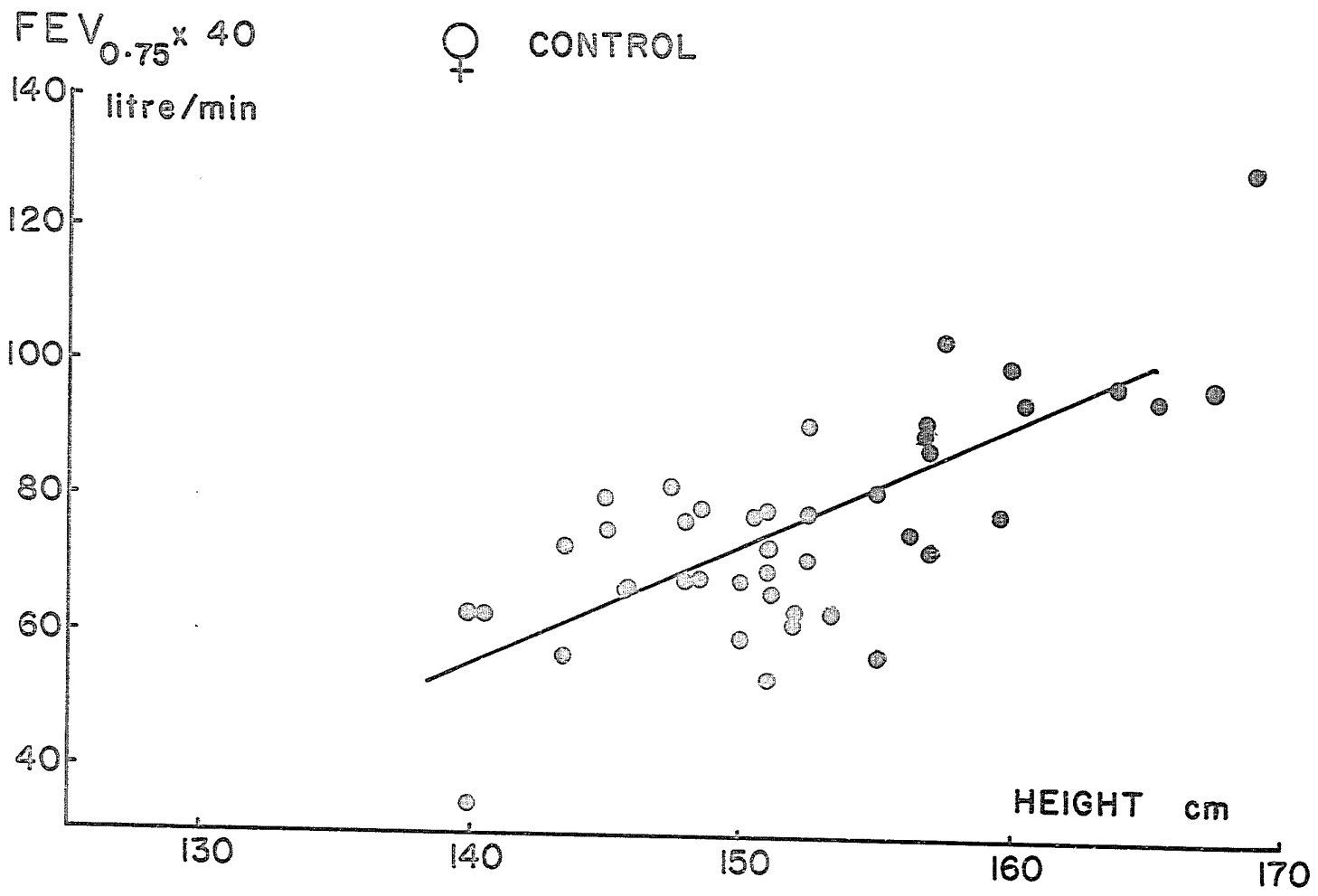


FIG. C_{20} - Individual results for $FEV_{.75}$X40 for Control girls.

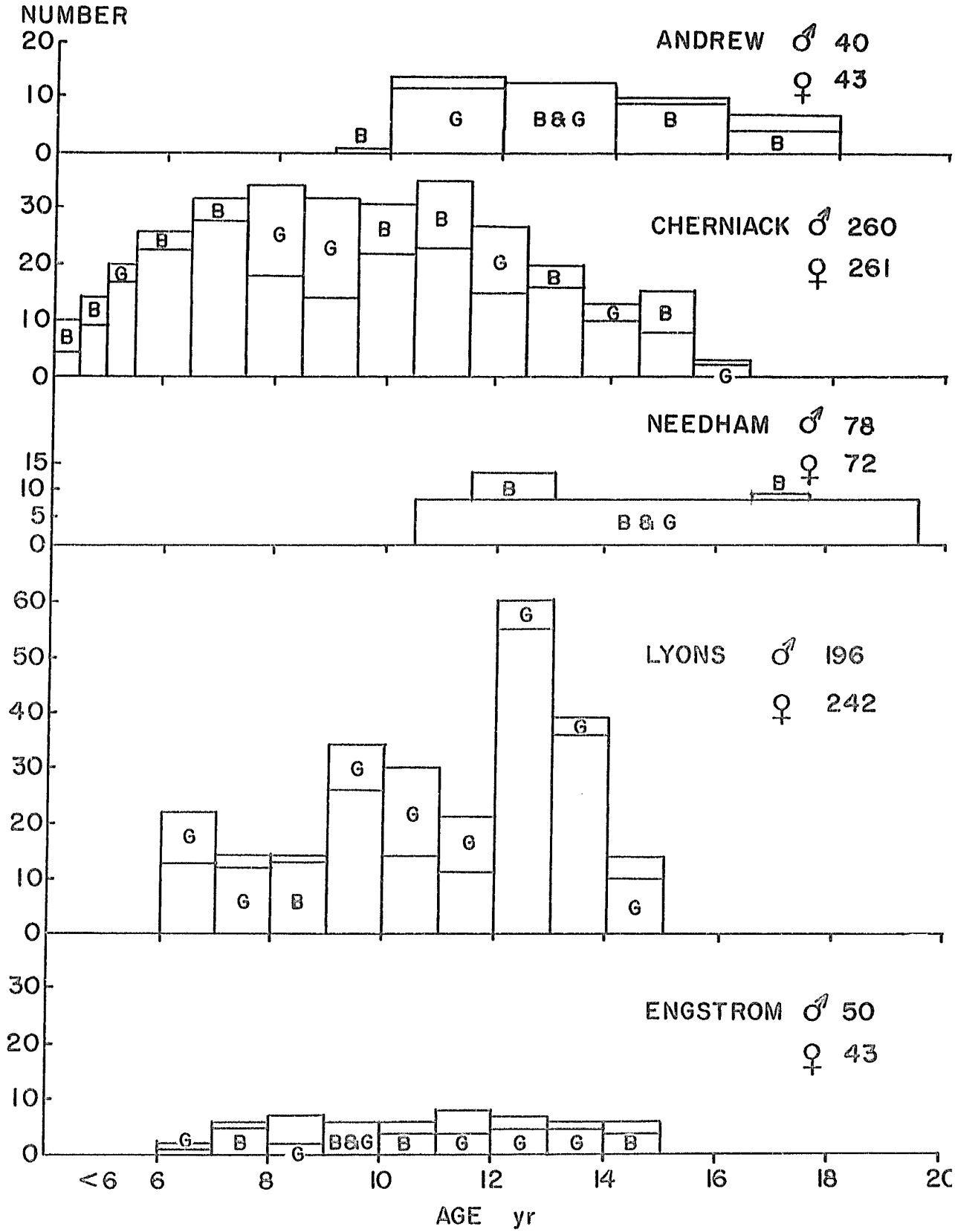


FIG. C_{21} - Comparisons of reported studies on lung function in children showing numbers and age included by each author. For each age, sex is indicated as B (boy) or G (girl); number is indicated on the ordinate.

the twenties (i.e. the lower age span in most adult studies). Since we could not be sure at what age the sex differences first become apparent (and therefore at what age data on the two sexes should be analyzed separately) it seemed advisable to analyze all the data separately for each sex. Indeed, little justification can be found for combined analysis.

An additional point of difference in opinion exists as regards the best means of describing the data. Some authors use the simpler linear regression, others employ logarithmetic and other transformations in the regression equations. To assess the merits of these treatments, a comparison of different regression equations for VC and FRC has been made. Table C4 shows the various correlation coefficients in which height has been used as the single independant variable. It is noted that the use of (height^{3}) gives the highest correlation and presumably best describes the data, for VC in both boys and girls, and for FRC in boys. However, it is also noteworthy that height is only slightly superior (as indicated by the correlation coefficient) to the simpler regression based on height^{1} which in turn gives a higher correlation than the considerably less convenient logarithmetric expression. From this it was concluded that there is little advantage to be gained by using height^{3} and height alone has thus been used to describe the present data.

The comparison of the physical characteristics of the children in the present study indicate our subjects were slightly

shorter, but of comparable weight, to published data on normal children. This suggests our children were "short and fat"; however, no measurements of obesity were made. The greatest difference was seen in the girls aged 13-15 years, suggesting they may have been late maturing. There is little doubt that differences in subject selection is an important consideration when different studies are being compared; this is particularily true when comparison of regression lines is being made, in which case the calculated regressions can be influenced by difference in numbers of a particular age in the study. Furthermore, the variations in growth rate with respect to age, make age a poorer basis for group comparison than height in children.

The number of children included in our Control group is small by comparison with some other studies (Fig. 21). Nonetheless, there is good general agreement with previously published data on lung volumes and flow rates. Closest agreement was invariably seen in the height range which includes the greatest numbers studied; perhaps differences in this respect accounts for our agreement being poorest at the shortest heights.

As might be expected, VC, because of its ease of measurement, shows the most consistent agreement with values reported by others. On the other hand, the FRC values of the present series were higher than those of other investigators, except for the data of Helliesen whose values were identical (171). Differences from other data becomes more apparent at taller heights. It is

well recognized that such measurements are more difficult, and the coefficient of variation wider, in children than adults (239). One would therefore have expected greatest disparity with published data to be evident in younger, rather than older children, the opposite of that shown above (Fig. 5-7). Only single determinations of FRC were made in the present study, a point which is in contrast to most other groups. Engstrom (128) found a significantly lower value for FRC in the second observation than in the first, and this difference was attributable to variation on ERV since RV was not different. We have made duplicates in only a small number of children and found no consistent difference. Engstrom cites that while the difference was significant, the error introduced by employing single determinations is small (2-3%) and well within the error of the technique itself.

The difference between sexes in respect to VC is in agreement with that found by Demuth (107). Although the difference was not significant, it was consistent for any given height. By contrast, no consistent sex difference was observed in FEV and MMFR. Cherniak (83) found values for MMFR higher in males but does not state if the difference was significant. Demuth (107) found values (for both sexes) lower than both ourselves and Cherniak and the difference in technique probably accounts for the difference.

Finally, the purpose for inclusion of Controls in this study was to permit comparison with other children (swimmers). It is concluded that the present children agree favorably with published data, both in respect to physical characteristics and static and dynamic lung measurements, and are adequate for subsequent comparison with other children in the present study.

$D_L CO$ Results - Controls:

Results of $D_L CO$ for the 40 boys and 43 girls in this study are shown in Table C6. From the table, it will be noted that not all subjects did identical loads; however, the majority in each sex was tested at load 150 KgM/min. (31 boys, 33 girls, see Table C9). The mean oxygen consumption for each sex, including all test loads, was .788 l/min. for the boys and .7241 for the girls. While $D_L CO$ is dependant on $\dot{V}O_2$, from the mean values at load 150 KgM/min., at which 80% of the D_L measurements were made, it is apparent that no consistent difference in $\dot{V}O_2$ for age (or size) was observed. Since there was no significant correlation between D_L and $\dot{V}O_2$ in these data (the range of VO_2 being presumably too small for this correlation to be demonstrated), a regression was calculated using height only as the independant variable.

Table C8 lists the regression equations thus calculated for $D_L CO$ for boys and girls separately and combined. Also included in this table are the regressions on height for $D_L CO$ per litre mid-lung capacity ($D_L CO/MCO$) and per litre $\dot{V}O_2$ ($D_L CO/\dot{V}O_2$). It will be noted that the inclusion of mid capacity ($FRC + 1/2\ V_T$) and oxygen consumption in the regressions as additional measured variables has increased rather than decreased the standard error (SE) of the predicted $D_L CO$ value.

TABLE (C 4) CORRELATION COEFFICIENTS FOR LUNG VOLUMES AND FLOW RATES

CONTROLS

SEX	Regression Used: Dependant Variable (Y)	Regression Used: Independant Variable Ht(cms.)	Dependant Variable (Y): FRC	VC	TLC	RV	ERV	MMFR	FEV
Boys	-	-	.865	.900	.902	.710	.820	.826	.835
	log	-	.861	.895	.906	.671	.804	.812	.848
	-	log	.857	.893	.894	.701	.814	.817	.825
	log	log	.857	.891	.901	.664	.803	.806	.840
	-	$()^3$	.877	.910	.913	.723	.830	.839	.852
Girls	-	-	.757	.809	.845	.597	.707	.518	.750
	log	-	.775	.804	.843	.625	.680	.477	.718
	-	log	.755	.806	.842	.597	.702	.509	.745
	log	log	.775	.802	.843	.626	.678	.470	.716
	-	$()^3$	.759	.813	.847	.595	.712	.535	.758

Highest correlation value underlined

- indicates no transformations.

TABLE (C 5) SUMMARY OF WORKLOADS USED IN D CO MEASUREMENTS

CONTROLS

Load KgM/Min.	Males	Females
100	6	7
150	31	33
200	1	2
250	1	1
350	1	
TOTALS	40	43

TABLE (C 6)

DIFFUSING CAPACITY RESULTS - CONTROLS

SEX	AGE Yr.	NO.	LOAD KgM/Min.	OXYGEN CONSUMPTION MN.	S.D.±	RANGE	DIFFUSING CAPACITY MN.	S.D.±	RANGE
Boys	10-12	6	100	0.645	.104	.55-.82	18.6	2.2	15.3-21.3
	10-12	7	150	0.752	.049	.69-.85	21.1	3.3	16.2-25.1
	10-12	1	200	0.89			18.2		
	12-14	12	150	.785	.084	.62-87	22.8	4.1	18.2-31.0
	12-14	1	350	1.420			33.1		
	14-16	9	150	0.834	.093	.73-.95	30.4	4.8	22.0-36.2
	16-18	3	150	0.678	.131	.54-.80	27.8	2.0	26.5-30.1
	16-18	1	250	1.110			36.3		
Girls	8-10	1	100	0.780			17.4		
	10-12	6	100	0.592	.121	.39-77	17.0	1.97	13.5-19.4
	10-12	6	150	0.761	.070	.39-.78	19.5	3.6	14.7-24.5
	12-14	11	150	0.754	.140	.59-1.06	21.0	2.1	17.9-24.2
	12-14	2	200	.881	.058	.84-.92	17.6	2.4	15.9-19.3
	14-16	10	150	0.678	.072	.58-.79	24.9	4.1	18.8-31.8
	16-18	6	150	0.727	.129	.53-.89	26.0	5.5	21.3-38.8
	16-18	1	200	0.909			29.2		

TABLE (C 7) TABLE OF 'P' VALUES SHOWING SEX COMPARISON - CONTROLS

VARIABLE	SEX		P
	MALE	FEMALE	
AGE		+	0.504
HEIGHT	+		0.640
WEIGHT	+		0.997
FRC	+		0.825
VC	+		0.064
TLC	+		0.293
RV		+	0.269
ERV	+		0.151
MMFR	+		0.901
FEV	+		0.234
$D_L CO/VO_2$	+		0.723
$D_L CO/MC$	+		0.112
$D_L CO/Kg$	+		0.009*
VO_2 /LOAD	+		0.041*

+ = higher values

* = significant

TABLE (C 8) REGRESSION FOR DIFFUSING CAPACITY ON HEIGHT - CONTROLS

SEX	Dependant Variable (Y)	Constant	Coef.(b) of Indepednant Variable (X)	Standard Error of (b)	Standard Error of (Y)	Correlation Coefficient (r)
M	$D_L CO$	-34.54	0.384	0.041	3.36	0.840
F		-47.97	0.457	0.082	3.70	0.660
M & F		-39.18	0.407	0.039	3.69	0.755
M	$D_L CO/VO_2$	-19.23	0.331	0.080	6.55	0.558
F		-56.29	0.572	0.162	7.29	0.483
M & F		-27.97	0.387	0.074	6.94	0.503
M	$D_L CO/MC$	-16.74	0.042	0.021	1.70	-0.313
F		(refused)				
M	$D_L CO$	5.11	5.22×10^{-6} *	0.555	3.36	0.837
F		-1.11	6.41×10^{-6} *	0.157	3.71	0.654
M & F		2.72	5.59×10^{-6} *	0.531	3.65	0.760

Independant Variable ..(X) - Height in cms.

* - Height^3 in cms.

TABLE (C 9) TABLE OF $D_L CO$ STATISTICS -
SEX COMPARISON - CONTROLS

AGE	LOAD	NOS. M/F	P
10-12	150	7/6	0.4336
12-14	150	12/11	0.2204
14-16	150	9/10	0.0276 *
14-18	150	3/6	0.5509
		31/33	0.0833

Likewise, in our data on $D_L CO$, the use of $Height^3$ as the independant variable (rather than the linear value of Height) had no effect on reducing the SE of the dependant variable.

The above data for $D_L CO$ are shown in graphic form in Fig.(C22). It is noted that the regression line for boys lies above that for girls for any given height. However, the two lines fall within one standard error for either line (SE for boys only shown). There was no significant difference in the slopes of the two lines although the intercept for the regression equation for girls was significantly less ($P < .001$) than for the boys. The results were tested for sex differences using the Student's t-test and comparing girls and boys of equivalent age and/or height (e.g. boys of 10 years tested against girls of 10 years) at a given workload (Table C9). The only significant difference was in the age range 14-16 years ($P=0.0276$); it was noted however that boys as a group had the higher diffusing capacities, a difference significant at the 8% level ($P=0.0833$), but not at the usually accepted statistically significant level of 5%. The correlation for D_L on height is higher for boys ($r=.840$) than for girls ($r=.660$), though both are significant (Table C8).

In Fig.(C23), Dl has been plotted using $Height^3$ as the independant variable to permit a comparison with the resting data of Demuth (107) who has choosen to express the relation of D_L to Height as an exponential function. The linear regression

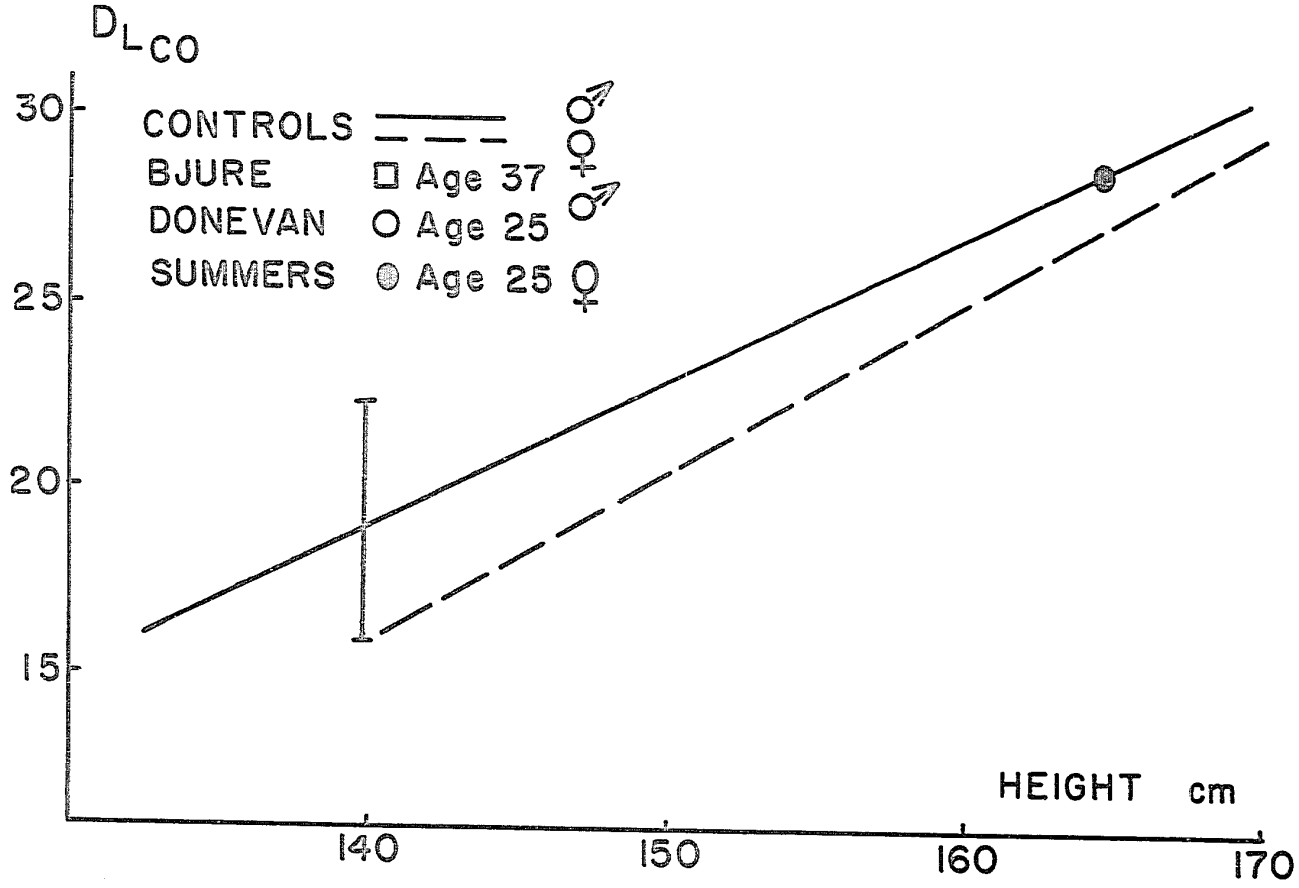


FIG. C_{22} - Exercise D_L in Controls ($\dot{V}o_2$ = ≃ .75ls) in relation to height. Bar indicate SE of boys regression line.

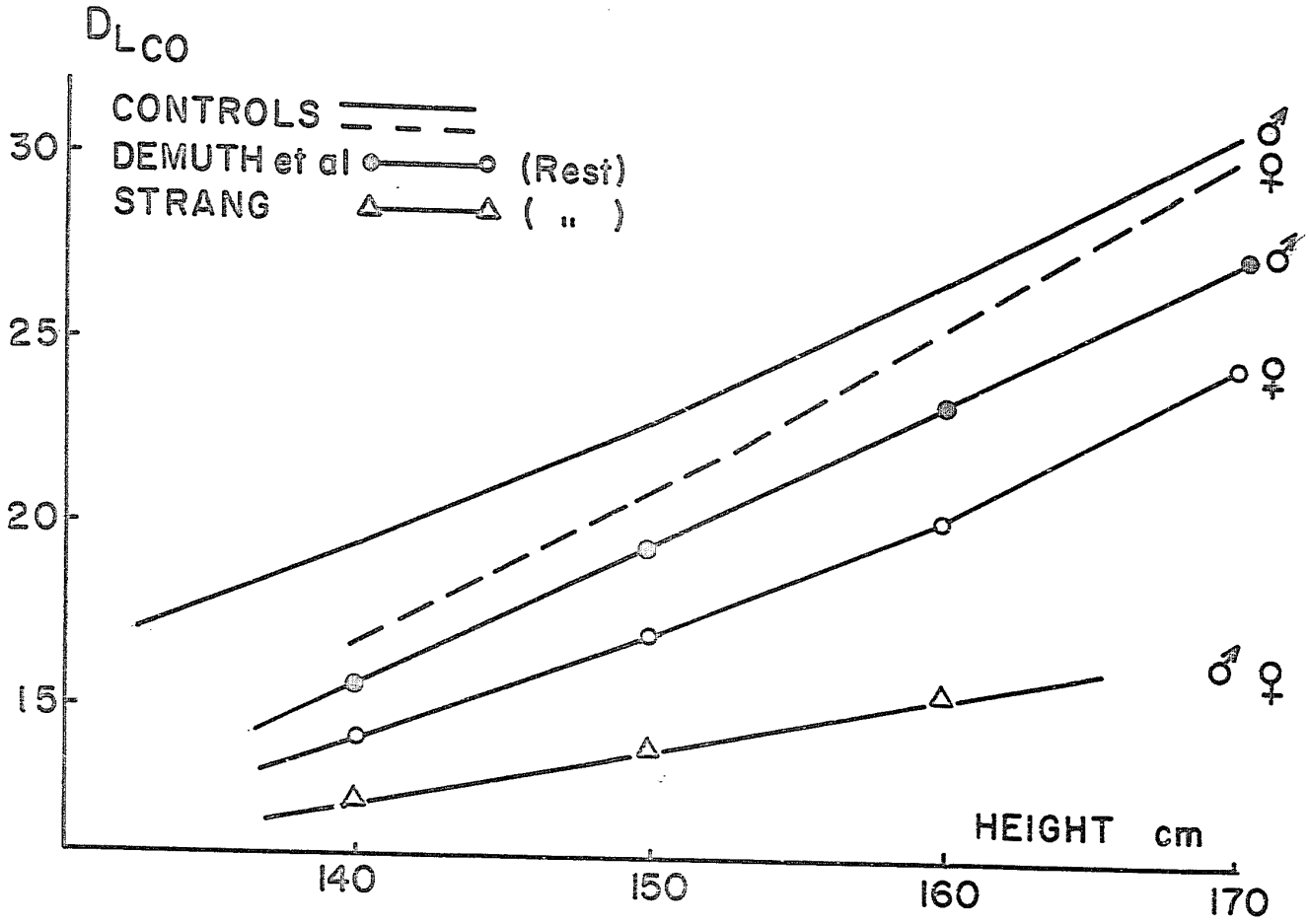


FIG. C_{23} - Exercise D_L of Controls to height and compared with resting data of other children.

for Strang's (333) data is also shown. Of interest here is that each study shows the similar effect of growth on diffusing capacity. The difference in resting values in the studies of Demuth and Strang can doubtless be attributed to the different methods employed. The exercise values of the present study bear the same relationship to height as do the resting data of Demuth through the height range studied, though they are of course higher because of recognized increase in $D_L CO$ on exercise. The relation of D_L to lung volumes is shown in Figures C25 - C26. The plot, showing the relationship of the two regressions for D_L and V_C, on height (Fig. C24) shows the lines for boys and girls cross and lie close to each other throughout the height range of the data. Also included on this figure is this relationship found by Demuth (107) in resting subjects and by Holmgren (182) in exercise of greater intensity than ours. The linear relation of these two variables appears remarkably constant whether in rest or in light to heavy exercise.

Fig.(C25) shows the scatter of individual points for D_L in relation to TLC, and with respect to the regression of Demuth (107) for resting D_L. In Fig. C26, D_L is expressed in relation to lung volume (D_L/TLC) against height, sexes separate. In this respect, beyond height 150 cms., the sexes are similar and this relation D_L/TLC does not alter in the taller subjects. At shorter heights however, this ratio is greater in boys.

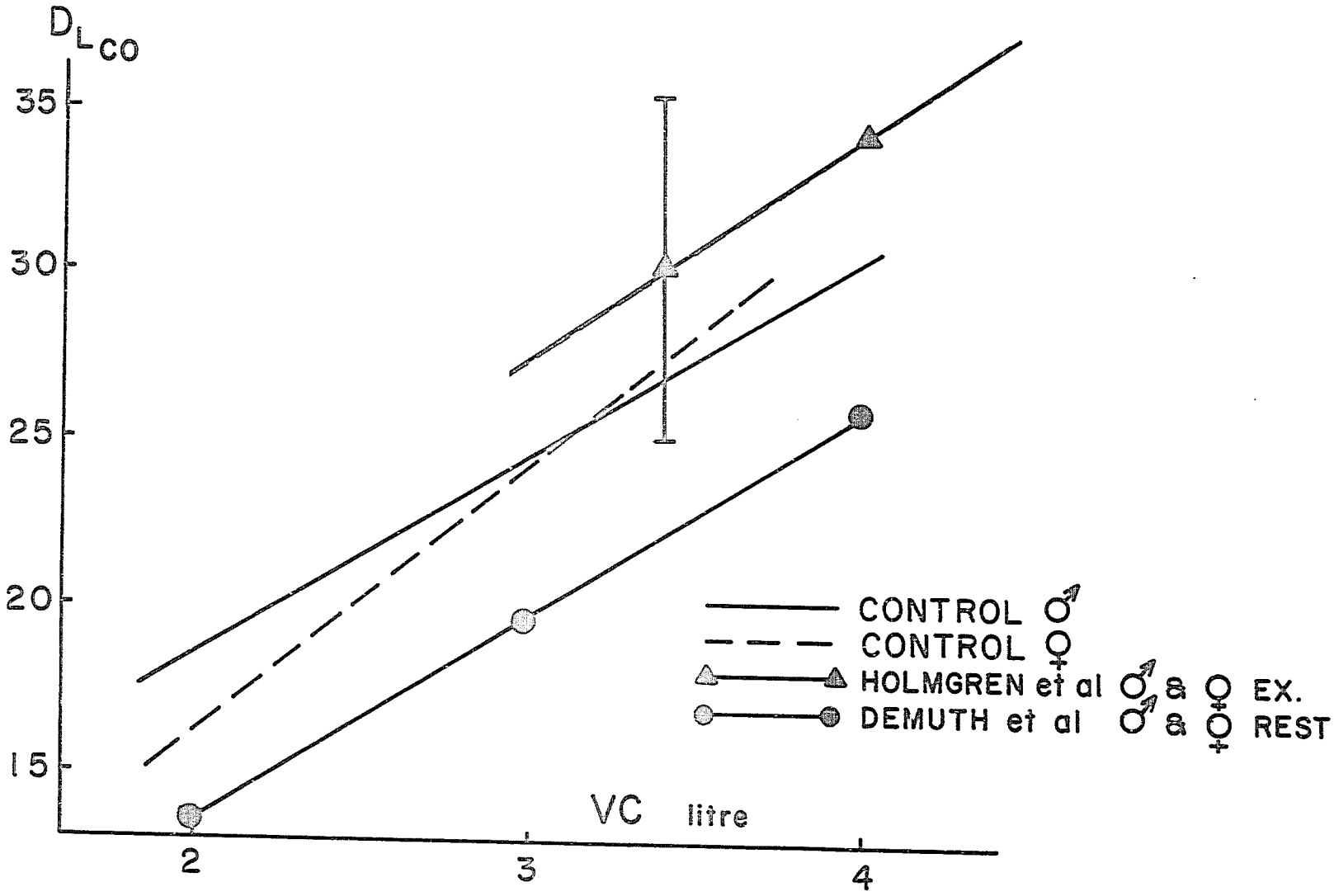


FIG. C_{24} - Exercise D_L of Controls in relation to VC and compared with results of others at rest (Demuth) and at higher exercise (Holmgren - Bar indicates 1 SD).

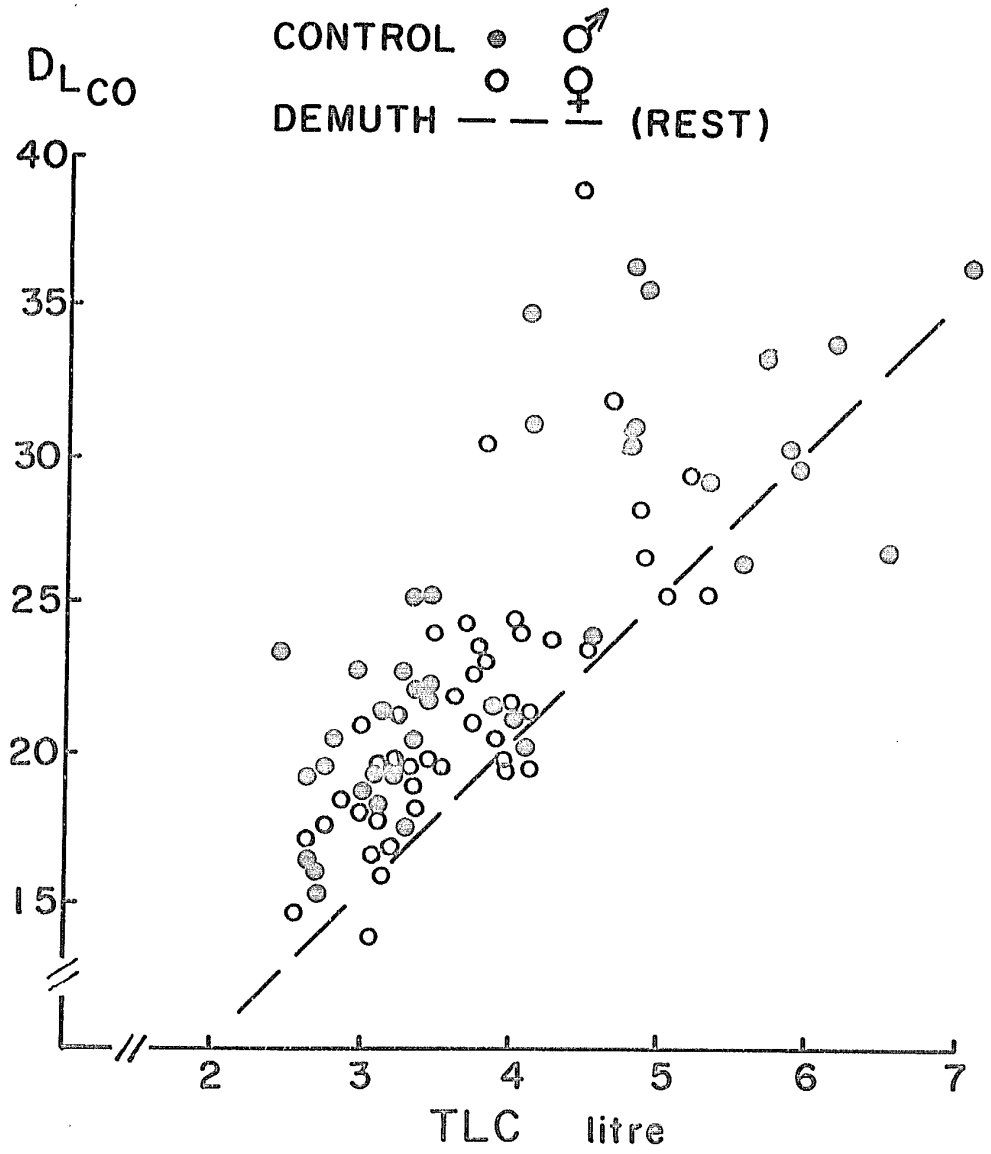


FIG. C_{25} - Individual results of exercise D_L Controls in relation to TLC and compared to resting data of others.

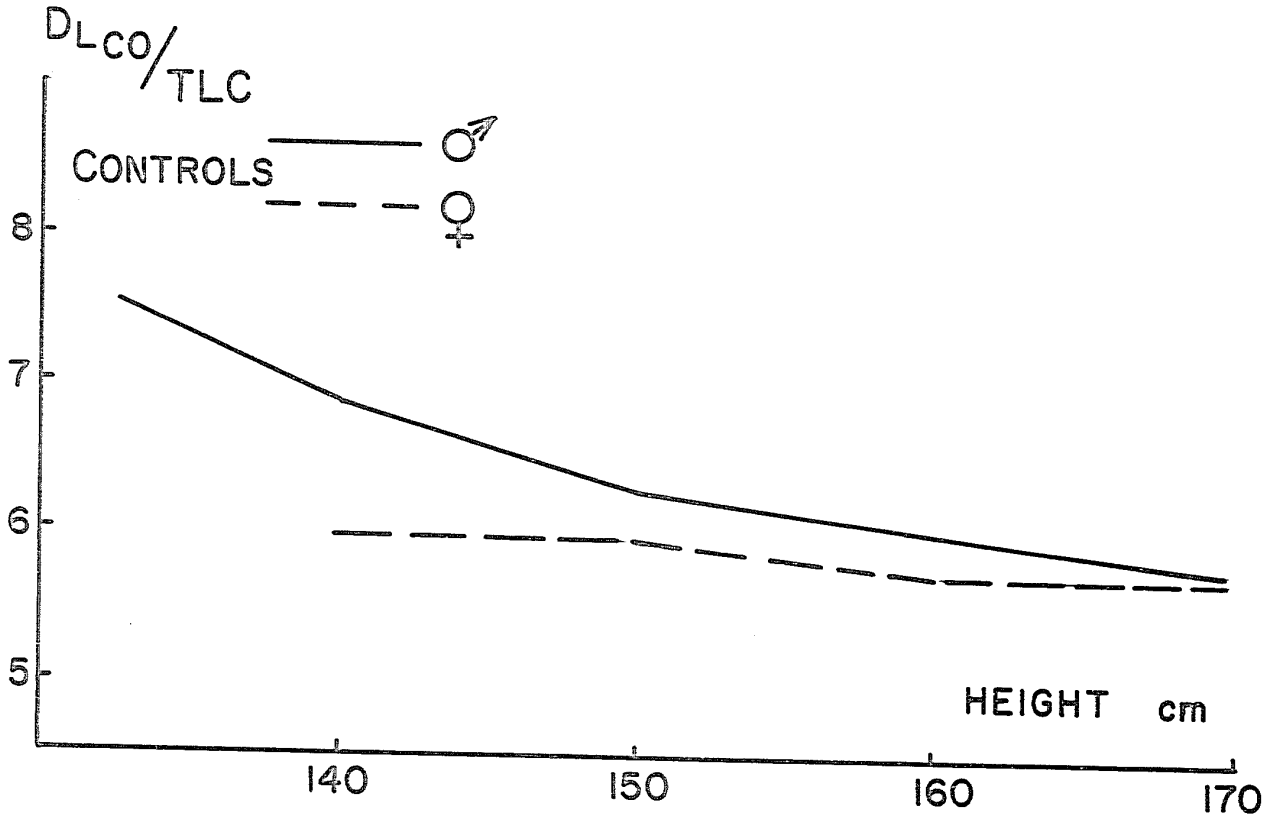


FIG. C_{26}- Rates D_L/TLC in boys and girls of Control group and related to height.

Discussion:

From the various analysis attempted, it is concluded that for this data, height alone is as good a predictor for exercise $D_L CO$ as any combination of multiple variables tried and is superior to any other single variable, even Height^3, for predicting $D_L CO$.

This is in contrast with lung volumes which, it has been shown (107,206,264), are best described by taking account of the 3-dimensional aspect of the lungs. Because of the high correlation of lung volumes to body size, the relationship of $D_L CO$ to lung volumes could be expected to be similar to that for body size, hence no attempts were made to include lung volumes in the regression analysis.

The original findings of Bohr (58) and Marie Krogh (225) that in an individual the exercise D_L was higher than that at rest has never been doubted. This has been attributed in part to an increased alveolar ventilation which accompanies exercise, but more particularily to an increase in pulmonary capillary blood volume (198.305) because of increase perfusion to the upper lobes of the lungs (115,358). It was therefore to be expected that for a given oxygen uptake, the child with the larger lungs, and presumably larger Vc, would have a higher exercise diffusing capacity. Indeed, the present study on 83 normal children indicates that there is a direct linear

relationship (Fig.C22) and a close correlation (Table C8) of exercise D_L to height.

Comparison with published data is shown in Fig.23 which includes the resting studies of Strang (333) and of Demuth et al(107), for comparison with the present exercise data. In general, the rest and exercise studies each show a similar relation of Dl to height, although the regression of Strang indicated less dependancy of Dl on height that that found by Demuth et al and ourselves. Three factors undoubtedly contribute to these differences: firstly, Strang has combined the sexes; secondly, his study does not include any subjects over age 14 years and thirdly, he has employed linear regression whereas data of Demuth and ourselves is described in Fig.C23 by a curvilinear function. The lower resting values of Strang compared to the data of Demuth and associates is doubtless attributable to the steady-state method which, as cited above, yields lower values at rest than the rebreathing method employed by Demuth et al.

Morphometric measurements have suggested that the number of alveoli in the lung does not increase after the age of 10. It was thought that the analysis of D_L (a function of surface area) in relation to VC or TLC (a function of lung size) in the growing child might throw some light on this postulate. Thus, it can be shown mathematically that if expansion alone accounted for the increasing volume of the lung with growth, and if changes

in D_L are a function of increase in surface area alone, the ratio of D_L to TLC would decrease with growth to the almost constant ratio found in the adult. Demuth's data showed however, that the ratio was constant in the growing lungs as well, and he argued from this that the lung must grow by the addition of new alveoli (even up to age 18 years). Our results on girls, and on boys of height 150 cms., are in agreement (see the constant relation of D_L/TLC in Fig.C26). However, this relation does not hold for our boys at the shorter heights. in whom the findings are certainly consistent with the view that their lungs (in the shorter boys) may contain more smaller alveoli/unit lung volume, and have as a consequence a greater effective surface area than the lungs of girls of equivalent height. In the above speculation, no mention has been made of Vc, which, it must be recalled, is much more significant as a factor for increasing D_1 than is Dm. Thus an increase in pulmonary capillary blood volume might affect a decrease in surface area (and Dm) caused by progressive expansion of existing alveoli and so maintain the constant D_L TLC ratio with growth; indeed this seems the more likely explanation.

The consistant sex difference in D_1 found in our exercise study is of the same magnitude as that found in adults (33) and children (107) at rest. This difference has been attributed to difference in lung volume, so that the ratios D_L/TLC and D_L/VC show no sex difference. Our exercise results are in

agreement with the above authors except in the shorter boys as discribed above.

Extrapolation of our findings on children to adult data is shown in Fic.C22 were points for adult subjects measured by a similar method and at the same oxygen consumption are shown. (55,117,338) Extensive comparisons cannot be made since our measurements were confined to this group to only one exercise level ($\dot{V}O_2$ = .75l/min); furthermore, our data does not permit extension of the regression line beyond height 173 $\pm$ 4.13 cms., and thus allow direct comparison of D_l with male adults of the heights indicated. However, this figure suggests that the boys at these heights might have a higher Dl for comparable $\dot{V}O_2$ than adults (age 25 years). One wonders if the aging process in respect to D_L, as found by Donevan (117) is already becoming apparent in males even at the age of 25 years. On the other hand, the single point for the adult female (338) lies slightly above that of the child.

3. CARDIO-RESPIRATORY FUNCTIONS - Results

A summary table (C10) describes the test exercise loads employed as well as numbers by age group studied at each level. As indicated, there were 176 determinations of exercise cardiac output included in the final results and from these results various regression equations were derived, as shown in Table (C11).

Recalling that there were 83 individuals in the Control group, and that each subject was tested at 3 exercise levels, it follows that 73 measurements of $\dot{Q}c$ were excluded. Criteria for exclusion of a measurement were as follows:

1) Failure to equilibrate with the test gas, as indicated by a falling $F_{A\,N_2}$ and rising $F_{A\,N_2O}$ during the test period. Both of these conditions could be determined directly from the tracing.

2) An $F_{E\,N_2O}$ which was equal to or slightly below the $F_{A\,N_2O}$ value. Since the expired sample contained the dead space gas (and therefore having a similar concentration to the test gas), the expired value should always have been of higher concentration than the alveolar gas. Incomplete expired bag rinsing, or leaks at the mouthpiece during the test are among the more feasible explanations for such conditions.

3) Miscellaneous technical errors accounted for rejection of some results. For example, if the oxygen consumption

TABLE (C10) CARDIO-RESPIRATORY TEST WORKLOADS BY AGE SHOWING NUMBERS - CONTROLS AND SWIMMERS

Sex	Age Group	LOAD* 100 C	100 S	150 C	150 S	200 C	200 S	250 C	250 S	300 C	300 S	350 C	350 S	400 C	400 S	450 C	450 S	550 C	550 S
Boys	8-10				1		1		1										
	10-12	4	1	8	2	9	1	4	1		2		1				1		
	12-14			8	2	3		6		3	2	4					2		
	14-16			6	4			1		5	3	1	1	1		4	4	1	
	16-18			3	4						3	4	1				3	3	1
	18-20				1						1						1		
TOTAL	C 78 S 45	4	1	25	14	12	2	11	2	8	11	9	3	1	0	4	11	4	1
Girls	8-10		1		2	1	1				1								
	10-12	4	4	9	2	9	5	4			4	1							
	12-14			10	5	2		7	2	2	3	6	2				3		
	14-16			6	4			5		4	4	5		1		3	4		
	16-18			5	2			2		5	2	3				4	2		
	18-20				2						1		1				2		
TOTAL	C 98 S 59	4	5	30	17	12	6	18	2	11	15	15	3	1	0	7	11	0	0
TOTALS	176 104	8	6	55	31	24	8	29	4	19	26	24	6	2	0	11	22	4	1

C-Controls
S-Swimmers

* Kgm/Min.

TABLE (C 11) CARDIO-RESPIRATORY REGRESSION EQUATIONS - CONTROLS

Sex	Y	Regression Equation	S.E. of Coef.(b) *		Correlation Coef (r) *		S.E.of Y
M	$\dot{Q}c$	= 1.64 + 5.82 ($\dot{V}O_2$) + 0.313 (Age)	0.721	0.091	.744	.528	1.55
		= 1.63 + 6.83 ($\dot{V}O_2$)	0.703				1.66
		=-3.91 + 5.96 ($\dot{V}O_2$) + (0.041(Ht).	0.741	0.015		.497	1.59
		= 3.21 + 0.386 ($\dot{V}O_2$ x Age)	0.036		.778		1.56
		= 2.54 + 0.038 ($\dot{V}O_2$ x Ht.)	0.0036		.767		1.59
F	$\dot{Q}c$	= 3.66 + 4.99 ($\dot{V}O_2$)	0.684		.599		1.71
		= 2.33 + 4.75 ($\dot{V}O_2$) + 0.114 (Age)				.260	1.70
M	HR	=198.8 +24.1 ($\dot{V}O_2$) -6.03 (Age)	6.76	0.853	.050	-.525	15.0
		=261.5 +23.1 ($\dot{V}O_2$) -0.921 (Ht.)	6.77	0.133		-.521	15.1
F	HR	=145.4 +45.5 ($\dot{V}O_2$) -2.755 (Age)	7.21	0.826	.454	-.137	18.4
		=278.9 +48.7 ($\dot{V}O_2$) -1.138 (Ht.)	6.88	0.231		-.233	17.5
M	SV	=-76.0 +31.1 ($\dot{V}O_2$) +0.681 (Ht.)	5.79	0.116	.635	.659	12.4
F	SV	= 33.9 +15.4 ($\dot{V}O_2$) +0.489 (Ht.)	5.20	0.189	.360	.334	12.4
M	$\dot{V}O_2$	= 0.460 + 0.0021 (Load)	0.0001		.889		0.122
		= 0.620 + 0.0022 (Load) -0.0146 (Age)		.0076		.438	0.120
F	$\dot{V}O_2$	= 0.410 + 0.0023 (Load)	0.0001		.864		0.125
		= 0.649 + 0.0025 (Load) -0.0222 (Age)	0.0001	0.0057		.261	0.119
M	$(A-V)O_2$	=10.10 + 2.02 ($\dot{V}O_2$)	0.95		.238		2.24
F		= 6.50 + 5.28 ($\dot{V}O_2$)	0.85		.538		2.12
M	$\dot{V}$	=10.70 +17.19 ($\dot{V}O_2$)	1.43		.791		3.52
F		= 5.69 +22.99 ($\dot{V}O_2$)	1.48		.828		3.91

Y - Dependant Variables

* S.E. and (r) follow same order as shown in regression equation.

Independant Variables - Age in years, Ht.in cms., Load in cms., Load in KgM/min., $\dot{V}O_2$ in litres.

determination was not acceptable, the cardiac output measurement for the test load was similarily discarded.

The regressions for $\dot{Q}c$ and the other values derived from this measurement (stroke volume, arterio-venous O_2 difference) were thus calculated from the 176 determinations. For $\dot{V}O_2$ there were 209 complete tests, for heart rate regressions 212, etc. Because of the variability of numbers employed, age, and test loads for each parameter, a summary table of mean values is not practical and results are presented by regression equations only.

Oxygen Consumption and Ventilation:

Regression equations, as given in Table C11, were derived from the 209 observations. These are plotted in Fig.C27 to show the relationship between sexes in the Control group.

Oxygen consumption (litres/min) is shown as a function of work load (KgM/min). The lines for each sex are virtually coincident and as would be expected,no difference in the regression euqations was found. In each sex the correlation coefficient of $\dot{V}O_2$ with load was high (males .889, females .864). Statistical comparison between sexes, the group divided by age, showed no significant sex difference at any workload, even when account was taken of the slight difference in body surface area (BSA). Similarily, when age groups within a sex were compared, this revealed no overall difference in O_2 requirements for a given exercise load for children of different ages. This is

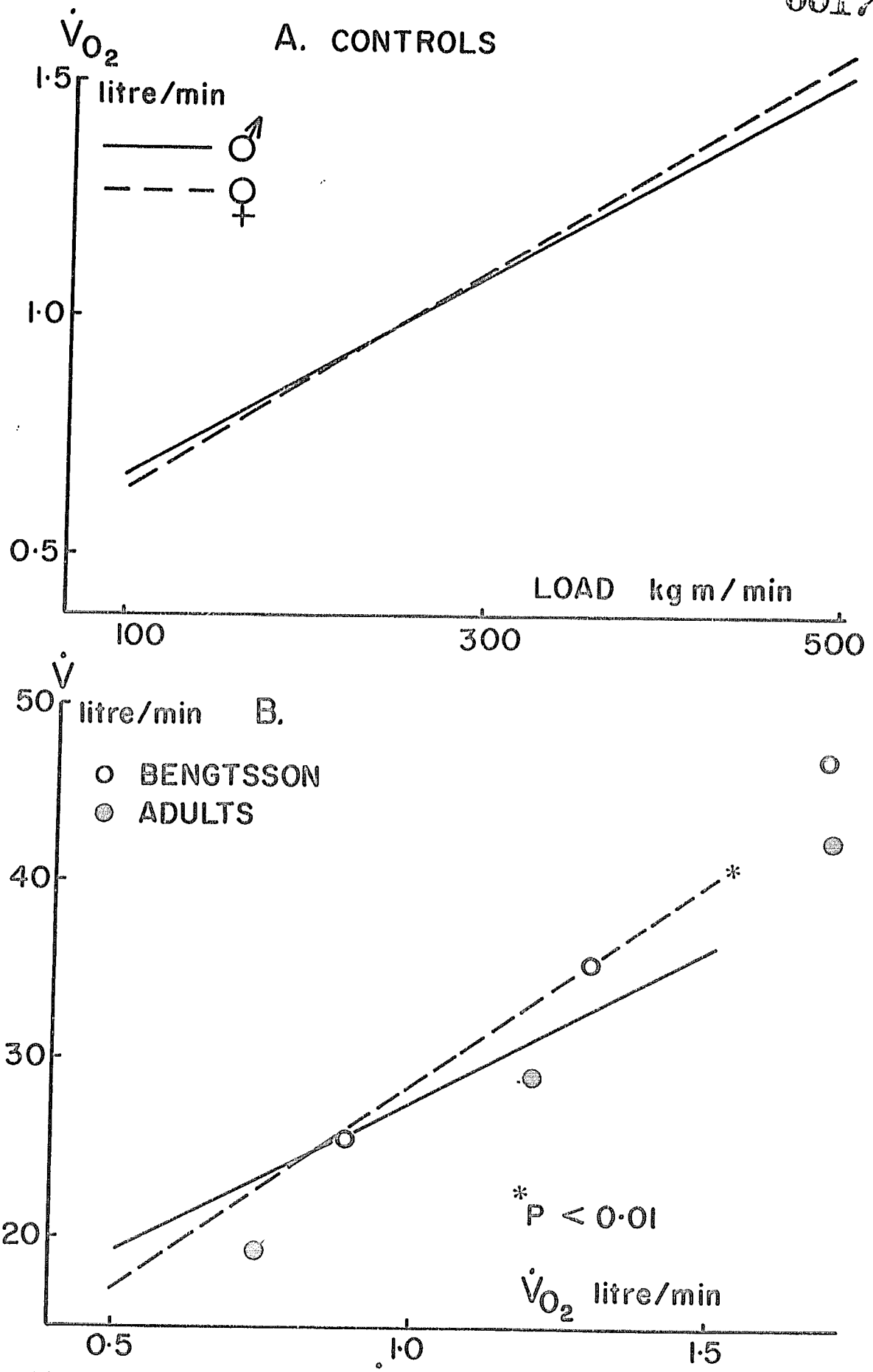


FIG. C_{27} - A. Relation of $\dot{V}o_2$ and work (KgM/min) in boys and girls of Control group

B. Sex comparison of $\dot{V}$ to $\dot{V}o_2$ in Controls and compared with mean values of other children and adults (39) ($^{M}P < .01$ indicates slope difference in regressions of Control boys and girls).

evident in Fig.C28 (B and C) where the multiple regressions for $\dot{V}O_2$ on load and age are shown in relation to workload. The difference with age was small in each sex, though slightly more marked in the females. The addition of age in the prediction equation had only a small effect on reducing the standard error of the predicted value (Table C11). The positive correlation of $\dot{V}O_2$ with age is then more an indication of the relationship of age to load, since the older subjects did more of the higher loads. It is of interest to note that at load 150 KgM/min., in both sexes when the 10-12 year age group was compared with the 14-16 group (numbers were 12 and 7 for males, 11 and 9 for females respectively), $\dot{V}O_2$ was significantly greater (P 0.0361) in the older boys, but lower (P 0.0364) in the older girls. Otherwise, in no case was there any difference in this respect.

Comparison of $\dot{V}O_2/M^2$ showed the younger boys consistently with higher values, often significantly so. This indicates the close relationship of $\dot{V}O_2$ to work rather than any real dependence of $\dot{V}O_2$ during exercise on body size. Support is seen for this in Fig.C28A. Here, mean values for adults (39) are shown in relation to our Control children with sexes combined. ($\dot{V}O_{2(adult)} = 0.432 +$ .0022 Load). The similarity is readily apparent. Also included are results of other studies made on children (42,99). It is noted the slopes of all lines are similar. Differences in the

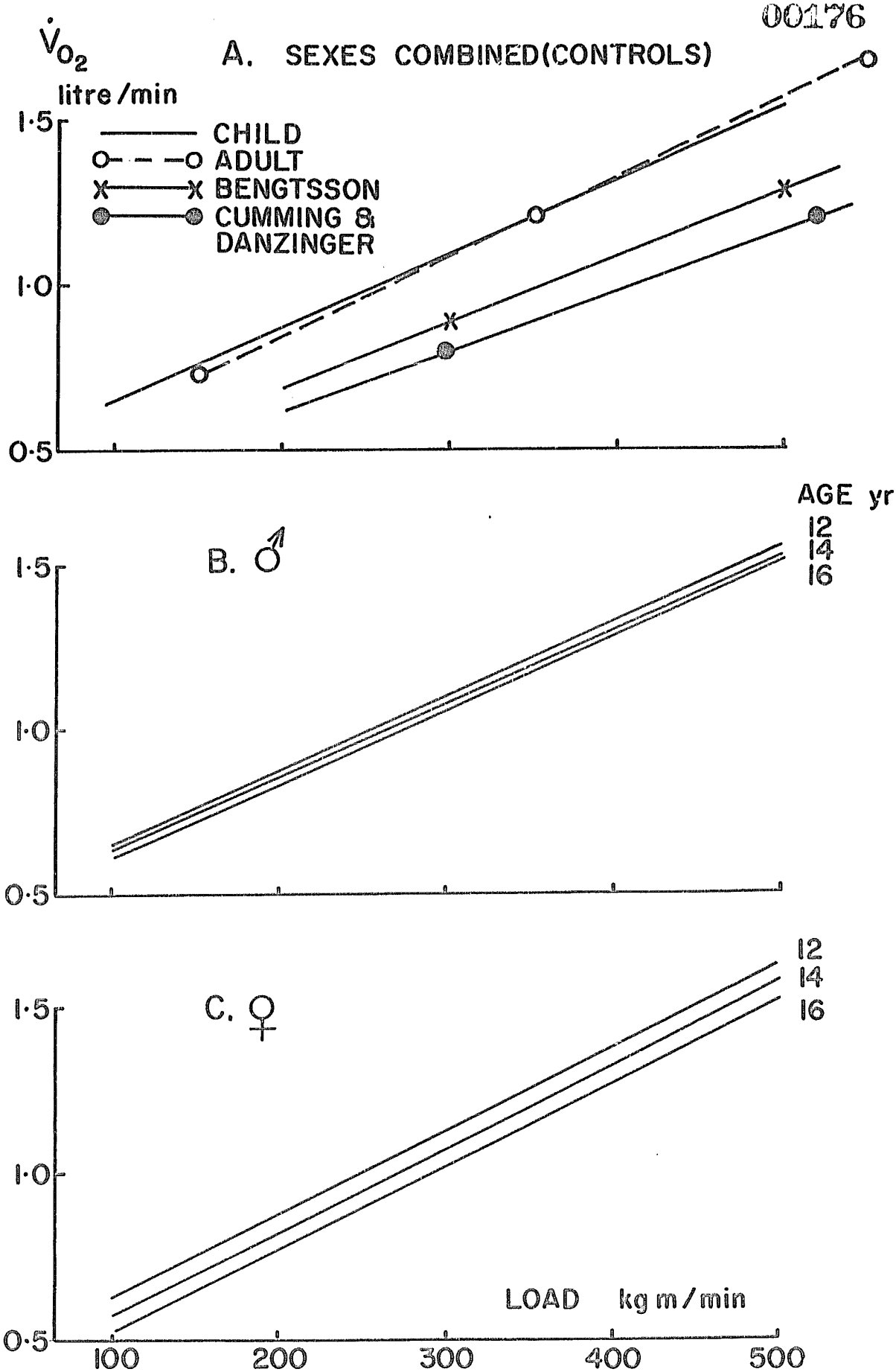


FIG. C_{28} - A. Comparison of Controls (sexes combined) with results of others, children and adults (39) showing $\dot{V}o_2$ - work relationship.

B & C. Age effect on $\dot{V}o_2$ - work relationship in Control boys (B) and

values for $\dot{V}O_2$ are attributable to ergometer calibration variations.

Ventilation (litres/min.) is plotted on the ordinate in Fig.C27B in relation to oxygen consumption. The two lines, showing the sex relationship cross at $\dot{V}O_2$ = .85 ls, which corresponds to the workload at which the greater number of determinations were made. The coefficient of regressions was found significantly greater in females ($P < .01$) indicating a higher ventilatory equivalent ($\dot{V}/\dot{V}O_2$) at the higher workloads in females. Conversely, the boys often, though not always, had the higher ventilation for the lower loads and this difference was significant at workload 150 KgM/min.(P 0.0244) where results on 30 males and 38 females are compared. The mean values for the combined sexes in Bengtsson's (42) study are shown to be in close agreement while those for adults (39) are lower.

Cardiac Output and Related Parameters:

Table C11 includes regression equations for males and females for cardiac output, and heart rate, the two measured values, as well as stroke volume and arterio-venous oxygen difference which were calculated.

Cardiac Output:

As shown by the above table, several regression equations for this function were derived. This analysis included the use

of single and multiple variables, with and without transformations. For comparison purposes, some of these are shown for males only. In the males the best fit of the data was with the multiple linear regression employing $\dot{V}O_2$ and age although this was only slightly superior to the regression using the product of these two predictors. The correlation of both age and $\dot{V}O_2$ with $\dot{Q}c$ was significant ($r = .528$ and $.744$ respectively) in the males though age was not significantly correlated to $\dot{Q}c$ in the females. Height correlated less well than age in males while in females the level of significance (F level) was too low to warrant inclusion of height in the regression equation.

Fig.C29 shows the plot of $\dot{Q}c$ as a function of age in relation to $\dot{V}O_2$. Three ages (10,13 and 16 years) are shown and illustrates the greater effect of age on $\dot{Q}c$ in males than in females. Values for a 25 year old adult (39) are shown (dashed line). Good agreement is seen in the predicted values for the 16 year old child and the adult males, especially at the higher levels of oxygen uptake, while in the girls the agreeement is best at the lower exercise levels. The slope of the regression line for adults was significantly less in males ($P < .05$) which again is in contrast with the females where no slope difference with the childrens' regression was found. Statistical analysis of $\dot{Q}c$ indicates that for a given workload $\dot{Q}c$ was consistently greater in the older boys though no such trend was observed in the girls. At no work level, where adequate numbers were available

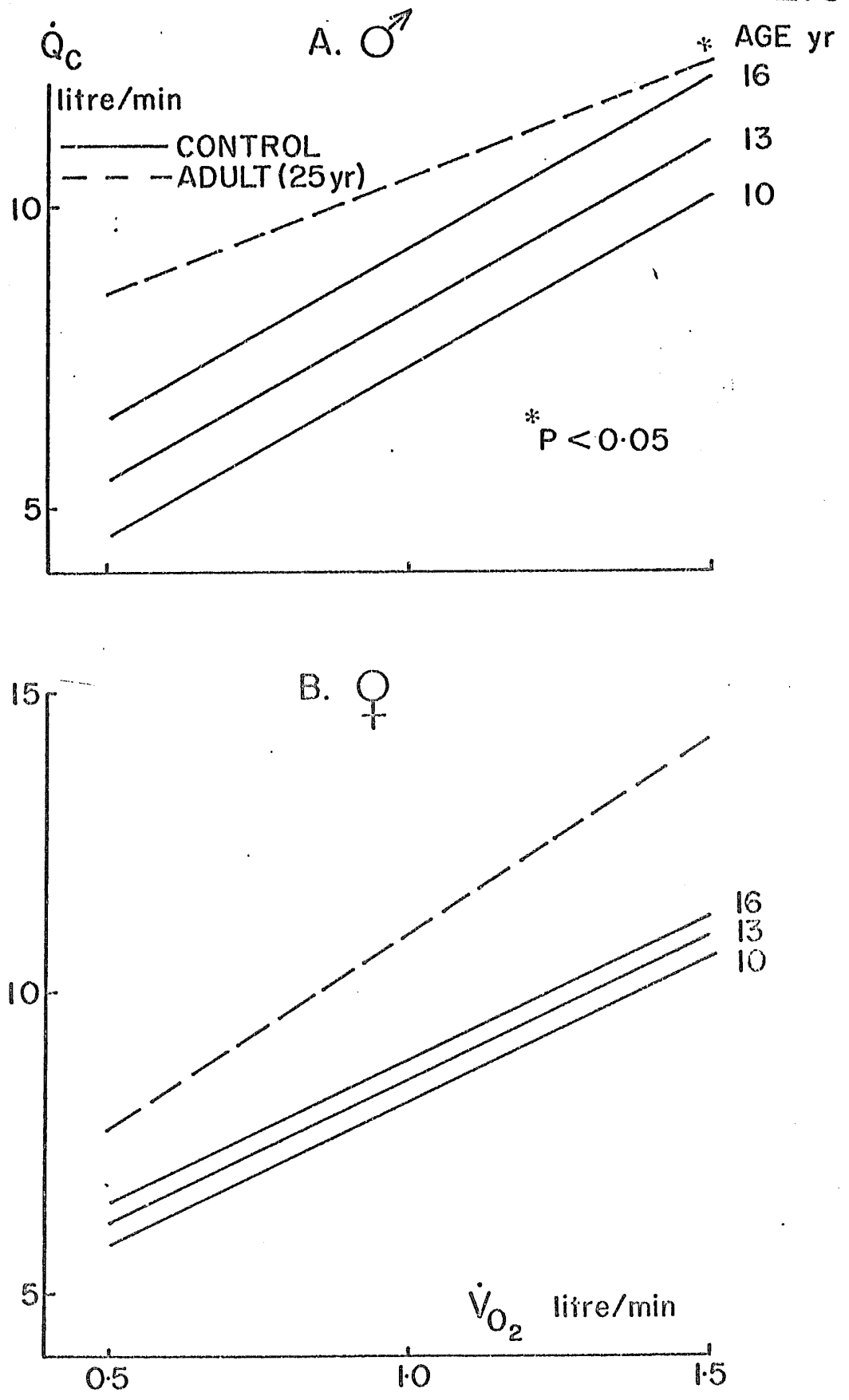


FIG. C_{29} - Relation of $\dot{Q}c$ to $\dot{V}o_2$ in Control boys (A) and girls (B). Results are also shown of the effect of age in children on this relationship and in comparison with adults (39)

to permit comparison, was this age difference in boys significant.

Fig.C30 shows the sex comparison in Controls at ages 10, 13 and 16 years. Because of the direct positive correlation of $\dot{Q}c$ with age in boys, and not in the girls, the comparison of sexes shows younger girls (age 10) to have higher cardiac output for a given $\dot{V}O_2$; this difference is reversed in the 16 year old child (i.e. boys greater). Predicted values for the 13 year old boys and girls are almost identical. Sex comparison by age group, using the 't' test, showed the same trend. $\dot{Q}c$ was higher in the younger females (up to age 14) at the lower workloads (up to 300 KgM/min.). However, older boys had consistently higher values at all worklevels and at the higher exercise loads this same trend was present in the younger boys as well. Rarely were these differences significant at the 5% level.

The relationship of heart rate to $\dot{V}O_2$, in respect to age, is presented in Fig.C31 and in respect to height in Fig.C32. The sex differences in exercise cardiac output as related to $\dot{V}O_2$ (see above) is shown to be similar in heart rate. The correlation with age was significant in boys but not in the girls.

Height correlated higher than age with pulse rate in girls although neither showed a significant relation (Table C11). The adult female predicted values lie below the line describing the HR-$\dot{V}O_2$ relationship for the 16 year old (Fig.C31) while the line for male adults crosses that of the 16 year old boy and

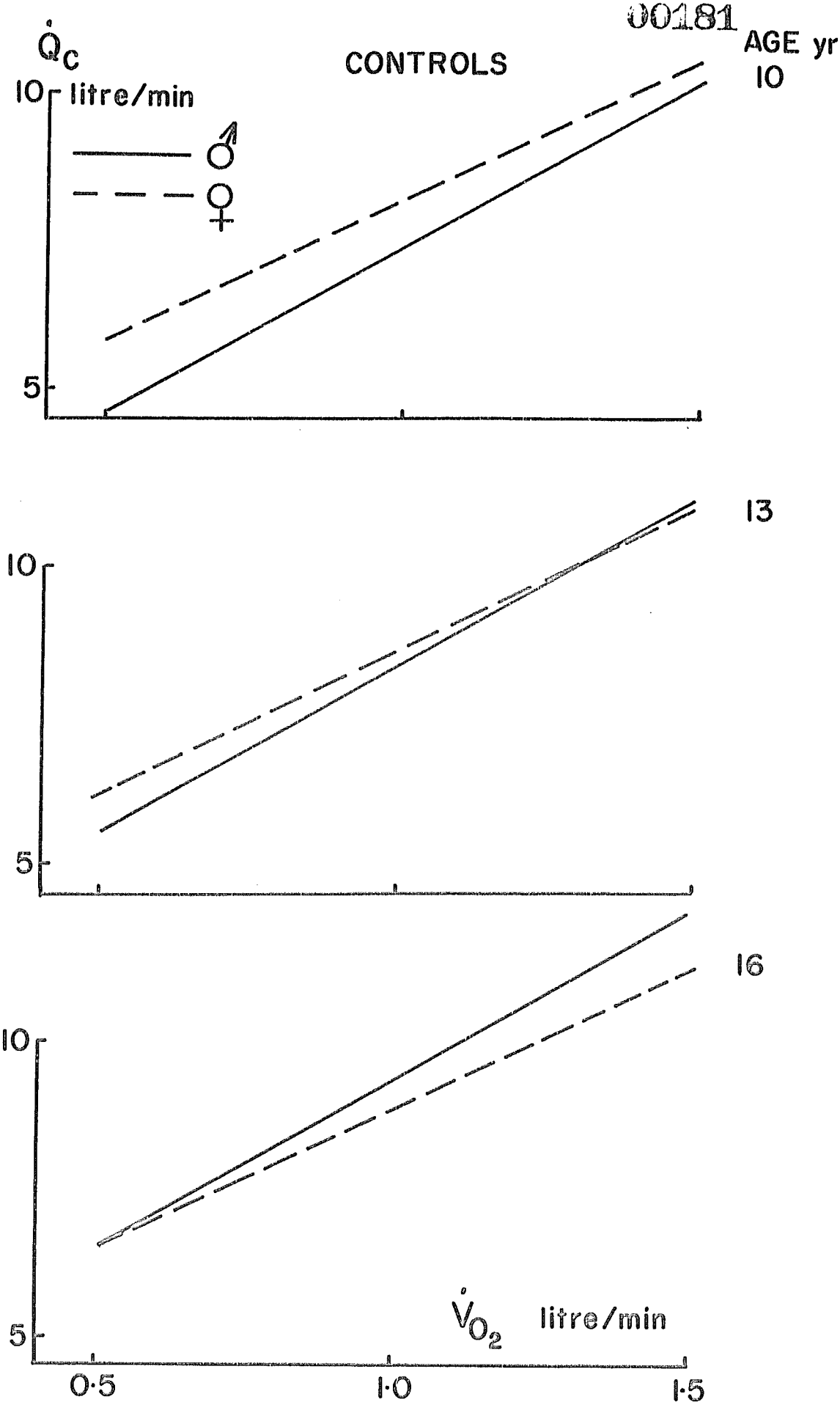


FIG. C_{30} - Sex comparison of $\dot{Q}c$ and $\dot{V}o_2$ in Controls at ages 10, 13 and 16 years.

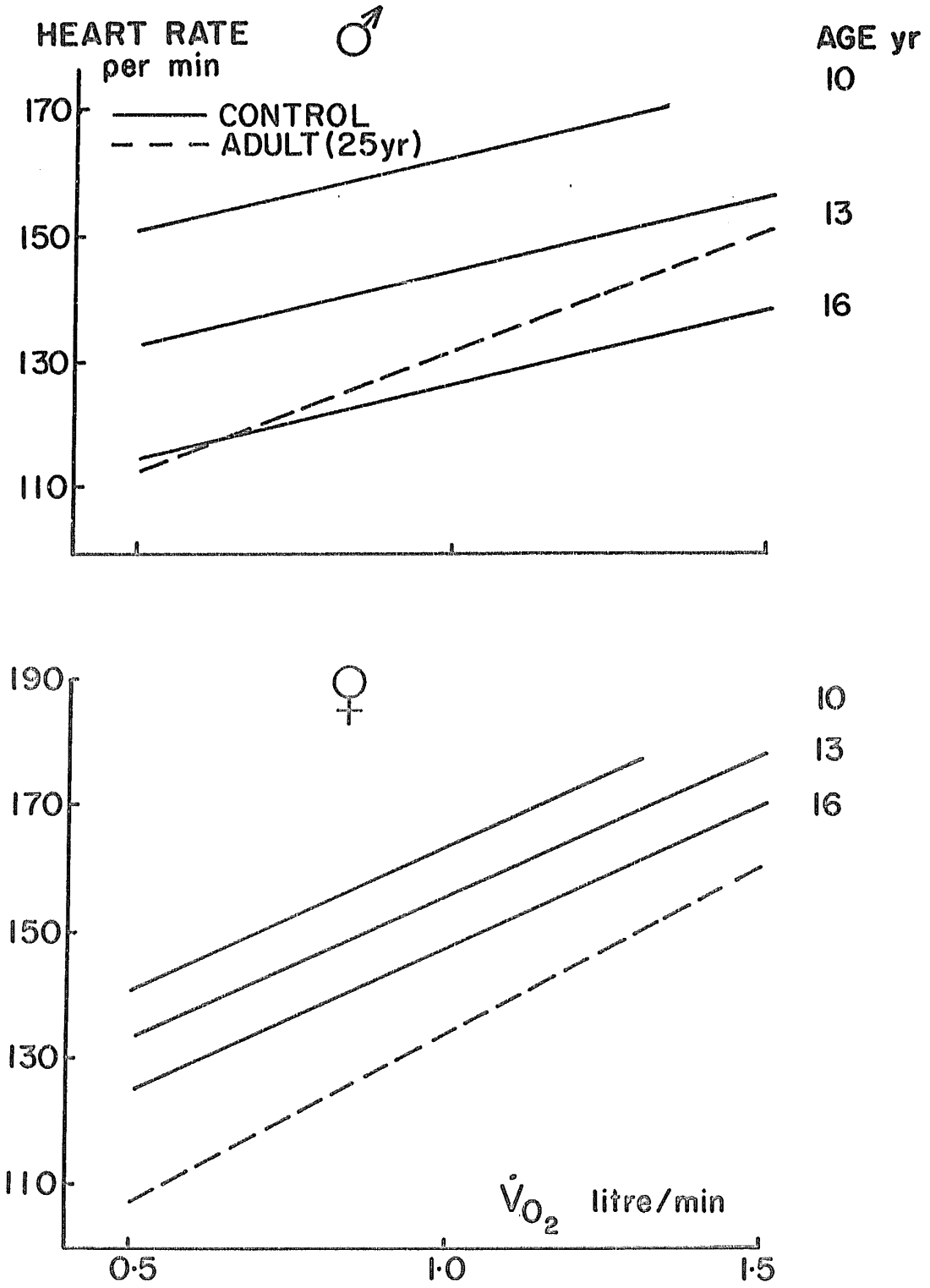


FIG. C_{31} - Heart rate in relation to $\dot{V}O_2$ in Control boys and girls and showing the age effect on same. Adults (39) indicated by dashed line.

has the steeper slope (i.e. adult has a greater increase in HR for given change in $\dot{V}O_2$). When adults are compared with children on the basis of height (Fig.C32) a similar relation as seen in age persists in males but the lines for the 170cm girl and 25 year old woman are coincident.

Stroke volume is shown in Fig.C33. As seen in Table C11 stroke volume correlated significantly with both $\dot{V}O_2$ and height in males (r=.635 and .659); these correlations in females were poorer (r= .360 and .334). Age was not tried in the regression analysis for stroke volume. It was indicated (above) that $\dot{Q}c$ was greater in the older (or taller) male subject while heart rate was lower in relation to $\dot{V}O_2$. This indicates that SV increase with growth has more than offset the reduction in rate as a factor effecting cardiac output. The 170cm boy, in respect to SV, is similar to the adult male except at the lowest levels of $\dot{V}O_2$. The change in SV with height is less in girls than in boys. The relationship of SV to $\dot{V}O_2$ is similar in girls and adults; however, even at height 170 cms., these values are greater in the adult, for a given $\dot{V}O_2$.

Fig.C34 shows the sex comparison of heart rate and stroke volume, illustrated here at one height only (155 cms.). This height corresponds closely to an age 13 year old child, the age at which the $\dot{Q}c$-$\dot{V}O_2$ relationship was similar in boys and girls (Fig.C30). This figure indicates the higher heart rate,

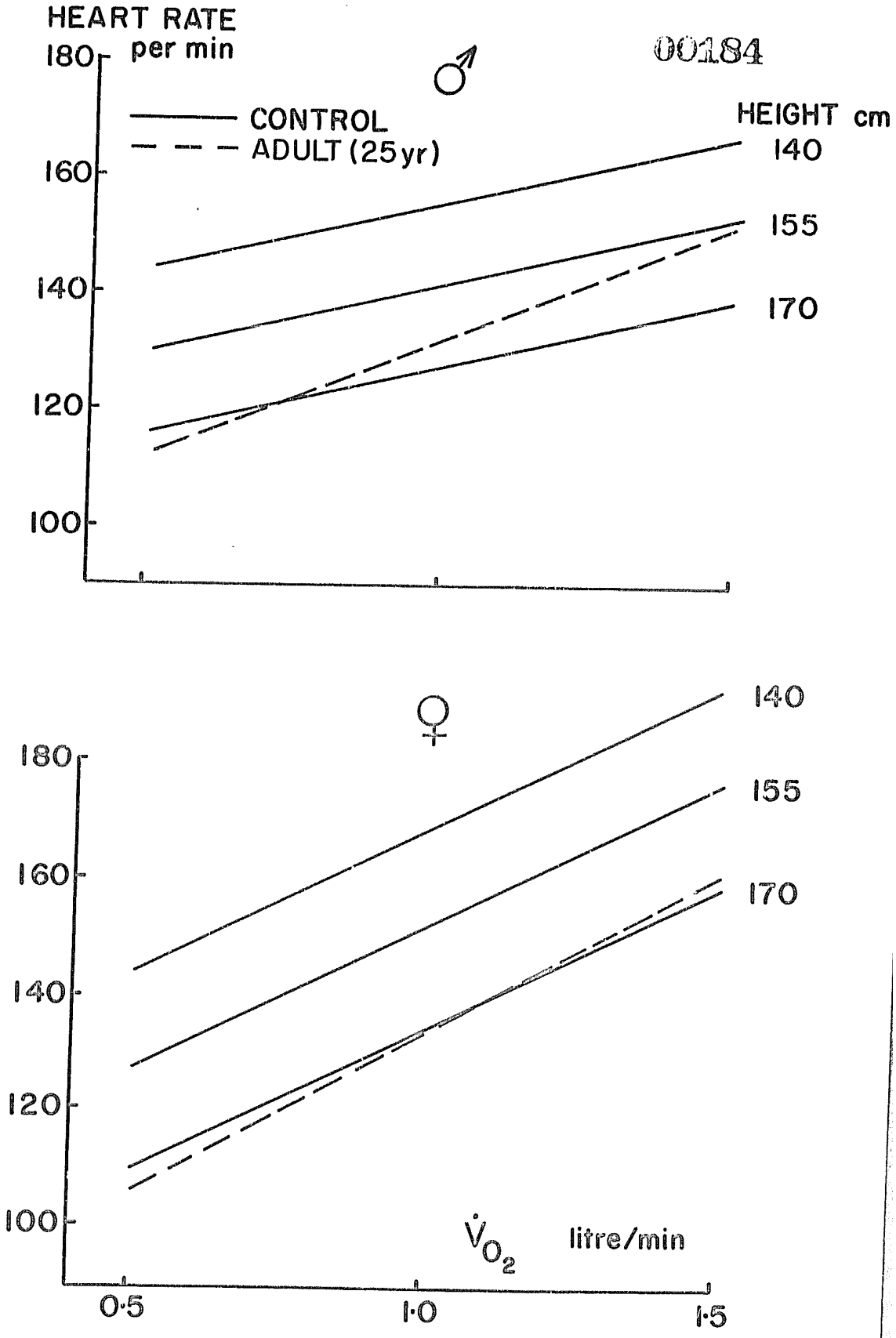


FIG. C_{32} - Heart rate in relation to $\dot{V}o_2$ in Controls, and showing the growth effect on this relationship. Comparison with adults (39) is indicated.

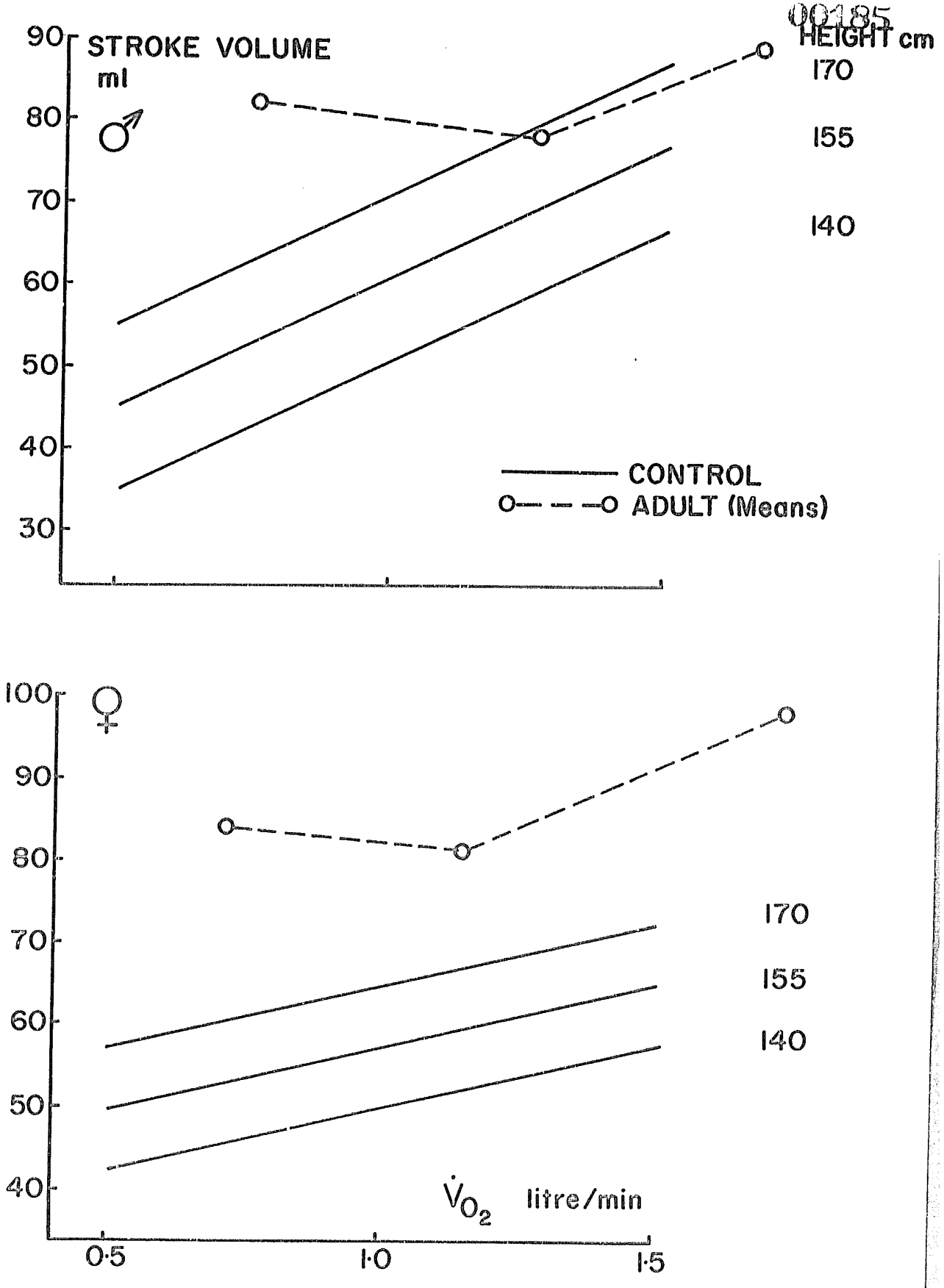


FIG. C_{33} - Stroke Volume - $\dot{V}o_2$ relationship in Controls showing the growth effect and compared with adults (39).

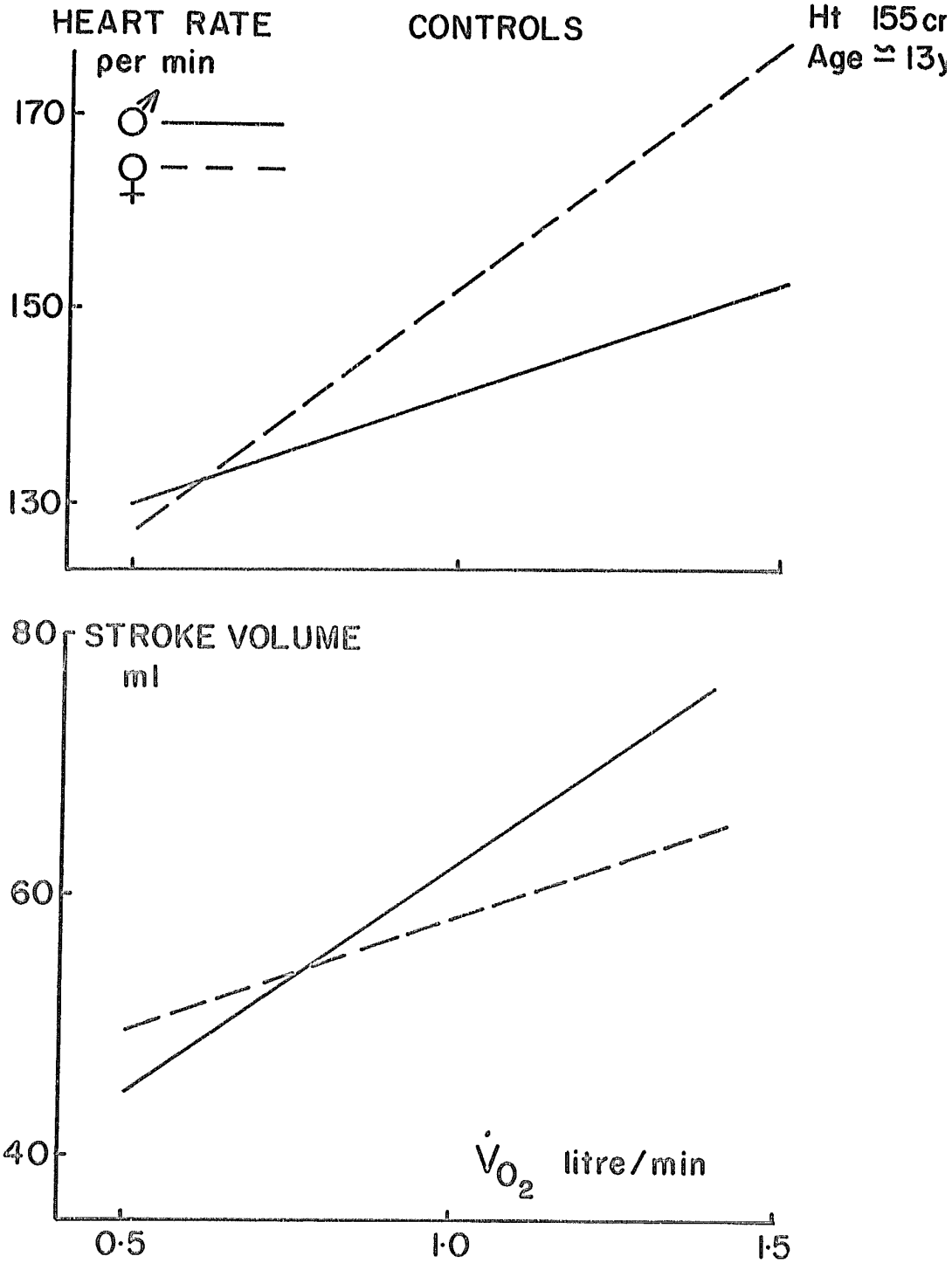


FIG. C_{34} - Sex comparison of H.R. and S.V. related to $\dot{V}o_2$ in Controls at age 13 years.

lower stroke volume of girls as compared with boys which becomes apparent at the higher exercise loads. Almost without exception, the heart rate in any age group and work level was higher in females, though never was this difference significant at 5%. Comparing ages within a sex however, for any work load the younger child had the greater heart rate and in most age group comparisons at different workloads this was found significant. Similar statistical analysis for SV showed the older child had higher values for any workload, and except in the youngest age group the males had larger values than the females.

Arterio-Venous O_2 Difference:

There being no sex difference in respect of $\dot{V}O_2$, any sex difference observed in $\dot{Q}c$ is therefore reflected in this calculated value. Thus, it is seen in Fig.C35 that the (A-V) O_2 difference..or O_2 extraction..is lower in females at lower workloads and greater at higher intensities of exercise. This indicates the regression coefficient on $\dot{V}O_2$ is greater in females and the difference in slopes is highly significant ($P < 0.02$). As expected, this same observation is evident when statistical comparison of sexes for any age is made. No consistent trend was found when ages within a sex were compared and for this reason age is not included in the regression equation. It is noted that there was a significant positive correlation of

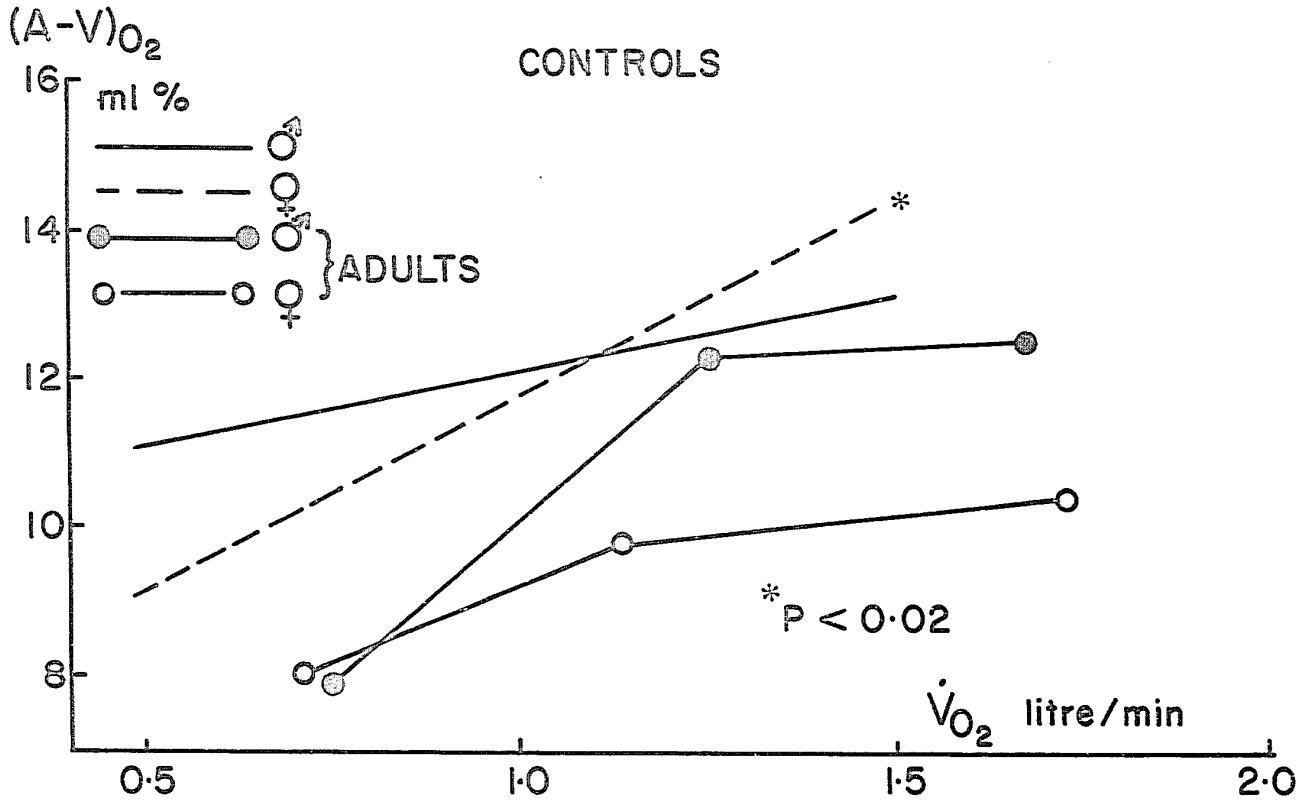


FIG. C_{35} - Relationship of $(A\text{-}V)_{O_2}$ Difference and $\dot{V}o_2$ in Controls and in comparison to adults (39) ($^{*}P < .02$ indicates slope difference in Control between boys & girls).

$\dot{V}O_2$ on $(A-V)_{O_2}$ in females (r= .538) which is in contrast with the males (r= .238).

Adult values (39) are shown (Fig.C35) and differences are the reciprocal of those seen above in $\dot{Q}c$ (i.e)adult females are markedly lower than the children; agreement in males is good except at low levels of $\dot{V}O_2$.

Discussion:

Ventilatory Functions: The close similarity of $\dot{V}O_2$ in child and adult clearly indicates the constancy of efficiency in exercising man, and in respect to ventilation as well as $\dot{V}O_2$ the adaptations to exercise in child and adult are similar, although minute ventilation is slightly greater in children (Fig.C27B). The age effect of $\dot{V}O_2$ in children was slight, and, in view of the directional trend (i.e. less in older) indicates the negligible effect of body surface area on the O_2 requirement in exercise.

Cardiac Functions:

In general, the adaptations to exercise in respect to $\dot{Q}c$ are similar in adults and children, with heart rate playing a greater role in this regard in the younger rather than older child. Or conversely, as the heart grows, and stroke volume becomes greater, the heart rate is reduced. These are expected findings. Also expected, and observed, was the sex difference in respect to heart rate (higher in females for a given $\dot{V}O_2$)

(see Fig.C34), which agrees with the results of others (13,256).

There are however a few findings which might not have been anticipated. However, conclusion should only be drawn in the light of the following precautions. The unexpected findings may in part be attributed to the distribution of ages studied in the children, in particular with respect to older children of which comparatively few are included. Also, we have perhaps not been fully justified in 'forcing' linear equations on the data; nonetheless, since the primary purpose of this control study was to permit comparison with swimmers of comparable age, this manoeuvre seemed justified.

The most surprising aspect of these results is the different relation of the male and female child to adults regarding cardiac output (Fig.C29). The results for males are as might be expected; thus as Fig.C29 indicates, the 16 year-old boy shows the response of $\dot{Q}c$ to work very similar to that of the man, indicating that at age 16 years he has almost reached maturity in this respect. The heart rate (Figures C31-32), stroke volume (Fig.C33) and O_2 extraction (Fig.C35) all support this conclusion. In contrast is the difference in $\dot{Q}c$ between Control girls and women (Fig.C29B) whereby, from the slope of the lines, as well as the slight age difference in children, no maturing effect on $\dot{Q}c$ is seen in the girls. The author is inclined to regard this more as 'artifact' than fact. The few older girls in the study (i.e. 10 age 15 + years) may allow the younger children to bias the regression

line and determine its slope. In addition, it is quite possible that these older girls are late maturers; this is suggested by their shortness (Fig.C1) and also by the fact that they were participants in a playgrounds summer program, which in general does not appeal to young post-puberty girls. It is perhaps not fair, in a study comparing child and adult, to mix pre-and post-puberty girls, particularily since the child-bearing age seemingly elevates $\dot{Q}c$ in relation to $\dot{V}O_2$(39). The heart rate response to $\dot{V}O_2$ however does suggest the 170 cm. girl is adult (Fig.C32) though the stroke volume for this height is below that of women.

The similarity of sexes in children up to age 13 years in respect to $\dot{Q}c$ is apparent, at which age the $\dot{Q}c$-$\dot{V}O_2$ relation is similar (Fig.C30). However, as shown in Fig.C34, a clear sex difference is already apparent not only in respect to heart rate (lower in boys) as shown by others (13) but in stroke volume which is larger in boys.

Finally, it is of interest to find that the young child for a given $\dot{V}O_2$ has a lower $\dot{Q}c$, and correspondingly higher A-V O_2 difference (since there was no difference in the $\dot{V}O_2$-work relation) than adults. Assmussen might regard this as a decreased efficiency of the O_2 delivery system in the young child as suggested in his review (8). If this were so, it would not seen compatible with some other physiological functions which deteriorate with age (33). A more feasible explanation to the author is as follows;for a given $\dot{V}$(

the young child is operating at a higher fraction of his maximal ability, and correspondingly greater A-V O_2. In relation to adults, the child must have a lower maximal cardiac output (as Johnson's study (198) suggests), has a lower maximal $\dot{V}O_2$ (13) while his maximal arterial O_2 content is not different. Hence, for a given $\dot{V}O_2$ he must perform at closer to his maximal levels in respect to this function. Presumably, if these functions were expressed as % of maximal, there would be no difference.

PART IV

Chapter 7. Project Swimmers
..subjects
..testing procedure

1. A.Physical characteristics - results

   B.Lung volumes - results

   C.Lung Flow Rates - results
   ..discussion

2. Diffusing Capacity - results
   ..discussion ..comparison of children and adults
   ..comparison of swimmers and control

3. Cardio-respiratory Functions
   ..results ..oxygen consumption and ventilation
   ..cardiac output and related parameters
   ..discussion

PROJECT SWIMMERS:

The children comprising this group were selected from three different swim clubs in the City of Montreal. Each was engaged in regular, strenuous year-round training. No effort was made to randomize their selection. Since the project was planned to permit study on a longitudinal basis, with testing at yearly intervals, more of the younger age group were chosen initially, in the hopes that these children would continue swim training and thus be available for follow-up studies.

At the onset, the coach of each team was approached and advised of the nature and purpose of the study. This was followed by distribution of letters of information and consent forms to parents. No member of a swim club who indicated a desire to participate in the program was refused. Because of this plan, the group referred to herein as swimmers was not comprised only of the best swimmers of each club although most of the best swimmers of each swim team did participate.

Initially, 70 children were studied in Year I, (38 boys and 32 girls). Forty-six (46) of the original group returned in Year II. Because of the number of withdrawals, 16 young swimmers were added to the group, making a total of 62 studied in Year II. Forty-seven of this number returned in Year III, 24 of whom were in the original 70 children at the start of the study. The high 'mortality' rate was due primarily to

out-of-town moves while several discontinued competitive swim training.

Table S1 summarizes their physical characteristics and includes any swimmer who was studied in the 3 year period; each was counted as a 'new' subject at each annual return visit. Thus, in Table S1, the 71 boys and 73 girls are comprised of 79 different individuals. The table below indicates the number of individuals, and years studied;

Years Studied	Boys	Girls
1	12	11
2	14	18
3	12	12
	38	41

Seven of the 86 individuals tested were excluded for technical reasons.

TABLE (S 1) PHYSICAL CHARACTERISTICS - SWIMMERS

SEX	AGE GROUPING (years)	NUMBER *	MEAN AGE (years)	MEAN HEIGHT (cms.)	MEAN WEIGHT (kgms.)
Boys	8-9.9	4	9.07	131.83	27.96
			.54	2.79	1.89
	10-11.9	16	10.98	141.26	35.22
			.51	5.20	5.06
	12-13.9	20	12.92	151.74	45.26
			.50	6.08	5.37
	14-15.9	16	15.09	168.96	58.66
			.50	8.07	9.54
	16-17.9	13	17.17	175.28	72.22
			.48	4.53	6.86
	18-19.9	2	18.50	175.5	76.55
				4.53	.29
Girls	8-9.9	7	9.00	129.81	28.10
			.52	11.13	5.97
	10-11.9	21	11.19	143.70	37.44
			.47	6.90	5.57
	12-13.9	26	12.83	155.57	45.40
			.47	6.75	5.92
	14-15.9	13	15.00	161.92	55.32
			.51	4.43	6.89
	16-17.9	5	16.80	163.17	59.20
			.48	4.13	4.17
	18-19.9	1	18.50	172.80	65.40

*..Repeats on an individual counted as a new subject.

Testing Procedure:

For testing, the swimmers were divided into two groups according to the month of the year in which they visited the Laboratory. The June group consisted of members from the two smaller swim clubs and testing was done during the last ten days of this month. Testing for the December group was planned to coincide with the mid-term school holidays and, except for Year II of the study, testing was done at this time. In Year II, because of out-of-town swim meets, testing was made during the following month.

In each of the 3 years, lung volumes and flow rate measurements were made. In Year I, determination of exercise $D_L CO$ and $\dot{V}O_2$ at one level of exercise (3 mph, 3% slope on the treadmill) were performed. In Year II, two determinations were made at different exercise loads on the bicycle ergometer, one of which required a similar oxygen uptake to that in the test exercise for Year I. The testing in Year III consisted of similar measurements ($D_L CO$ and $\dot{V}O_2$) at exercise levels similar to Year II plus an additional exercise load of higher intensity. In addition, exercise cardiac output measurements were made at each of these exercise loads in Year III.

The procedure followed during the testing was similar to that described above for the Control group, except that when repeat $D_L CO$ measurements were made (Years II & III) the re-breathing procedure as described by Henderson and Apthorp (172).

was followed after each test to permit COHb correction.

Results:

In presenting results of the longitudinal study of the swimmers, comparisons are made with the Control group. Both groups were studied in the same laboratories under similar conditions. Because of the duration of the study, it was not possible to have the same technical assistants throughout. However, each technician had been trained in the same department and followed similar testing procedures; furthermore, the techniques used, and for the most part the equipment employed, was the same for the duration of the study. It was hoped that these precautions minimized the effects on results due to technical variation.

Data processing was carried out in a manner similar to that for Controls. For purpose of group comparisons, multiple statistical anlysis were performed; in addition a comparison was also made using regression analysis.

PHYSICAL CHARACTERISTICS:

The physical characteristics of the swimmers are presented in Table S1, and these are graphically displayed in Figures S1 and S2. Mean values for height and weight are shown in relation to age. Table S5 summarizes the statistical findings, showing the group differences with sexes separate and combined.

In respect to age, there was no overall difference (P 0.5325) although male swimmers and Control females were slightly older than those of the same sex of the opposite group. The swimmers were taller at any given age after 12 years, a significant difference prevailing in girls between ages 12-16 years. They also weighed more in relation to age than did the Controls (Fig.S2) although the differences are less marked than for height and in no age group were the differences statistically significant at the 5% level. This meant that the Controls tended to be slightly heavier for a given height than the swimmers. In general, however, overall results of their physical characteristics showed few marked differences from the Controls.

Table S4 summarizes the sex differences among swimmers. The males were significantly older than the females (P 0.0217) which also resulted in significant differences in both weight (P 0.0038), and height (P 0.0274). The growth pattern of the sexes was similar to that for the Controls (Controls shown in Fig.C3).

TABLE (S 2) MEAN VALUES FOR LUNG VOLUMES AND FLOW RATES

SWIMMERS - MALE

	AGE (yrs.)	NO.	HT. (cms.)	WT. (Kgms.)	VC (ls)	ERV (ls)	FRC (ls)	RV (ls)	TLC (ls)	MMFR (l/sec.)	FEV l/min.)
	8.00	1	128.5	26.00	1.86	0.26	1.19	0.93	2.79	1.56	45.00
	9.57	7	134.09	29.17	2.21	0.71	1.44	0.73	2.94	1.85	57.86
SD±	.98		2.88	2.00	.23	.06	.31	.30	.47	.39	9.84
	11.50	20	144.35	42.39	3.01	0.88	1.63	0.76	3.76	2.72	85.26
SD±	1.36		3.20	9.40	.84	.32	.65	.41	1.15	.79	24.54
	12.50	12	153.40	45.00	3.20	0.92	1.62	0.69	3.89	2.74	87.40
SD±	.80		2.94	4.67	.40	.16	.33	.29	.52	.63	11.65
	14.00	9	164.92	55.87	4.25	1.25	2.54	1.23	5.52	3.98	116.13
SD±	1.50		2.47	6.90	.78	.25	.63	.38	1.15	.62	22.65
	16.00	20	175.02	69.63	5.18	1.81	3.30	1.49	6.68	4.86	152.89
SD±	1.21		2.54	6.72	.81	.31	.41	.30	.90	1.10	26.64
	16.00	2	183.00	56.10	5.94	1.85	3.63	1.89	7.83	5.07	176.50
SD±	1.41		4.24	28.14	.06	.67	.20	.33	139	189	10.61

TABLE (S 3) MEAN VALUES FOR LUNG VOLUMES AND FLOW RATES

SWIMMERS - FEMALE

	AGE (yrs)	NO	HT. (cms.)	WT. (Kgms)	VC (ls)	ERV (ls)	FRC (ls)	RV (ls)	TLC (ls)	MMFR (l/sec)	FEV (l/min.)
+	8.50	2	115.55	21.15	1.36	0.41	0.94	0.99	2.36	1.86	45.50
SD-	.71		.07	1.63	.09	.06		.60	.69	.65	10.61
	8.00	1	129.5	24.50	1.83	0.56	1.01	0.45	2.80	1.69	54.00
+	9.91	11	135.95	32.69	1.92	0.63	1.42	0.77	2.69	2.27	58.87
SD-	1.14		3.25	4.38	.21	.09	.24	.25	.31	.57	11.01
+	11.20	15	146.01	37.85	2.53	0.79	1.55	0.76	3.29	3.16	80.96
SD-	1.01		2.36	3.61	.23	.19	.27	.26	.36	.78	12.26
+	12.36	22	154.53	45.24	3.01	1.03	1.98	1.07	4.08	3.46	97.34
SD-	1.47		3.00	4.88	.60	.16	.30	.64	.58	.65	16.49
+	14.11	19	163.78	55.44	3.82	1.26	2.35	1.16	4.92	4.14	117.38
SD-	1.45		2.85	6.12	.51	.28	.43	.34	.59	.91	18.35
+	16.33	3	172.27	64.13	4.83	1.27	2.45	1.18	6.01	3.75	131.00
SD-	1.53		0.68	1.10	.16	.10	.36	.26	.34	.69	3.61

TABLE (S 4) TABLE OF 'P' VALUES SHOWING

SEX COMPARISON.- SWIMMERS

VARIAVLE	MALE	FEMALE	'P'
AGE	+		.0217*
HEIGHT	+		0.0274*
WEIGHT	+		0.0038*
FRC	+		0.0108*
VC	+		0.0001*
TLC	+		0.0005*
RV	+		0.4787
ERV	+		0.0035*
MMFR	+		0.5887
FEV	+		0.0167*
$D_L CO/VO_2$	+		0.0029*
D CO 3/3	+		0.0174*
L 150	+		0.0021*
300	+		0.0008*
D CO/MC 3/3	+		0.0257*
L 150		+	0.7402
300		+	0.8392
$D_L CO/Kg$ 3/3	+		0.0733
150	+		0.3860
300	+		0.3461
VO_2 /LOAD 3/3	+		0.0821
150	+		0.0957
300	+		0.9807

+ higher values
* significant level

TABLE (S 5) TABLE OF 'P' VALUES SHOWING GROUP COMPARISON

VARIABLE	GROUP CONTROL	GROUP SWIMMERS	BOYS	GIRLS	COMBINED
AGE		+	0.3097		
	+			0.0585	0.5325
HEIGHT		+	0.2360		0.4588
	+			0.6376	
WEIGHT		+	0.0631		0.2876
	+			0.4524	
FRC		+	0.1078		0.2675
	+			0.6199	
VC		+	0.0007*	0.0315*	0.0001*
TLC		+	0.0034*	0.2051	0.0015*
RV		+	0.3454		0.9141
	+			0.3900	
ERV		+	0.0623	0.2515	0.0276*
MMFR		+	0.0454*	0.0100*	0.0017*
FEV		+	0.0033*	0.0007*	0.0001*
#$D_L CO$		+	0.0332*		0.1705
	+			0.6267	
$D_L CO/VO_2$		+	0.6708		
	+			0.1212	0.3781
$D_L CO/MC$	+		0.0020*	0.2697	0.0031*
$D_L CO/Kg$	+		0.1653	0.1987	0.0680
VO_2 (150 Kg)		+	0.7812		0.9326
	+		0.7418		

+ - Higher values
* - Significant
# - $D_L CO$ at loads 150 KgM/Min. only

TABLE (S 6) SEX COMPARISON IN RELATION TO HEIGHT - SWIMMERS

HEIGHT (cms.)	NUMBERS MALES/FEMALES	'P' Value VC	TLC
130-140	7/11	0.0227*	0.2358
140-150	20/14	0.0308*	0.1074
150-160	12/21	0.2827	0.3569 (-)
160-170	9/19	0.1455	0.1549
170-180	19/3	0.2332	0.1405
TOTAL	70/71	0.0001*	0.0005*

(-) females larger

* statistically significant

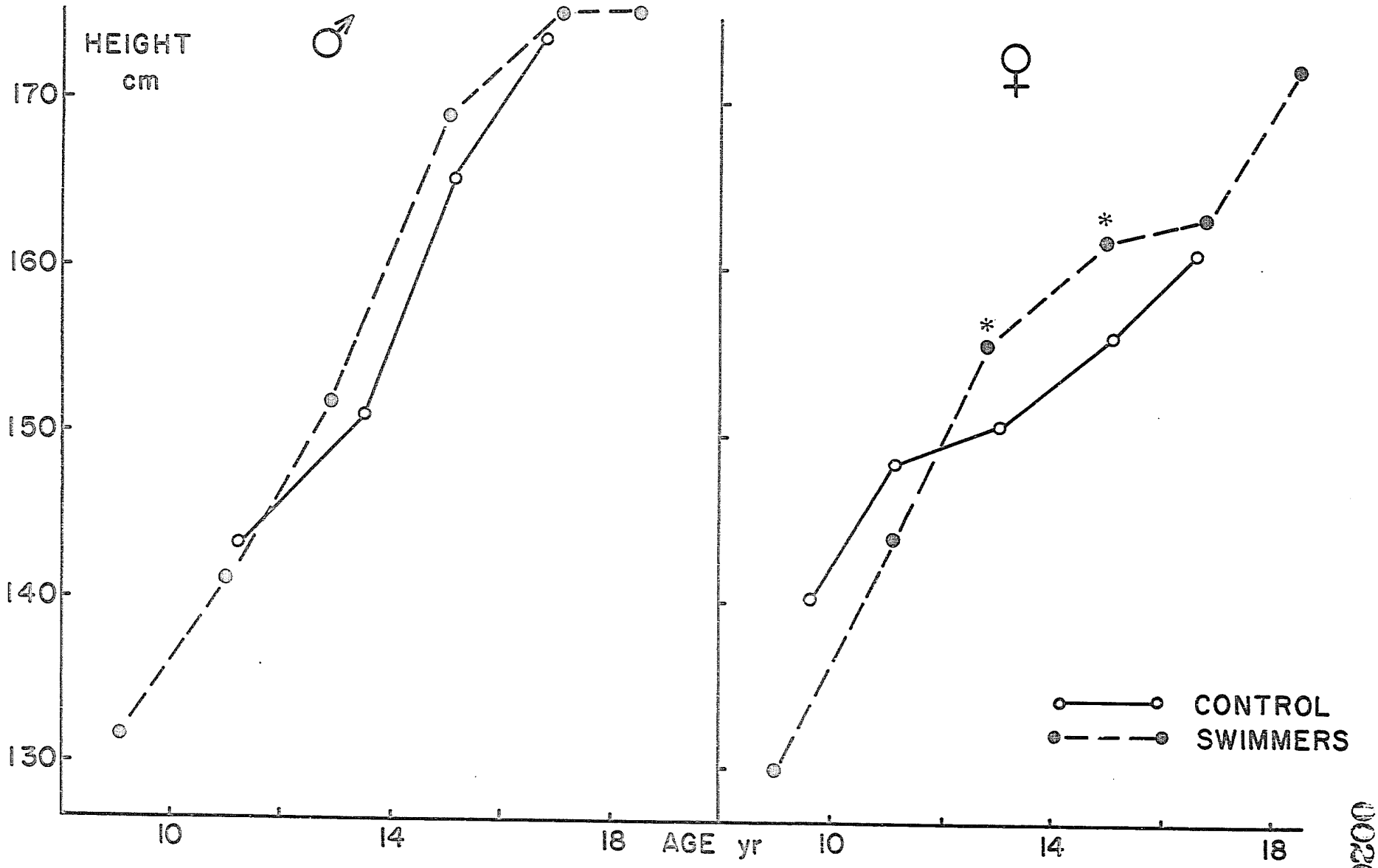


FIG. S_1 - Relations of height and age in swimmers as compared with Controls (* indicate difference in means $P < .05$).

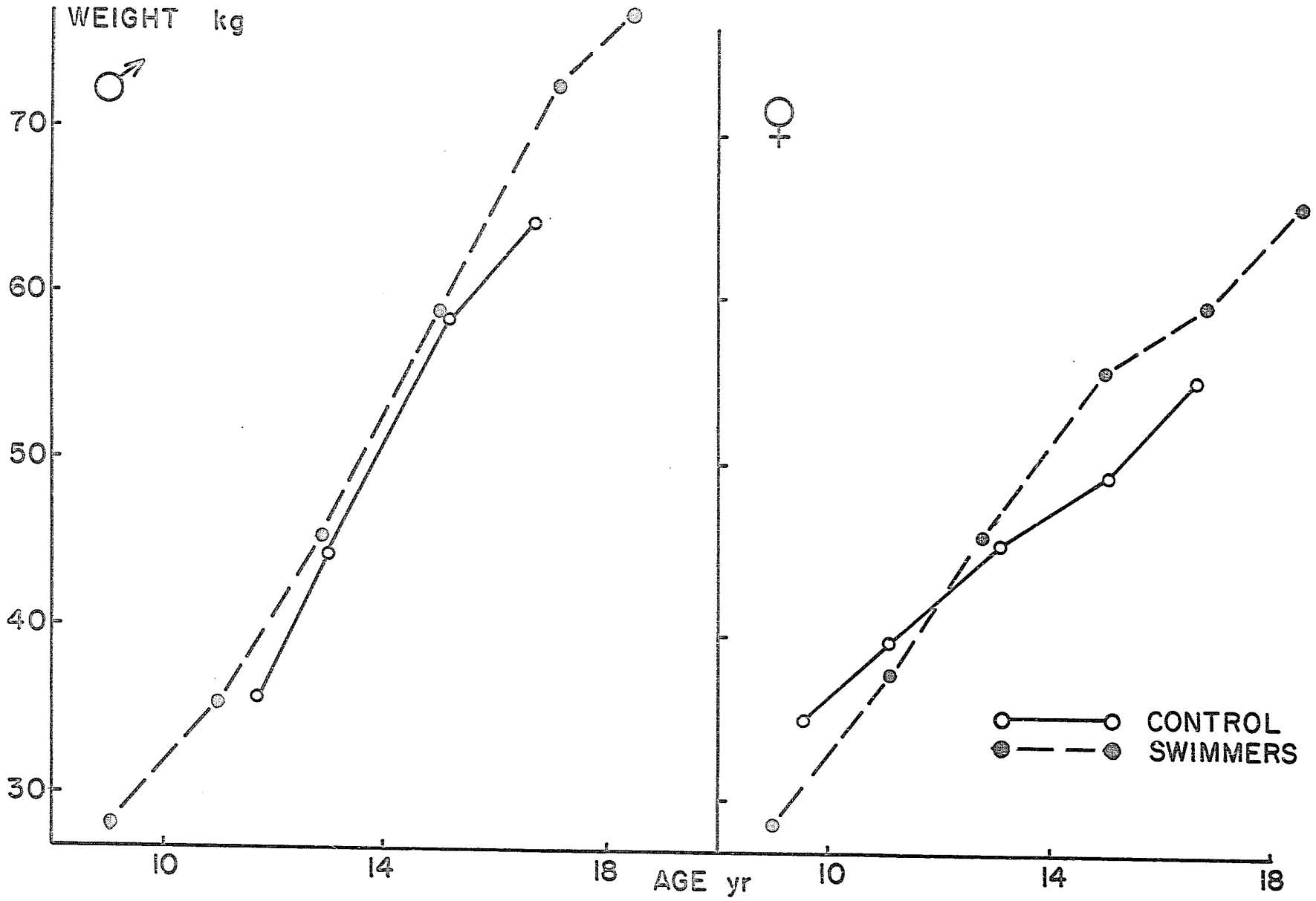


FIG. S_2 - Relation of weight to age in Swimmers and Controls.

LUNG VOLUMES:

Since lung volumes are directly related to height, analysis was made between groups divided according to height rather than age.

Table S2 and S3 show mean values with SD, for the subdivisions of lung volumes and flow rates for boys and girls swimmers respectively. Mean values for physical dimensions and age are also included. It will be noted that these values differ from those shown in Table S1, only because the group was divided according to height in 10 cm.units, whereas in Table S1 they were divided by age in increments of 2 years.

Fig.S3 shows the plot of linear regressions (Table S7) describing the relationship of lung volumes and height for each sex and Table S8 summarizes the correlation coefficients for the different regression analysis performed. No consistent sex difference was seen in respect to RV although at shorter heights girls had slightly greater values. In each of the other subdivisions, males had significantly larger volumes as a group (see Table S4). In part, this overall sex difference in the swimmers can be attributed to the larger number of taller males in the group. However, when sex comparison is made for any particular height, male swimmers had larger VC and this difference was significant in the younger children too (heights 130-150 cms) (see Table S6). Except at height 150-160 cms., where the number of females was greater (21/12), males had larger total lung volumes but at no height was this difference significant (i.e. at 5%).

TABLE (S 7) LUNG VOLUME AND FLOW RATE REGRESSIONS - SWIMMERS

SEX	Dependant Variable (Y)	Constant		Coef. of Indep. Var. (b) (X)		Corr'n (r)	SD of Coef. (b)	SE of (Y)
		Ht	$(Ht)^3$	Ht	$(Ht)^3$			
Boys	FRC	-5.68		.0505		.843	.0039	.503
			- .486		.685	.855	.0503	.484
	VC	-7.64		.0728		.863	.0052	.665
			- .093		.977	.866	.0685	.659
	TLC	-10.23		.0960		.863	.0068	.875
			- .308		1.295	.871	.0886	.852
	RV	-2.53		.0227		.712	.0027	.350
			- .201		.313	.732	.0353	.339
	ERV	-3.14		.0276		.830	.0023	.290
			- .287		.372	.836	.0297	.285
	MMFR	-7.35		.0689		.792	.0066	.833
			- .242		.929	.797	.0873	.825
	FEV	-239.85		2.2143		.836	.1778	22.55
			-11.066		29.868	.842	2.3424	22.18
Girls	FRC	-3.16		.0334		.774	.0033	.324
			.122		.494	.776	.0487	.323
	VC	-6.46		.0621		.851	.0046	.484
			- .434		.955	.866	.0665	.462
	TLC	-7.17		.0723		.864	.0051	.538
			- .086		1.128	.882	.0727	.504
	RV	-0.91		.0125		.341	.0041	.433
			- .280		.196	.356	.0621	.431
	ERV	-2.02		.0197		.784	.0019	.196
			- .095		.298	.787	.0282	.195
	MMFR	-4.68		.0528		.677	.0071	.735
			.506		.791	.671	.1077	.740
	FEV	-221.78		2.085		.852	.1148	19.11
			- 6.758		27.812	.859	2.0393	14.01

TABLE (S 8) CORRELATION COEFFICENTS FOR LUNG VOLUMES AND FLOW RATES

SWIMMERS

SEX	Regression Used: Dependant Variable (Y)	Regression Used: Independant Variable Ht(cms.)	Dependant Variable (Y): FRC	VC	TLC	RV	ERV	MMFR	FEV
Boys	-	-	.843	.863	.863	.712	.830	.792	.836
	log	-	.827	.878	.872	.641	.826	.800	.837
	-	log	.833	.879	.857	.670	.842	.787	.830
	log	log	.820	.879	.869	.631	.826	.780	.837
	-	$()^3$	.855	.866	.871	.732	.836	.797	.842
Girls	-	-	.774	.851	.864	.341	.784	.677	.852
	log	-	.805	.849	.891	.438	.821	.708	.866
	-	log	.768	.839	.849	.331	.778	.657	.843
	log	log	.803	.844	.881	.424	.820	.711	.864
	-	$()^3$	.776	.866	.882	.386	.787	.671	.859

Higher correlation value underlined
- indicates no transformation.

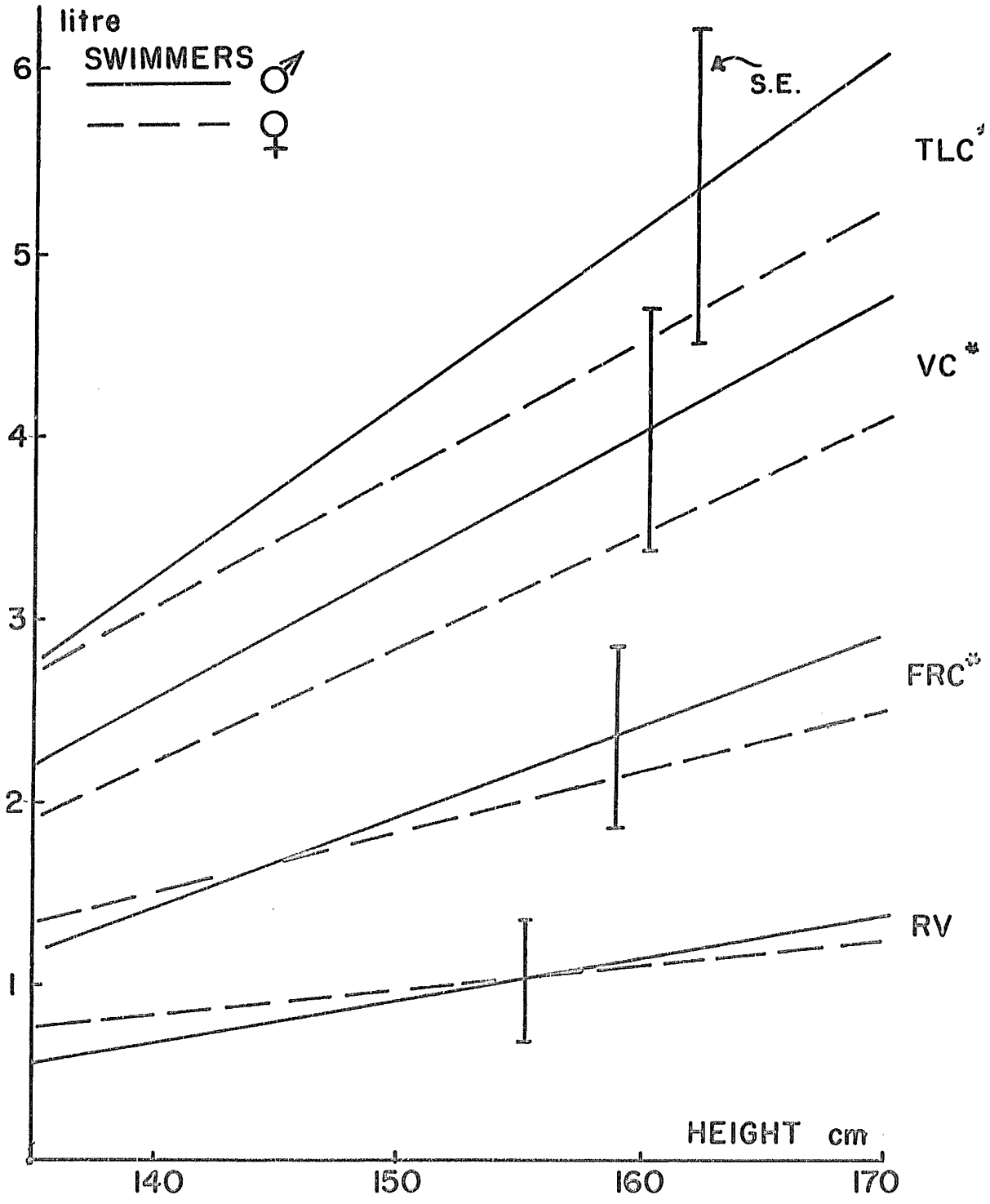


FIG. S_3 - Sex comparison in Swimmers of subdivision of lung volume in relation to height (Bars indicate S.E. of regression lines of males, * indicates sex difference in mean values - $P < .05$).

Comparison with Controls is shown in Fig.S4 (males) and Fig.S5 (females) were linear regressions, using height as the independant variable, are plotted,and in Table S5, it can be seen that swimmers have significantly larger values for VC, TLC and ERV. In respect to FRC and RV, there was no difference between groups nor was there a significant intergroup sex difference, although in the females these values (FRC & RV) were larger in the girl Controls than in the girl swimmers. This was opposite to that for the boys (Table S5) where it is seen that the swimmers had higher values for all subdivisions of lung volumes. While the difference in the females was not significant at the 5% level, in each case (FRC and RV) the slope of the regression lines (Fig.S5) were different ($P < 0.01$).

On Figures S4 and S5, regressions for 20 year old adults (152) are plotted. It is noted that in no case has the line for the children -- swimmers or Controls-- reached that for adults. VC in swimmers of 170 cms. comes closest to adult values; the greatest difference between adults and children is in respect to FRC.

FLOW RATES:

Mean values for flow rates in swimmers are included in the lung volume tables indicated above. Linear regressions are plotted describing sex differences in swimmers (Fig.S6) and group differences in Fig.S7 (males) and Fig.S8 (females).

In Fig.S6, it is seen that values for FEV in boy and girl

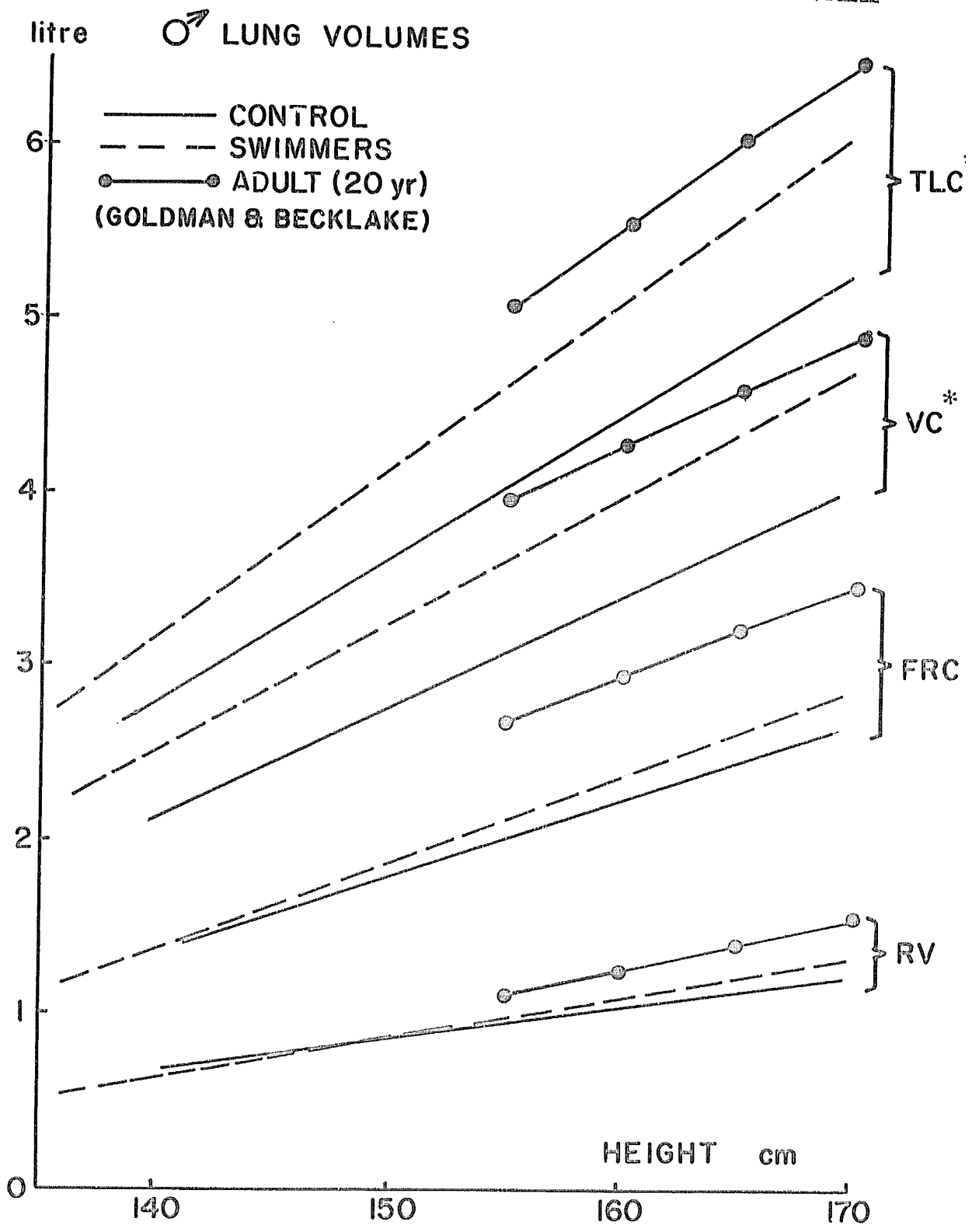


FIG. S_4 - Subdivisions of lung volumes related to height comparing male swimmers, Controls and adults. (* indicates group difference of mean in children $P < .05$).

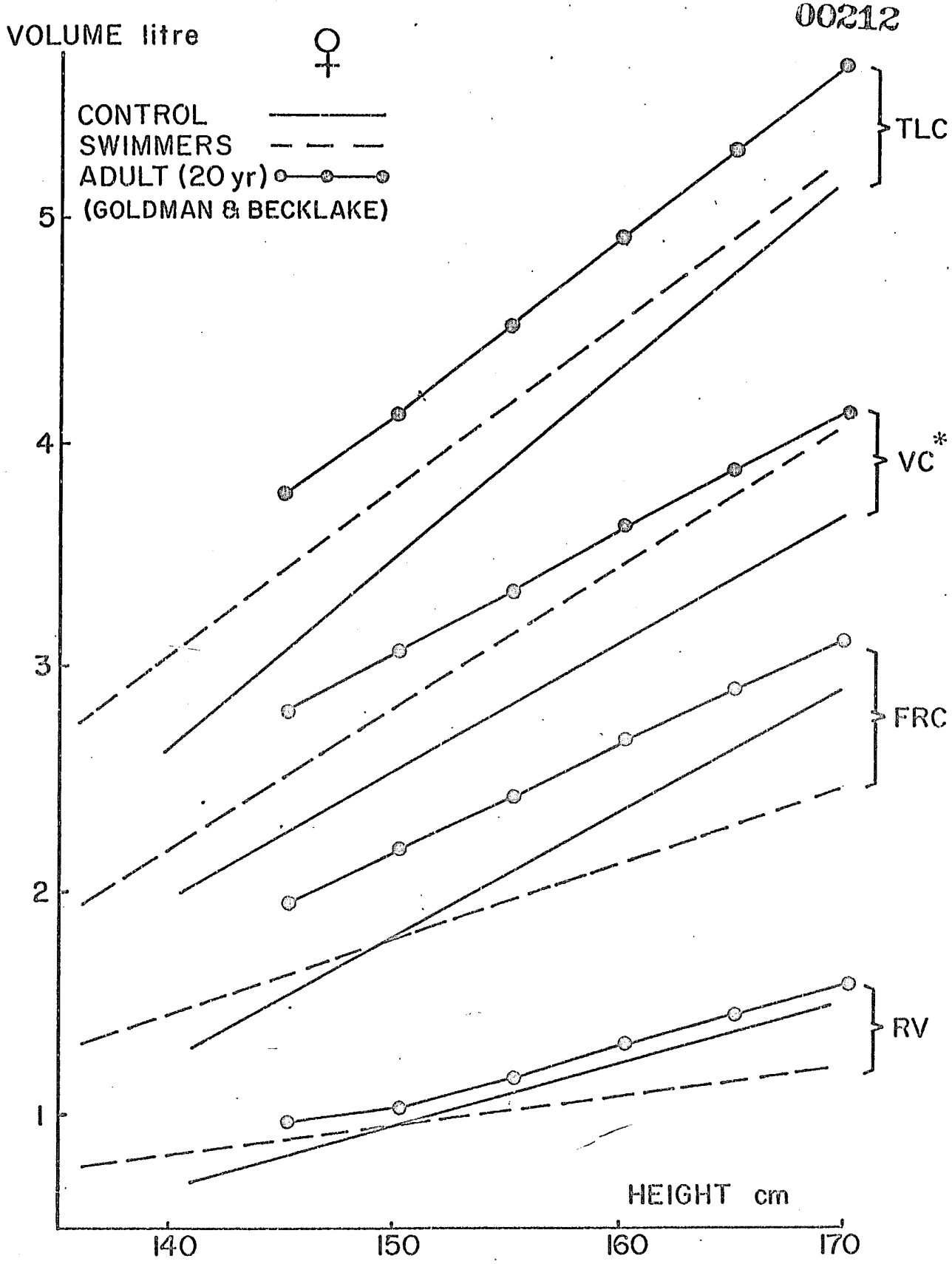


FIG. S_5 - Subdivisions of lung volumes related to height comparing female swimmers, Controls and adults. (* indicates group difference in mean values in children $P < .05$).

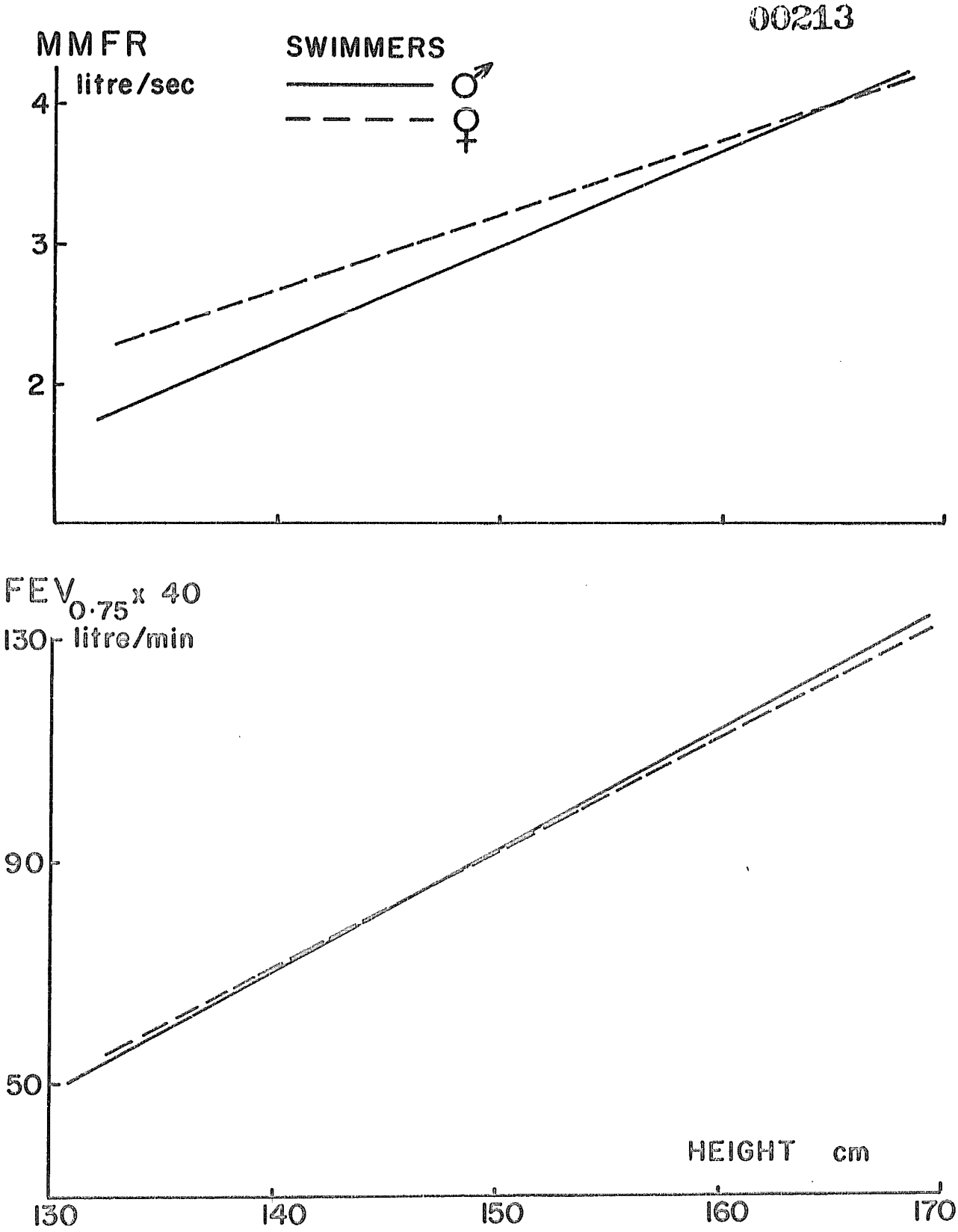


FIG. S_6 - Sex comparison in Swimmers of MMFR & FEV, in relation to height.

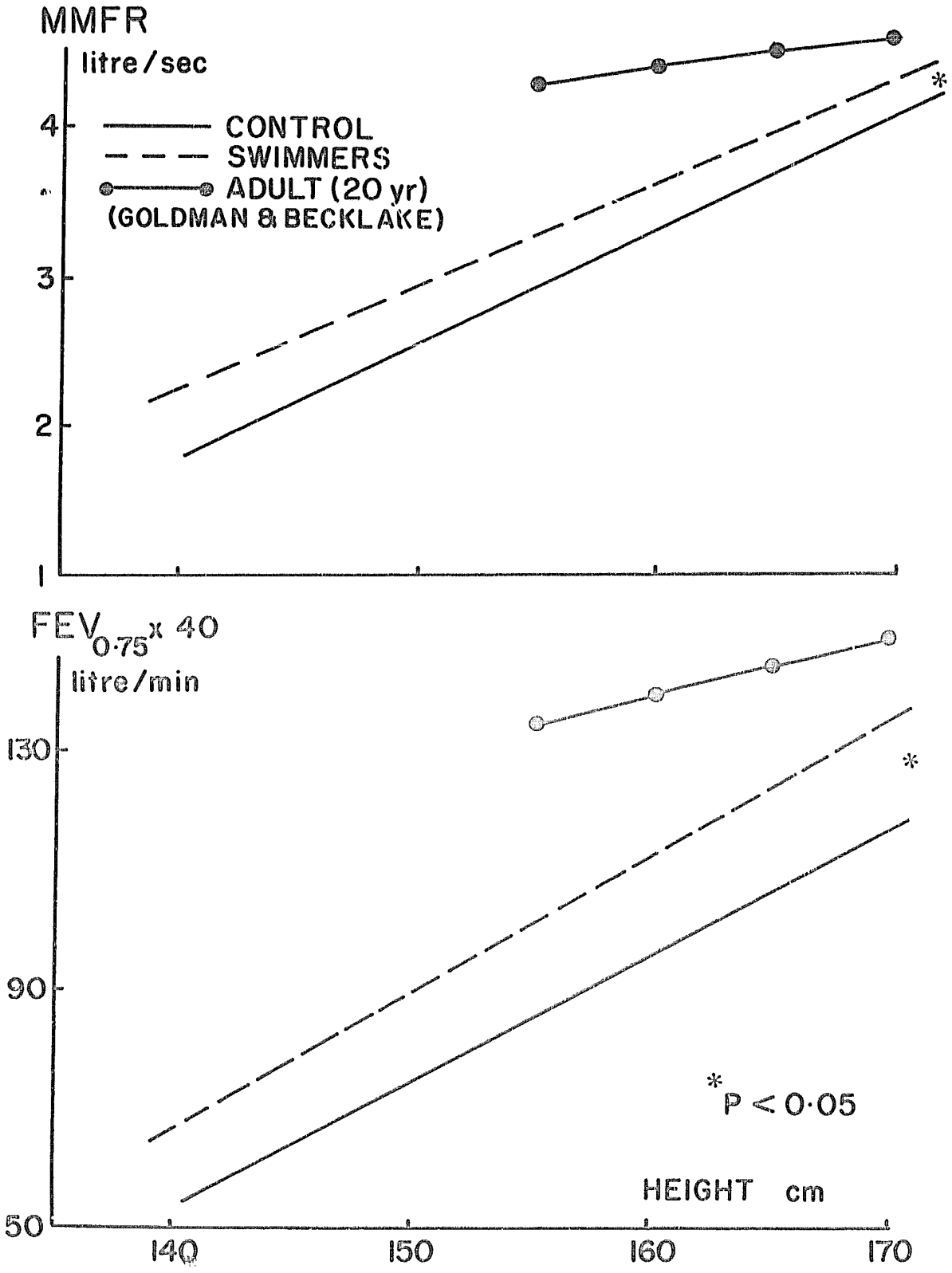


FIG. S_7 - Comparisons of MMFR & FEV as related to height in male Swimmers, Controls and adults.

(* indicates group difference in mean values in children $P < .05$).

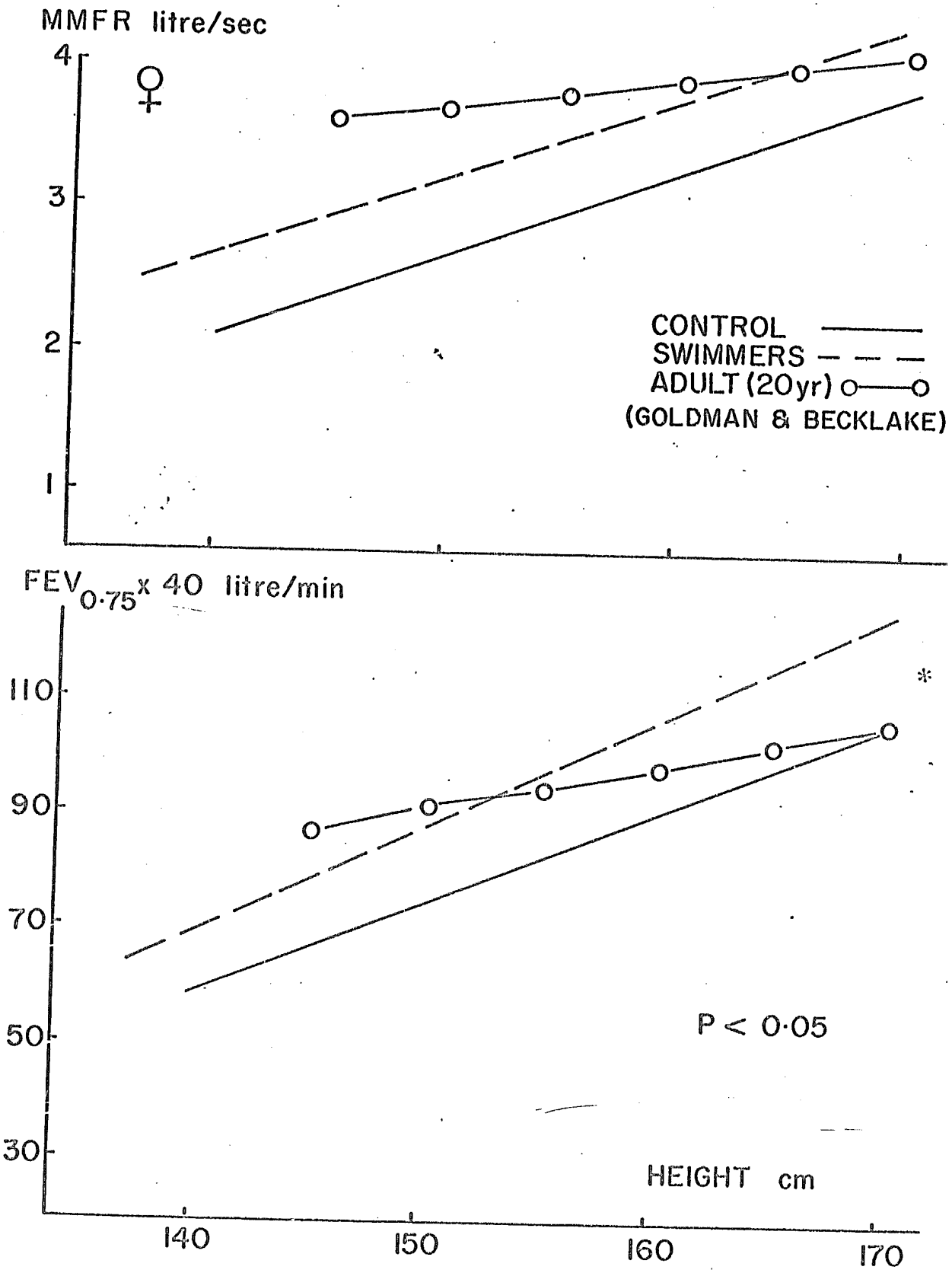


FIG. S_8 - Comparison of MMFR and FEV as related to height in female Swimmers, Controls and adults
(* indicates group difference in mean values in children $P < .05$).

swimmers are similar. MMFR was higher in the girls at shorter heights. As shown in Table S4, the overall values for males were higher in each case, attributable to more taller boys in the group.

In addition, swimmers of both sexes are shown (Table S5, Figures S7 & 8) to have significantly larger values than Controls for both MMFR and FEV. Furthermore, this difference was found at any given height, and in most cases (i.e. at most height sub-groups) was significant.

As was the case for lung volumes, neither group of male children, even at height 170 cms., had values for flow rates comparable to adults of a similar height (Fig.S7). The Control girls however, have reached adult values for FEV, and nearly so for MMFR, at height 170 cms., while the values for female swimmers is greater than for adults at this height.

Individual Growth ...Volumes and Flow Rates

The comparison of linear regressions, as in the presentation of results above, was considered appropriate for group comparisons (i.e. swimmers and controls) as the groups involved were similar in age and physical dimensions. This method, because it linearizes the collected data, cannot show clearly the individual growth patterns which may differ from year to year and may be altered by strenuous athletic training during the growing period.

To illustrate growth of lung volumes and flow rates, results on individual swimmers are compared with control regressions in Fig.S9-14. Each point representing the first measurement on

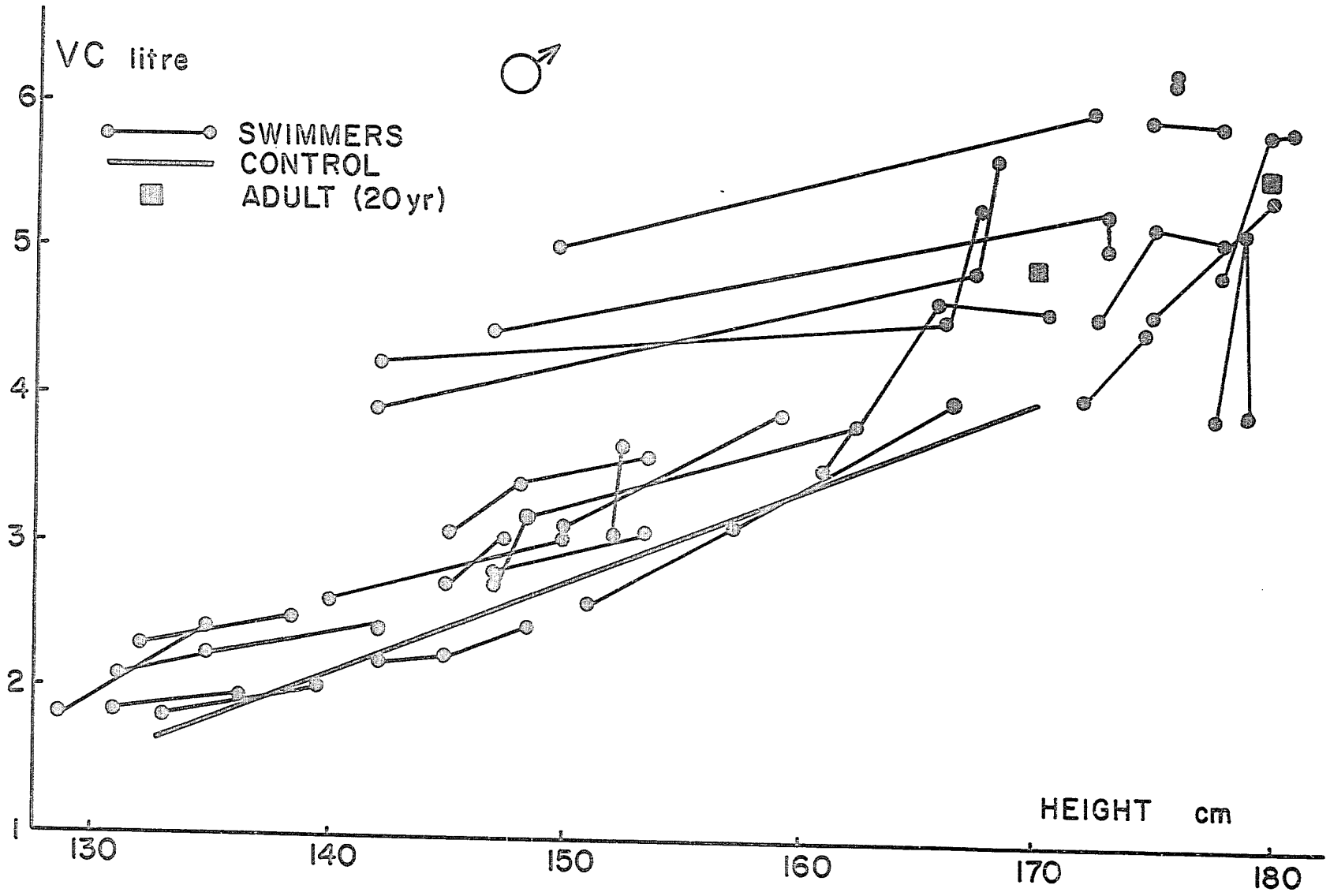


FIG. S_9 - Individual results of VC in relation to height (growth) for Boy Swimmers. Each point represents a measurement on one subject, made at yearly intervals. Comparison is made with the regression line for Controls and means for adults (152).

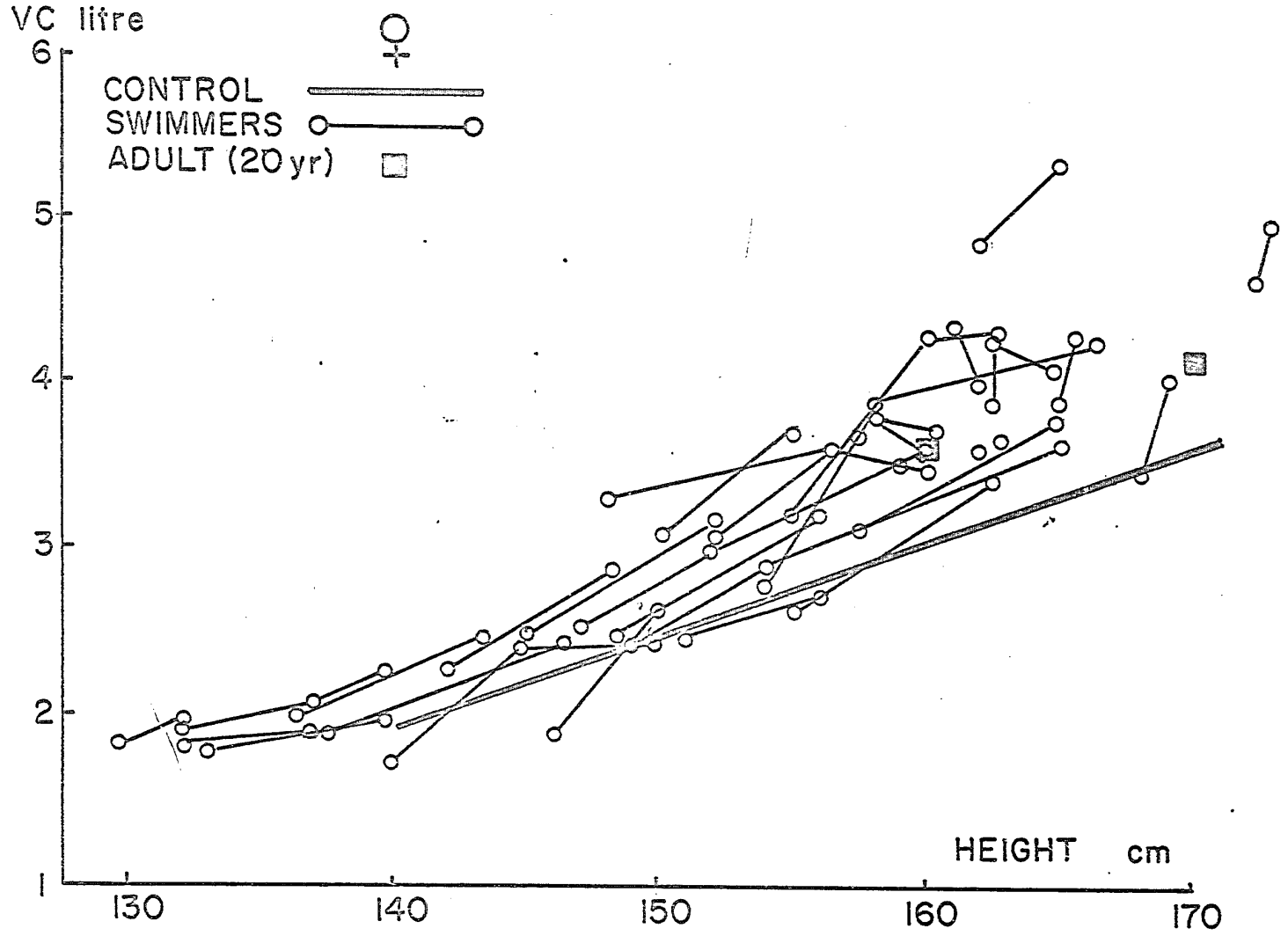


FIG. S_{10} - Individual results of VC, as related to height (growth) in girl swimmers. Points joined by lines, represent measurements on one individual made at yearly intervals. Comparison is made with the regression line for Controls and means for adults (152).

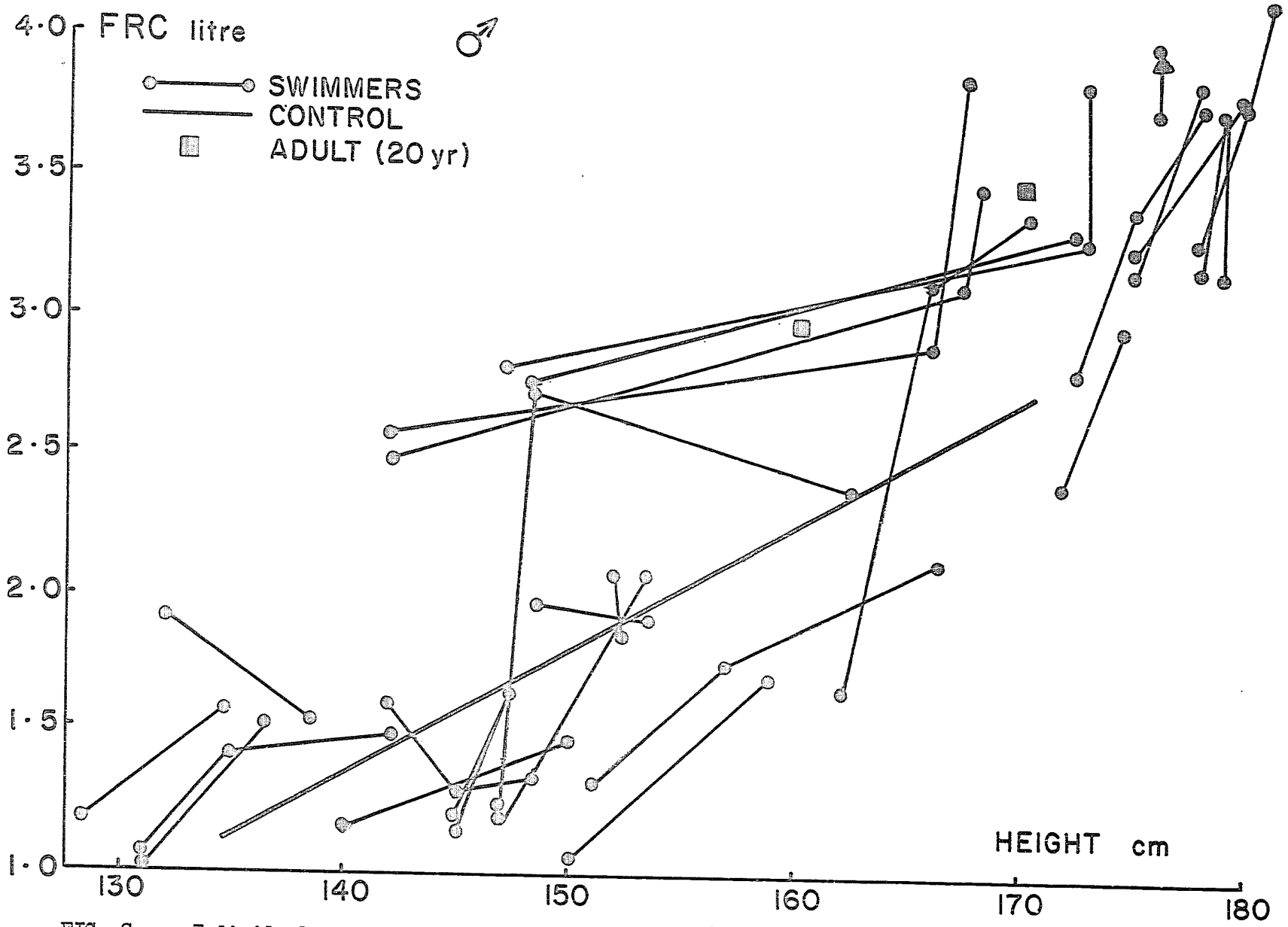


FIG. S_{11} - Individual results for FRC in boy swimmers, (c.f. Fig. S_9).

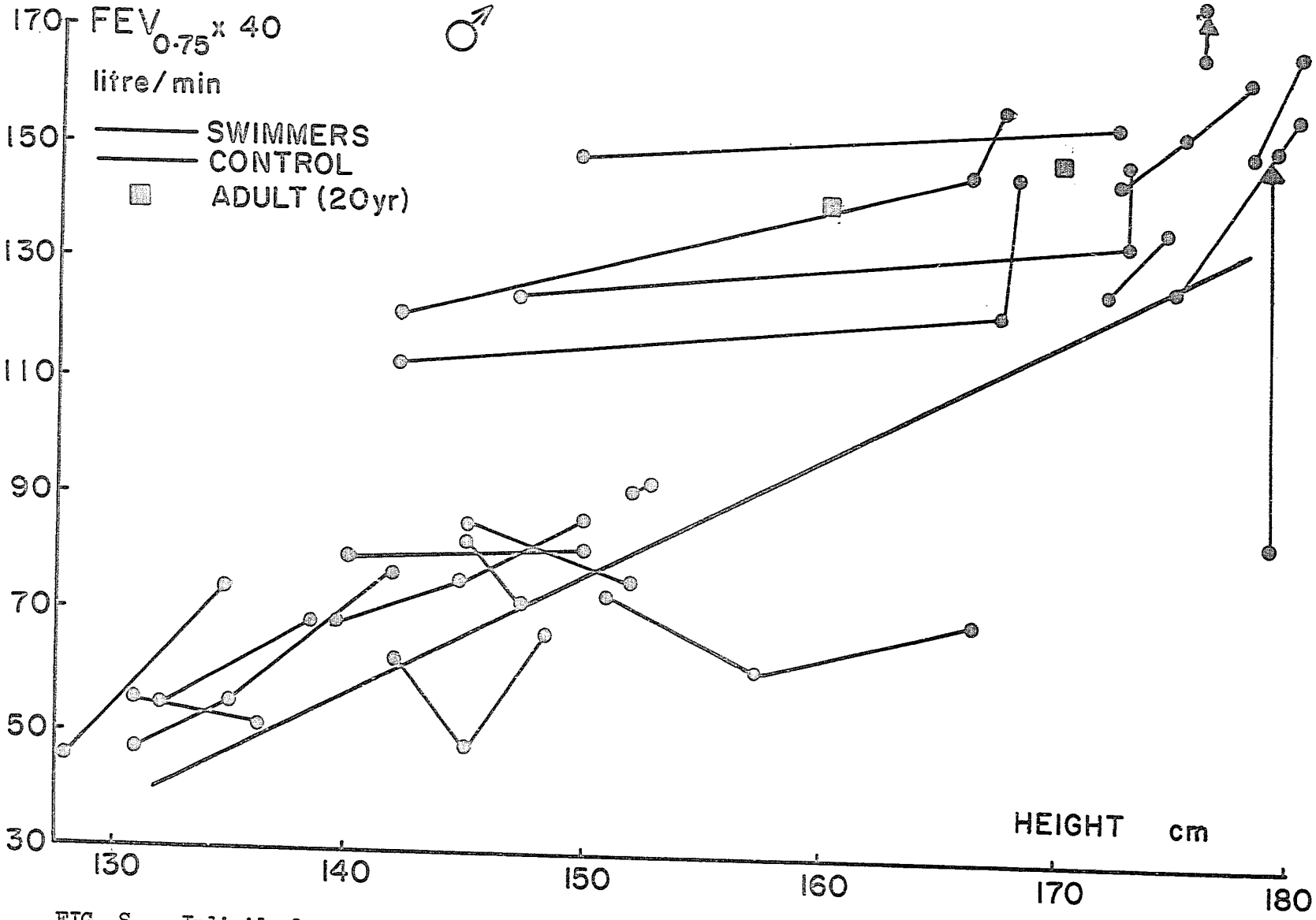


FIG. S_{12}- Individual results for FRC in girl swimmers (c.f. Fig.S_{10}).

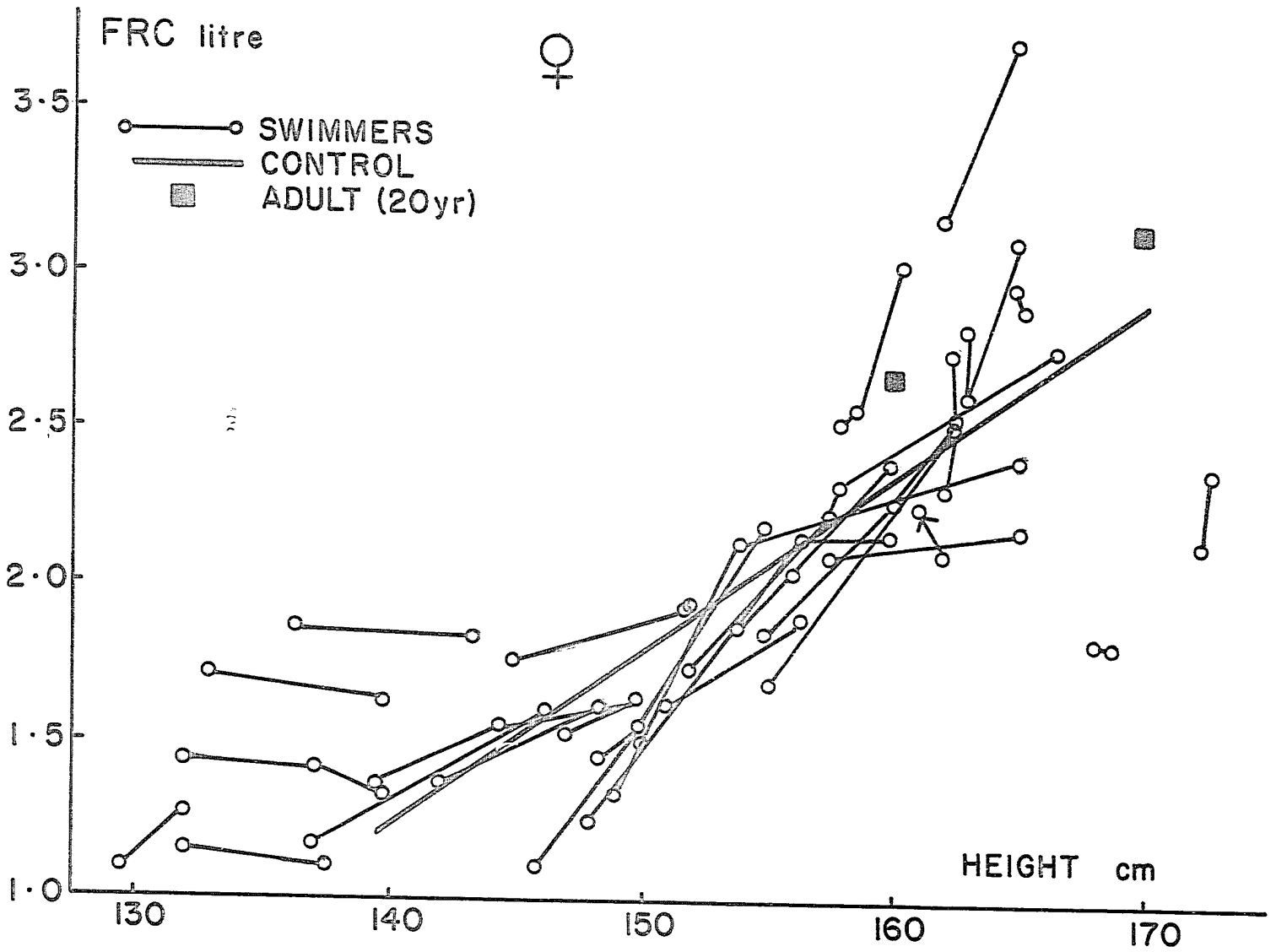


FIG. S_{13} - Individual results for FEV in boy swimmers (c.f. Fig. S_9)

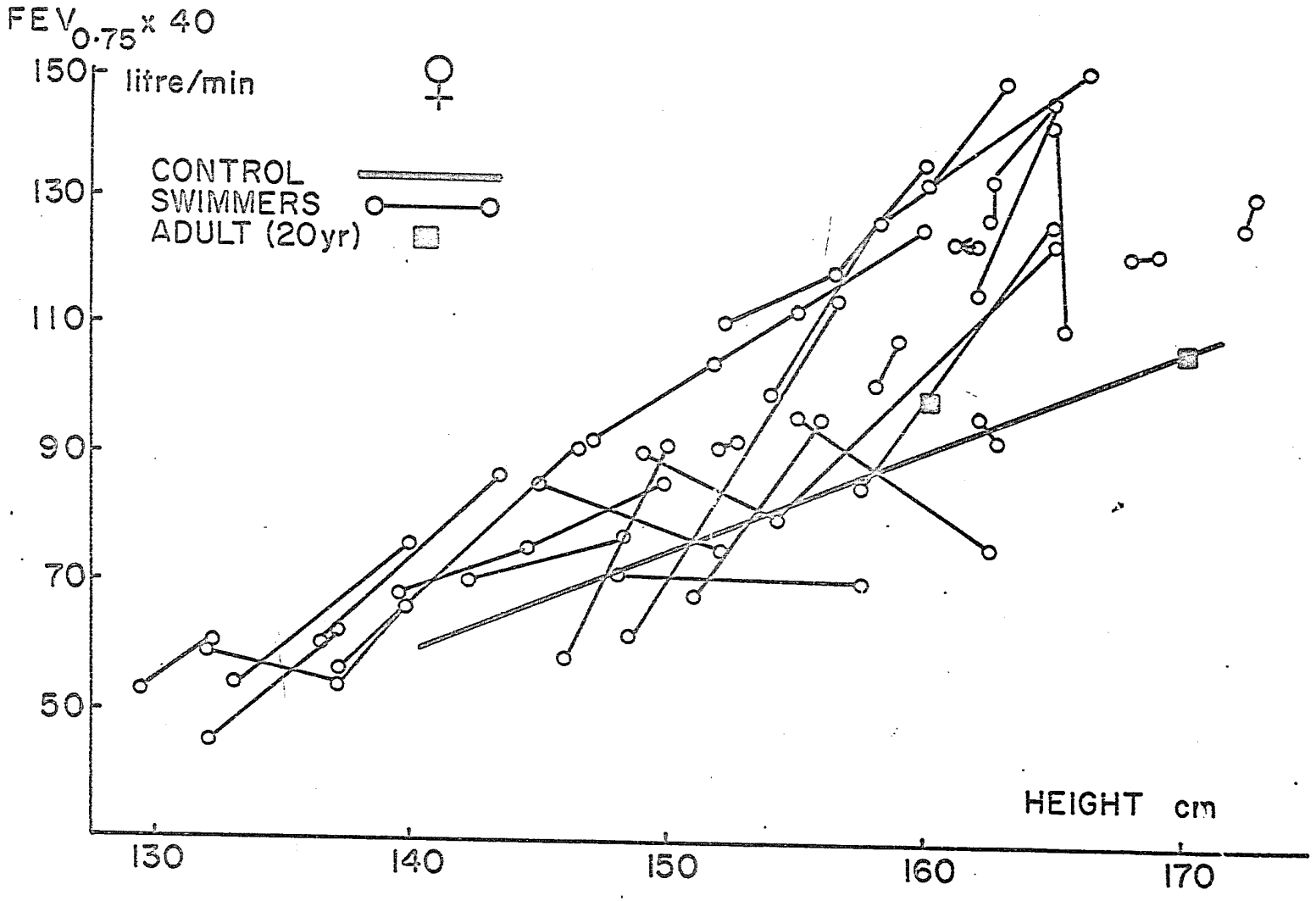


FIG. S_{14} - Individual results for FEV in girl swimmers (c.f. Fig. S_{10}).

any child is connected to subsequent measurements in the same subject, VC, FRC and FEV values are shown. Vital Capacity, with few exceptions, is higher in swimmers (In Fig.S9-S10 most points lie above the regression line for Controls). In the taller boys there is an increase in slope in the individual lines relating VC to height, suggesting a transition from child to adulthood. In other words, although the growth rate, as indicated by height change, has slowed, VC continues to increase perhaps as a consequence of increasing development of the shoulder girdle musculatu

It was noted that in the shorter (younger) girls (Fig.S10) their initial values lay close to the regression line for Controls, but training during the growth period has increased the rate of growth of VC (i.e. the individual lines have steeper slope than Controls). It was also noted with interest that many individual values of the swimmers lie above the predicted adult values, a point which is not evident from the linear plots above (Figures S4 and S5).

In Figures S11 & S12, the FRC-Height relationship in the swimmers at annual intervals are plotted for comparison with the regression of FRC on height in the control group. A wide scatter noted in the boy swimmers is not seen in the data for the girls. An increase in slope at the taller heights, as noted above in VC, is again shown here, while in the shortest girls there was no change in FRC with increasing height.

Individual points for FEV (Figures S13 & S14) in general lie above the Control regression line, even at the shortest heights,

and this group difference, which is especially well shown in the ℜamles, (Fig.S14) becomes more apparent with growth, and presumably with swim training.

DISCUSSION:

It has been reported (20,273) that the degree of physical development is greater in leading swimmers than controls not engaged in special physical training programs. These observations were deduced by comparing the small groups (30 in each study) with controls or established norms of comparable age. The present study compares swimmers (79 individuals), studied on 1, 2 or 3 occasions at yearly intervals during the growth and training period, with 83 'controls'. With such small numbers, caution must prevail when attempting to draw conclusions. However, it is evident there is no clear indication that the physical dimensions, in relation to age, were different in the swimmers. Nor was there evidence of a change in growth pattern in the children in swim training who were studied annually for 3 years. Although it is true that our swimmers, for a given age were on the whole taller, and slightly heavier, than our controls, by comparison with more extensive data (66,336) our controls were 'short and fat' and our group differences in physical characteristics can probably be attributed to sample selection. Our swimmers are comparable in height and weight to the mean values of others for normal children (66,336). In contrast with the other studies (20,273), our swimmers group did not include only champion swimmers and this may account for our different observations.

Swimming has long been recognized by lay, physical education and medical people as being among the best activities for exercising

simultaneously, virtually all muscle groups of the body. Likewise, it has been long established that repeated heavy exercise will result in hypertrophy of muscles. It is thus not surprising to find that these sub-divisions of lung volume which relate to voluntary effort (i.e. IC and ERV) and therefore depend on the muscle power available, are greater in the trained child swimmer. Indeed, it is apparent that the only difference in lung volumes between groups was in respect to VC, and as a consequence of this, TLC was greater. In this regard, however, it was of interest that this difference was detectable in even the youngest boy swimmers who had in fact been engaged in swim training for, in most cases, less than one year.

The present study does not enable one to separate distinctly the relative importance of genetic and training factors in the development of an athlete. There is some evidence however that training modifies growth pattern of lung volumes, at least with respect to VC. This is indicated in the girls particularily (Fig.S10) where there is a distinct increase in the slope on the VC-Height relationship in swimmers.

There are two distinct advantages accruing to a swimmer, from stronger 'essential' and accesssory respiratory muscles: a) a greater volume of air can be contained in the lungs and b) faster flow rates can be developed. Because of the limitation imposed on the breathing pattern by the water in swimming, a larger inspiration should mean a higher fractional alveolar O_2 concentration/unit time, thereby permitting better arterialization

of the pulmonary capillary blood during the time the swimmers respiration is restricted. In addition, a swimmers efficiency as a performer is highly dependant on skill and if his stroke pattern had to be varied to accommodate inspiration, valuable time would be lost during the course of the competition. Because of this, higher flow rates, particularly inspiratory flow rates, can permit a larger tidal volume to be inspired during the "recovery" phase of the arm cycle. This larger tidal volume might also be expected to afford an additional advantage to the swimmer in that he would be more buoyant, thereby reducing the 'drag' of the water on his body.

To permit maximum inspiratory time during the "recovery" phase, the process of expiration must be effected with the head immersed. This necessitates development of higher intra-pulmonary pressures during expiration which must inevitably result in hypertrophy of the expiratory muscles as well.

These findings(a larger VC and higher flow rates in swimmers) are in agreement with Newman et al (273) and Astrand et al (20) and supports the concept of increased dimensions of this aspect of the O_2 transport system in trained persons as found by Holmgren (182).

Diffusing Capacity Results -Swimmers

Regressions describing the exercise D_L in relation to height and oxygen uptake are presented in Table S9. Because of the number of repeat measurements made, and the use of several different exercise loads (Table C10) it is not practical to attempt to include a table of absolute values.

Fig.S15 describes the relation between sexes in respect to $\dot{V}O_2$ and height. The relation of Dl to $\dot{V}O_2$ is seen to be similar in both sexes, in that the slopes of the regression lines are not different. The difference in constants in the regression equations is evident since for any level of exercise where comparisons of sexes were made (see Table S4) the observed values were statistically higher in males than females, whether comparing $D_L CO$ or $D_L CO/\dot{V}O_2$. This sex difference disappeared when account was taken for body size (e.g. $D_L CO/Kg$ in Table S4) or when Dl was related to lung volume ($D_L CO/MC$).

Comparison with Controls is shown in Fig.S16. Such comparison is made for only one level of oxygen consumption (i.e. .75-1/min) which corresponds to the mean value of $\dot{V}O_2$ for the control group. No significant differences in slopes of the regressions was found in males or females ($P < .20$). When group comparison was made by height or age, at load 150 KgM/min., the observed values for Dl were greater in boy swimmers ($P < 0.0332$) while no such difference was found between the girls of the two groups.

In Fig.S17, the relationship of $D_L CO$ to $\dot{V}O_2$ in boy swimmers

TABLE (S 9) REGRESSIONS FOR $D_L CO$ - SWIMMERS

	Sex	Dep. Var.	Constant	Indep.Var. Coef.(b) Ht.	Indep.Var. Coef.(b) VO_2	SD of (b) Ht.	SD of (b) VO_2	Corr'n Ht.	Corr'n VO_2	SE of Dep.Var.
A.	M	$D_L CO$	-40.57	0.462	6.77	0.036	1.70	.826	.552	5.26
	F		-30.77	0.323	6.27	0.025	1.15	.807	.609	3.43
	M&F		-45.65	0.428	6.65	0.023	1.09	.827	.583	4.71
	M	$D_L CO/MC$	13.16	-0.028	0.892	0.009	0.449	-.222	.068	1.36
	F		14.91	-0.034	--	0.011	--	-.255	-.122	1.56
	M&F		13.97	-0.030	0.424	0.007	0.347	-.244	-.048	1.48
B	M	$D_L CO$	5.75	$\frac{(Ht)^3}{5.10}$*	4.02	0.466	1.81	.783	.472	4.97
	F		2.81	5.29	3.39	0.574	2.09	.715	.440	4.75

* - (b) x 10^{-6}

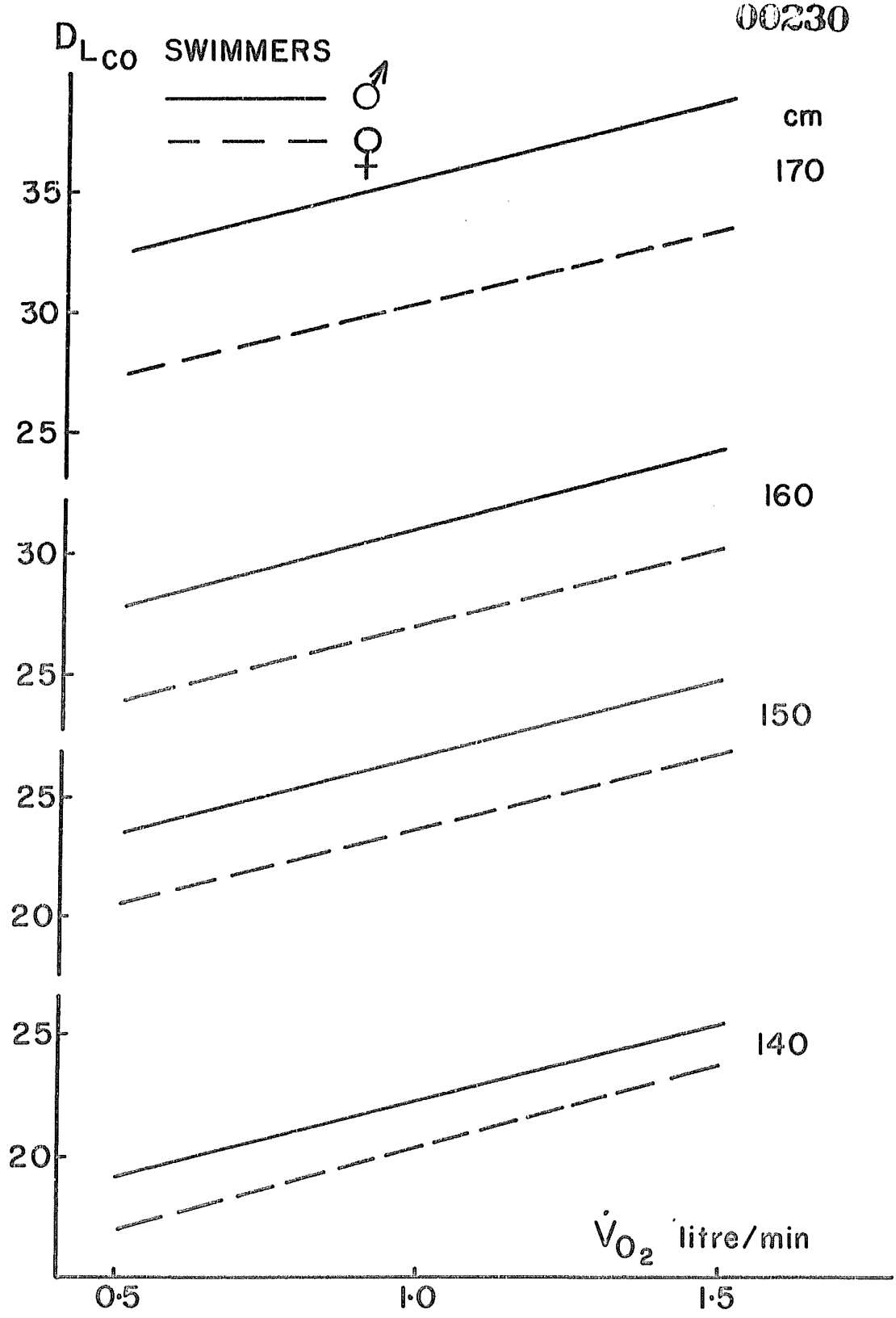


FIG. S_{15} - Sex comparison in swimmers of regressions for exercise D_L in relation to $\dot{V}o_2$ and showing effect of height.

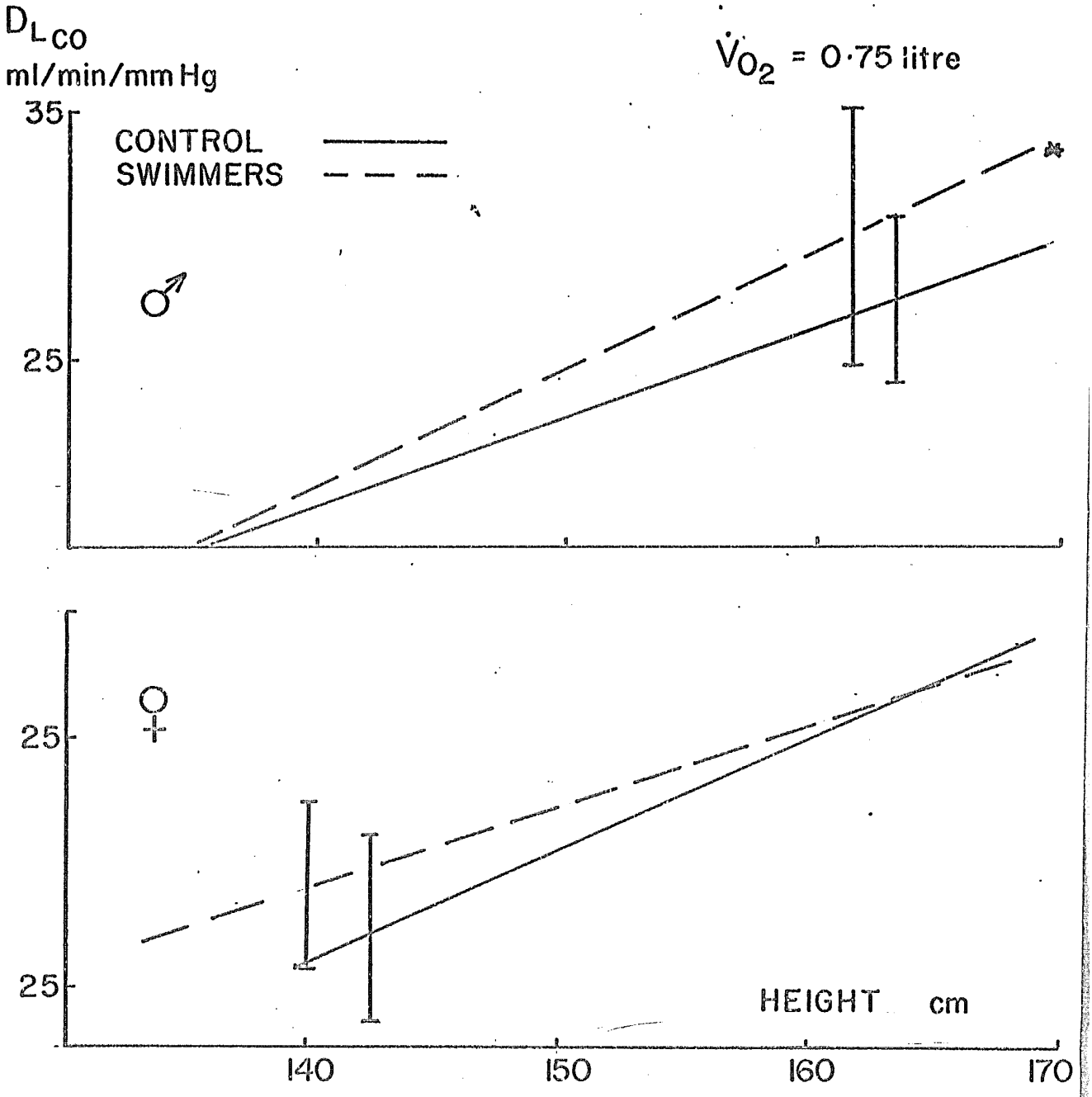


FIG. S_{16} - Comparisons of swimmers and Controls of exercise D_L ($\dot{V}o_2$ = .75) in relation to height. Bars indicate S.E. of regression lines, (* indicate difference in mean values P-0.0332).

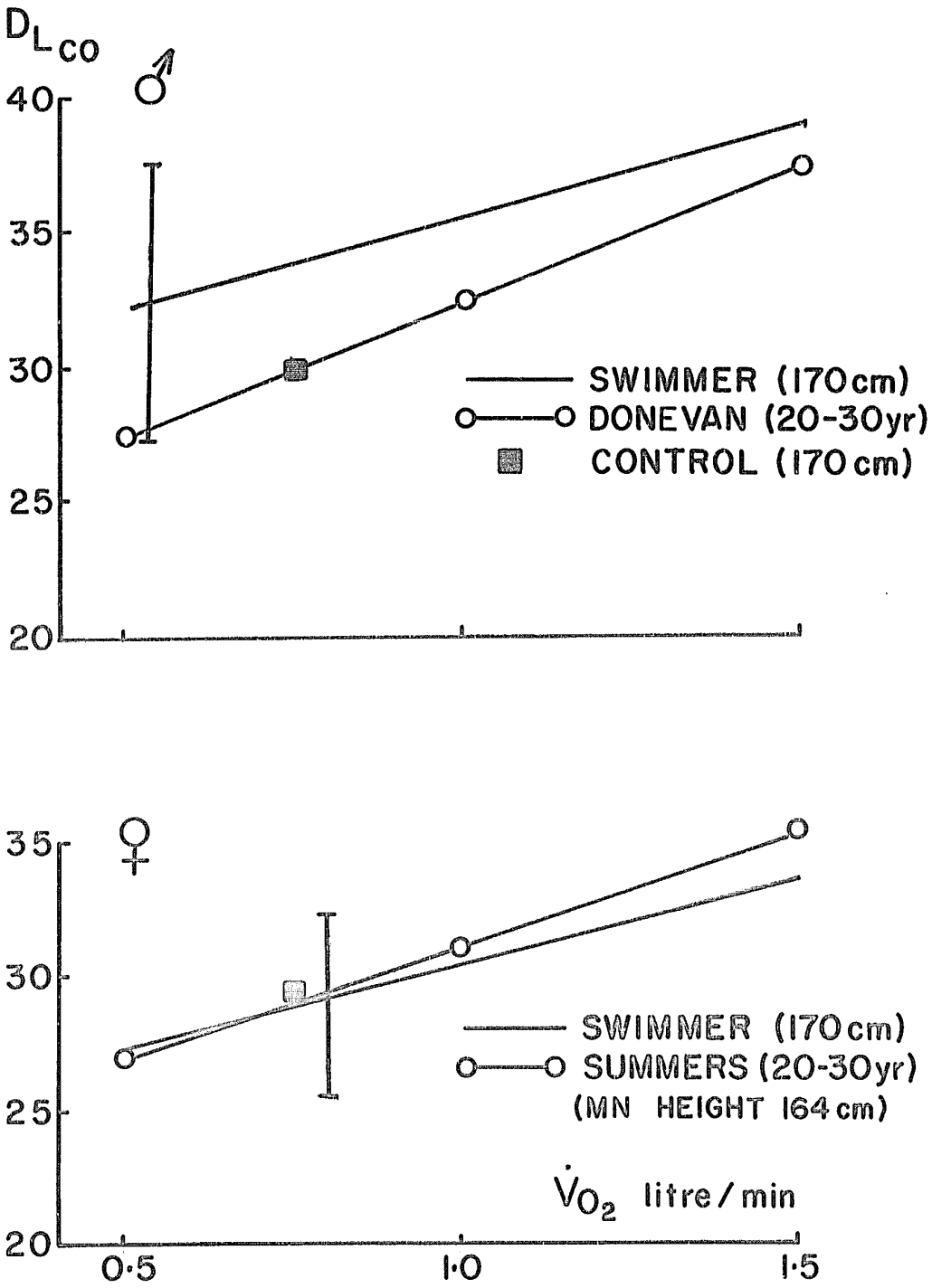


FIG. S_{17} - Comparison of exercise D_L $\dot{V}o_2$ relationship between swimmers and adults. (Bar indicates SE of swimmers).

of height 170 cms.is compared with values for men in their twenties studied by Donevan et al (117), while similar comparisons are also shown between the girl swimmers and unpublished data for women (data collected by Summers and Guzman in our laboratory using similar methods). The similarity of the results on girl swimmers and on adult women is obvious; also the single value shown for our Controls (i.e. $\dot{V}O_2$ .75 l/min.) falls on the line of the adult women. However, the regression line for the boy swimmers lies clearly above that for adult males (mean height 178 cms) even though the boys were on the average shorter. Note however that these differences are not statistically significant since the adult line falls within 2SE of the line describing the data on children.

Further comparison between Controls and swimmers is made in Fig.S18 (boys only shown) which shows D_L/MC and D_L/TLC, at similar oxygen consumption levels, in relation to height. In each case, Control values are greater and the difference is consistent throughout the height range. It should be noted that the SD of the D_L/MC is wide (Table S5), yet the difference between boys (P.0020 though not girls (P.2697) in this respect is significant (P .0031).

Figures S19 and 20 show the individual values (boys and girls respectively) for successive diffusing capacity measurements at 2 or 3 levels of exercise, correction being made for COHb in each case. The individual scatter along the vertical axis illustrates the great dependence of D_L, for a given $\dot{V}O_2$, on height. Although

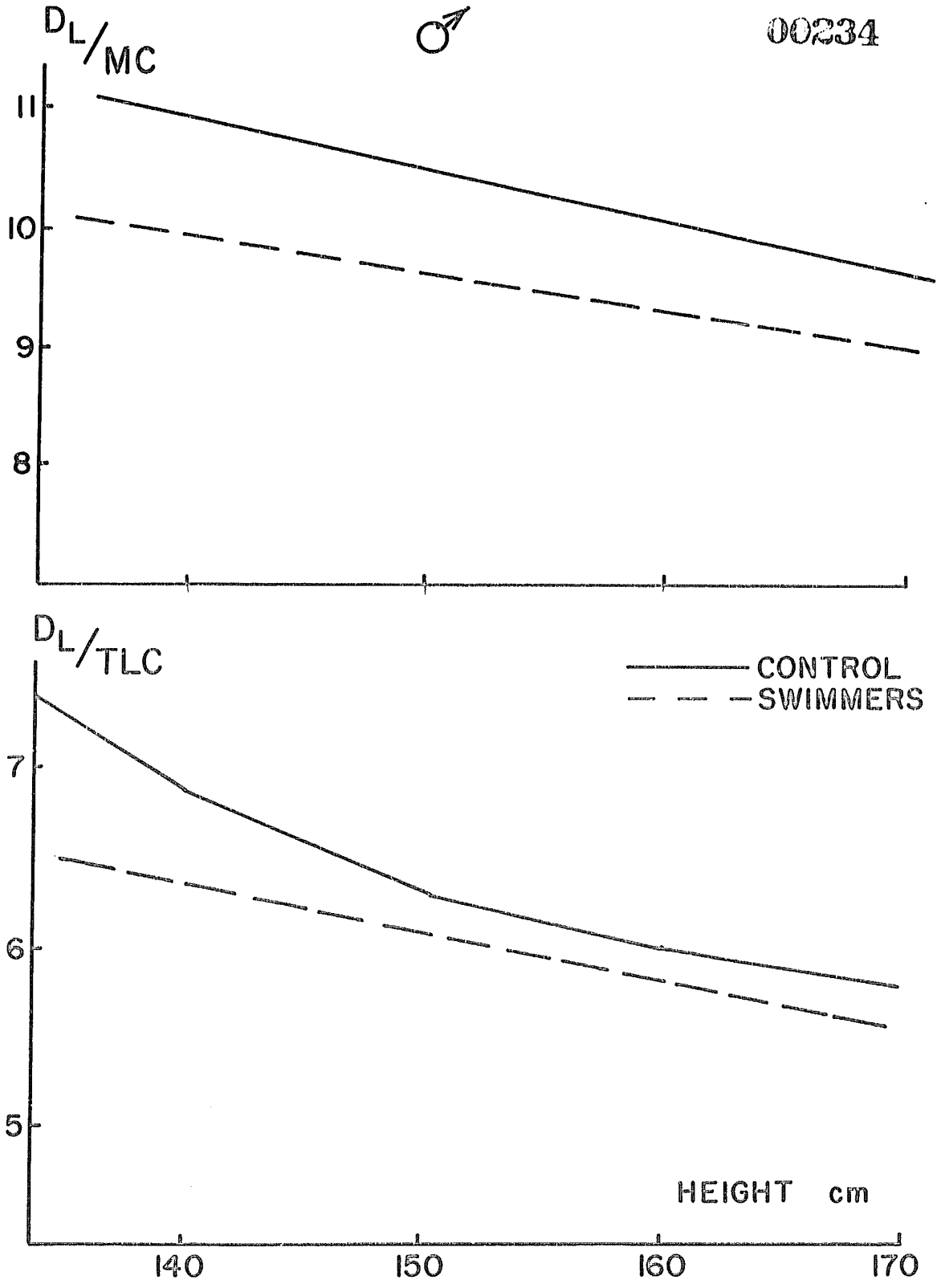


FIG. S_{18} - Relation of D_L/MC and D_L/TLC to height in boy of swimmer and Control groups.

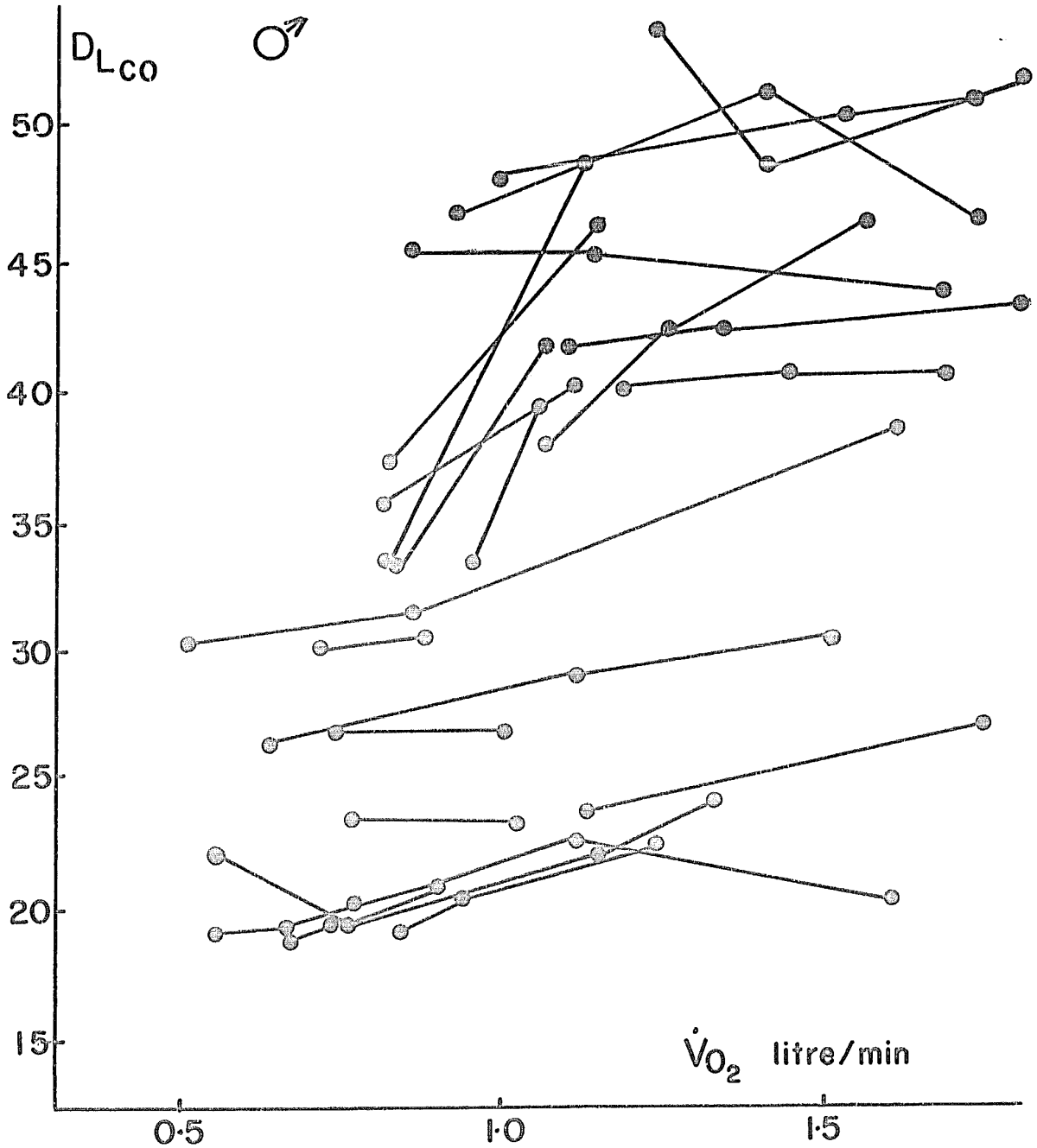


FIG. S_{19} - Individual results of exercises D_L at different levels of $\dot{V}o_2$ in boy swimmers of different heights.

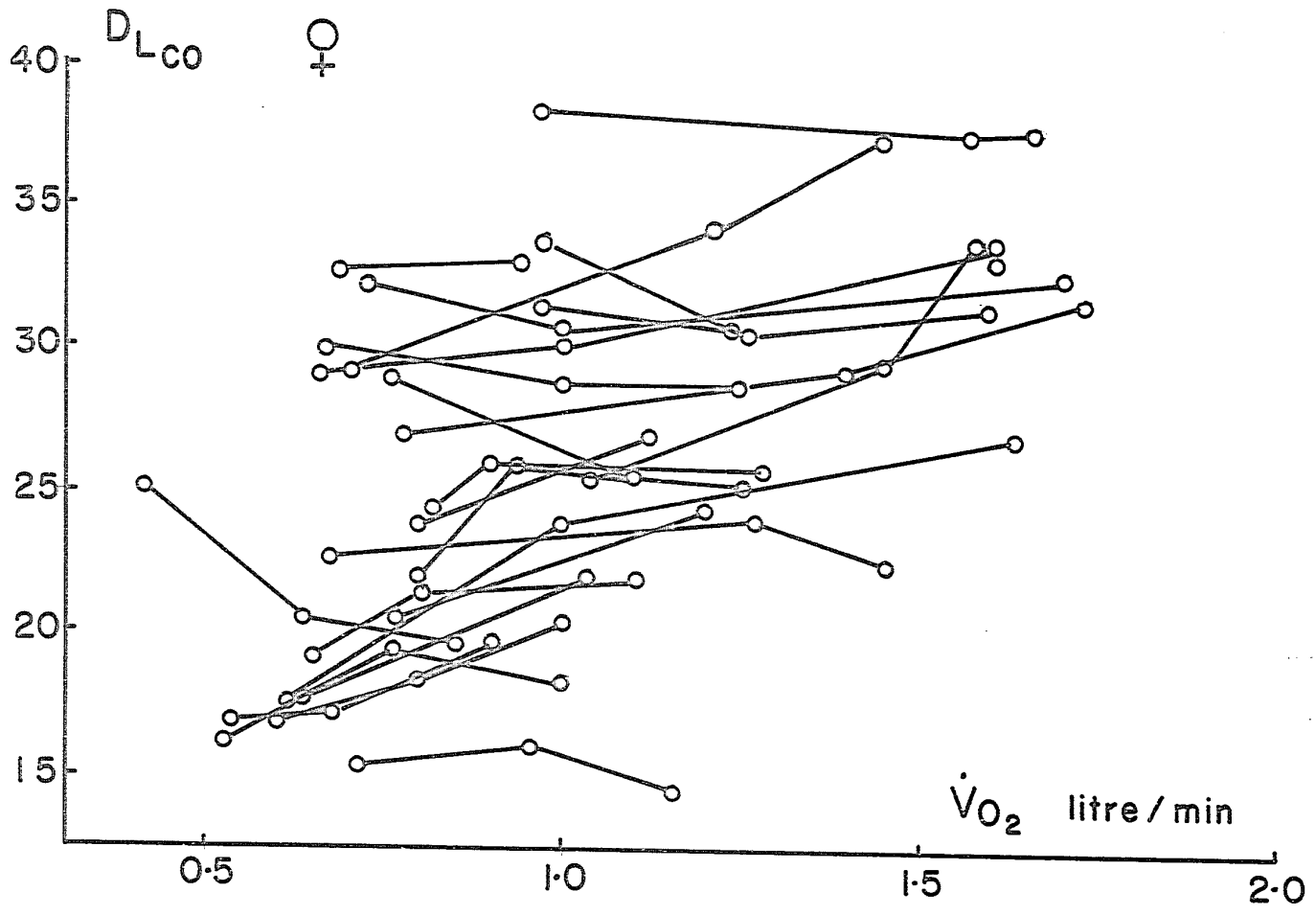


FIG. S_{20} - Individual results of exercise D_L at different levels of $\dot{V}o_2$ in girl swimmers of different heights.

the increase in D_L with higher levels of exercise (and higher $\dot{V}O_2$) is not always seen (i.e. lines joining individual points have zero, or occasionally negative slope), the general trend of an increase in D_L with $\dot{V}O_2$ is evident. It is noted too that the slopes of these lines is greater at $\dot{V}O_2$ 1 l/min., thereafter flattening with further increments of $\dot{V}O_2$.

Fig.21 shows individual points for D_L in selected swimmers considered by their coaches as having superior ability or potential These "elite" subjects are shown in relation to the regression line of their own group, and the line for Controls ($\dot{V}O_2$ comparable in all). The majority of these individual results lie above predicted values for both groups.

Discussion:

Comparison of D_L in children (swimmers and Controls) and in adults.

Although the relationship of D_L and $\dot{V}O_2$ has been well defined in adults, especially males, studies of exercise diffusing capacity at submaximal exercise levels in children have not been reported. The present findings indicate that this relationship in children (swimmers) is similar to that observed in adults (Fig.S17). The increase in D_L, per L O_2 consumption observed was 6.77 ± 1.7 in males and 6.27 ± 1.15 in females. These ratios are similar to those found by Newman (274) and Ogilvie (277) though slightly less than reported by Donevan (117) and Linderholm (236) in adults.

The age at which a child becomes an adult in terms of lung

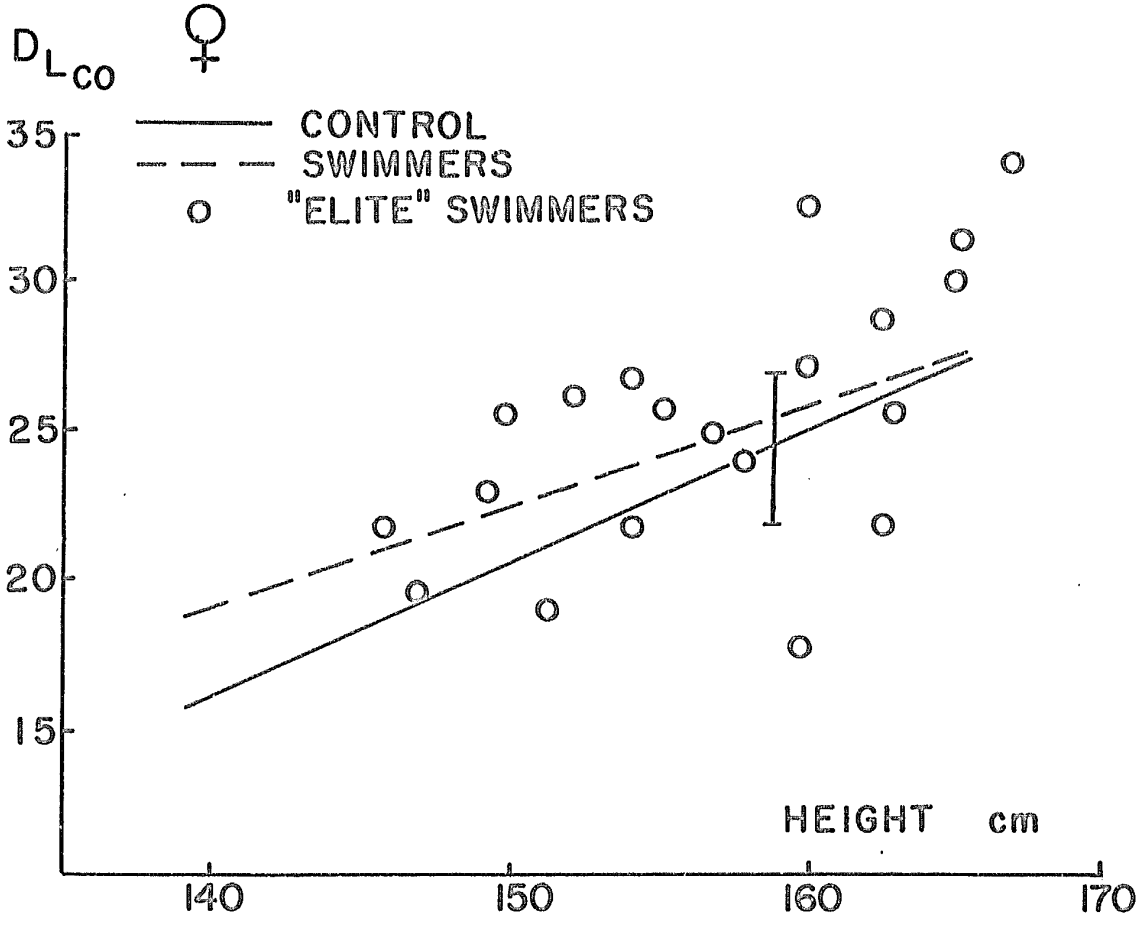


FIG. S_{21} - Individual points of selected 'elite' girl swimmers showing D_L, as related to height, and in comparison to regression lines for swimmers and Controls ($\dot{V}o_2$ for all $\simeq$ .75 l).

functions has not been clearly demonstrated. Berglund et al (44), analyzed the combined results of several studies (53,54,160) and concluded that peak values for FEV and VC are reached in males at age 25 years, and in females at age 20 years. This is in agreement with our finding in the control group (all under 20 years) that, in respect of lung volumes and flow rates, their values were lower than those for adults of comparable heights. By contrast D_L in the 170 cm.tall control "child" is comparable to that in an adult of similar height at the single level of $\dot{V}O_2$ at which comparison can be made, while the girl swimmers have values comparable to those of adult women over a wider range of $\dot{V}O_2$ (Fig.S17).

The difference in boy swimmers and adults is of interest. The higher values in the boy swimmers might suggest that one of the early events related to the aging process is a decline in exercise $D_L CO$ although this idea is not supported by the similarity of the single value for Controls with the regression line for male adults. A more likely explanation is that the swim training or endowment has conferred on the older male child, though not the female child, the advantage of a higher D_L, an advantage which apparently is all too short lived! (226)

The dependence of D_L on body size, or lung volume, has been suggested to account for the slight sex difference in adults (137) and our findings support this view. However, the exact relationship of this measurement to height in adults has not been defined.

The present findings, showing a marked dependence on height of D_L in children, suggests that height differences may account for some of the intersubject variation found among adults.

Comparison of D_L in Swimmers and Controls

Exercise diffusing capacity was significantly greater in boy swimmers than in Controls of comparable age and size at one exercise level of moderate intensity. No group difference in respect to D_L was observed in females. No ready explanation is at hand to account for the difference between sexes. The severity of training for boys and girls was comparable and no differences in age of onset of training or training technique were apparent.

It might be argued that the difference in boys may be related to differences in lung volumes prevailing during the testing. This is suggested in Fig.S18 where it is seen that D_L/MC is higher in Control boys. Since no difference was observed in FRC (Fig.S4), the higher V_T of the swimmers accounts for this reversal (i.e. D_L higher in swimmers, D_L/MC higher in Controls). The larger V_T of swimmers is unlikely to account for the higher D_L in boy swimmers, however, since doubling V_T had a negligible effect on D_L (266); nor can the group difference be attributed to variations in minute ventilation since these were negligible (see Fig.S25).

When the sexes are combined, it is evident that the group difference in D_L are not striking. Perhaps it was presumptuous to expect to find clear and striking differences between our groups. It is easy to propose reasons for our failure to observe well

defined changes. Firstly, The differences observed by Mostyn (266) were apparent only in the Champion swimmers of the swim group which included 3 of Olympic calibre (one of whom was a finalist in the 17th Olympiad). Our "Swimmers" group doubtless includes many who, in the vernacular of swimming, are'also swams'..and their effect would be to normalize this group. Figure S21 suggests that this might have been the case in the girls. As shown, most of the points for the few 'elite' girl swimmers lie above the regression line of their own group, a line which they have influenced, as well as the line of Controls. Perhaps there were fewer proficient girl swimmers and this accounts for the difference between boy and girl swimmers and Controls (i.e. boy swimmers higher than Controls, but not girl swimmers).

A second factor which might obscure differences, if indeed there are differences, might be the effects of growth, in particular variation in growth rate, which can make interpretations of results difficult. Thirdly, more striking differences might be apparent had comparison with Controls been made at several and higher test exercise levels.

A higher diffusing capacity, it can be reasoned, would be advantageous to competitive swimmers. It has been shown by Goff and Bartlett (149) that the trained underwater swimmers have a higher end-tidal CO_2 concentration (which can rise to 8%) than the untrained. These authors point out also that the trained employ a greater V_T, breathe more slowly with prolonged pauses,

and have a lower ventilatory equivalent. These differences suggest that the mean alveolar O_2 concentration must be low because of the interdependance of these two gases, as shown by the O_2-CO_2 diagram. Under such hypoxic conditions, it has been suggested that a high D_L is essential (288,359). Similar hypoxic conditions might be expected in competitive swimmers, who perform at about their maximal aerobic capacity as measured on land (20). Furthermore they exercise in the horizontal position, when cardiac output, which has often been blamed in limiting of performance, might be greater (48) and thus less likely to impose the limitation. If this reasoning is correct, development of a greater ability to diffuse O_2 in the face of lowering pressure gradients in the lungs would be a useful adaptation to the swimmer. Swimmers regularly employ in their training routine some underwater swimming which must expose the swimmer to periods of hypoxia. Chronic exposure to hypoxia has been shown to effect an increase in diffusing capacity (357); perhaps the same adaptations might occur in young swimmers who regularily exercise at maximal work levels.

On the other hand, arguments can be developed to show that such adaptations in swimmers may not be necessary. These include:

1) The improved uniformity of $\dot{V}/\dot{Q}$ ratios throughout the lung, and the higher Vc associated with the prone position would favour gas exchange in the lung even without an improved D_L/per se.

2) If arterial desaturation were to occur at maximal effort, a high D_L would be beneficial to a 'swimmers' performance.

However, there is little evidence (99) in the literature that this occurs even in maximal endurance exercise in healthy subjects at normal sea-level O_2 concentrations.

3) Despite the limitations imposed on respiration by partial immersion as in swimming, it would seem that these effects on the breathing pattern are negligible. In general, most champion swimmers breathe on each or alternate arm cycles, occasionally with a cadence of 1:3. Thus in a typical 100M race, requiring about 55-60 secs.to perform, it is estimated* a champion swimmer will breath at a rate of 50/min. It becomes apparent that the period of breath-hold in such cases would be brief and therefore a marked lowering of alveolar O_2 concentration during the swim stroke would be surprising.

However, it is also clear that the difference between the winner and others in a championship event is often a matter of several small differences, which can summate to produce the champion. There can be no doubt then that the swimmer with the greater ability to diffuse O_2 would have a slight advantage. It is possible that this advantage may play its' part in the first ten meters or so of the race, during which time he performs without breathing. However, in swimming, where skill or technique and motivation play such a key role in determining performance, it is doubtful that this advantage would be crucial.

* George Gate, Canadian Olympic Swim Coach,1968.

RESULTS: Cardio-Respiratory Functions

The regression equations for Qc, SV, HR, $\dot{V}O_2$, $\dot{V}$ and (A-V) O_2 difference are given in Table (S10).

Ventilatory Results:

The sex relation in swimmers in respect to $\dot{V}O_2$ and $\dot{V}$ is shown in Fig.S22. No difference is seen in $\dot{V}O_2$ - work relation although the girl ventilates more for a given $\dot{V}O_2$ than does the boy. The difference was more marked at higher loads, making the regression slope for females steeper ($P \leq .05$) although the statistical analysis for any work load showed the sex difference not significant.

Fig. 23A shows no difference in efficiency between swimmers and adults although for a given work load, $\dot{V}O_2$ was slightly greater in the swimmers. Fig. 23 B & C show the age effect on $\dot{V}O_2$ within the swimmers. As shown, the difference with age in girls is slight but considerable in males, suggesting that efficiency is lower in the older swimmers, especially males (the opposite was observed in Controls).

Comparison with Controls of $\dot{V}O_2$ and work is shown in Fig.S24. Higher values for $\dot{V}O_2$ in male swimmers were found significant at load 150 KgM/min. only (P .0476); a similar trend was found in females at higher, though not at lower work loads but in no case was the difference significant. No difference in ventilation was observed in females (Fig.S25) although ventilation, and

TABLE (S 10) CARDIO-RESPIRATORY REGRESSION EQUATIONS - SWIMMERS

Sex	Y	REGRESSION EQUATION	S.E. of Coef.(b) *		Correlation Coef (r) *		S.E.of Y
M	$\dot{Q}c$	= 6.23 + 4.03 ($\dot{V}O_2$) - 0.195 (Age)	0.587	0.080	.695	.197	1.17
		= 4.39 + 3.20 ($\dot{V}O_2^2$)	0.505				1.23
F		= 2.82 + 3.78 ($\dot{V}O_2$) + 0.083 (Age)	0.581	0.080	.720	.414	1.41
		= 3.66 + 4.06 ($\dot{V}O_2$)	0.518				1.41
M	SV	= 49.5 + 8.61 ($\dot{V}O_2$) + 0.657 (Ht.)	6.30	0.151	.518	.688	12.60
F		= 53.5 + 8.37 ($\dot{V}O_2$) + 0.634 (Ht.)	5.02	0.130	.472	.654	11.80
M	HR	=348.5 +43.84 ($\dot{V}O_2$) - 1.697 (Ht.)	6.33	0.151	.046	-.681	12.02
		=203.5 +39.46 ($\dot{V}O_2$) - 8.59 (Age)	8.19	1.12		-.595	16.3
F		=325.2 +41.8 ($\dot{V}O_2$) - 1.407 (Ht.)	6.47	0.168	.223	.515	15.2
		=200.7 +35.5 ($\dot{V}O_2$) - 6.398 (Age)	7.11	0.981		-.468	17.2
M	$\dot{V}O_2$	= 0.430 + 0.0025 (load)	0.0002		.868		0.185
		= 0.260 + 0.0023 (load) + 0.053 (Age)	0.0001	0.007		.580	0.121
F		= 0.278 + 0.0028 (load)	0.0001		.925		0.136
		= 0.036 + 0.0026 (load) + 0.021 (Age)	0.0001	0.007		.442	0.126
M	$(A-V)_{O_2}$	= 6.62 + 6.59 ($\dot{V}O_2$)	0.835		.769		2.04
F		= 6.96 + 5.97 ($\dot{V}O_2$)	0.798		.704		2.17
M	$\dot{V}$	= 7.95 +17.78 ($\dot{V}O_2$)	1.52		.872		3.70
F		= 5.73 +22.28 ($\dot{V}O_2$)	1.54		.885		4.19

* S.E. and (r) follows same order as shown in regression.

Independant Variables - Age in years, Ht.in cms., Load in KgM/Min., $\dot{V}O_2$ in litres.

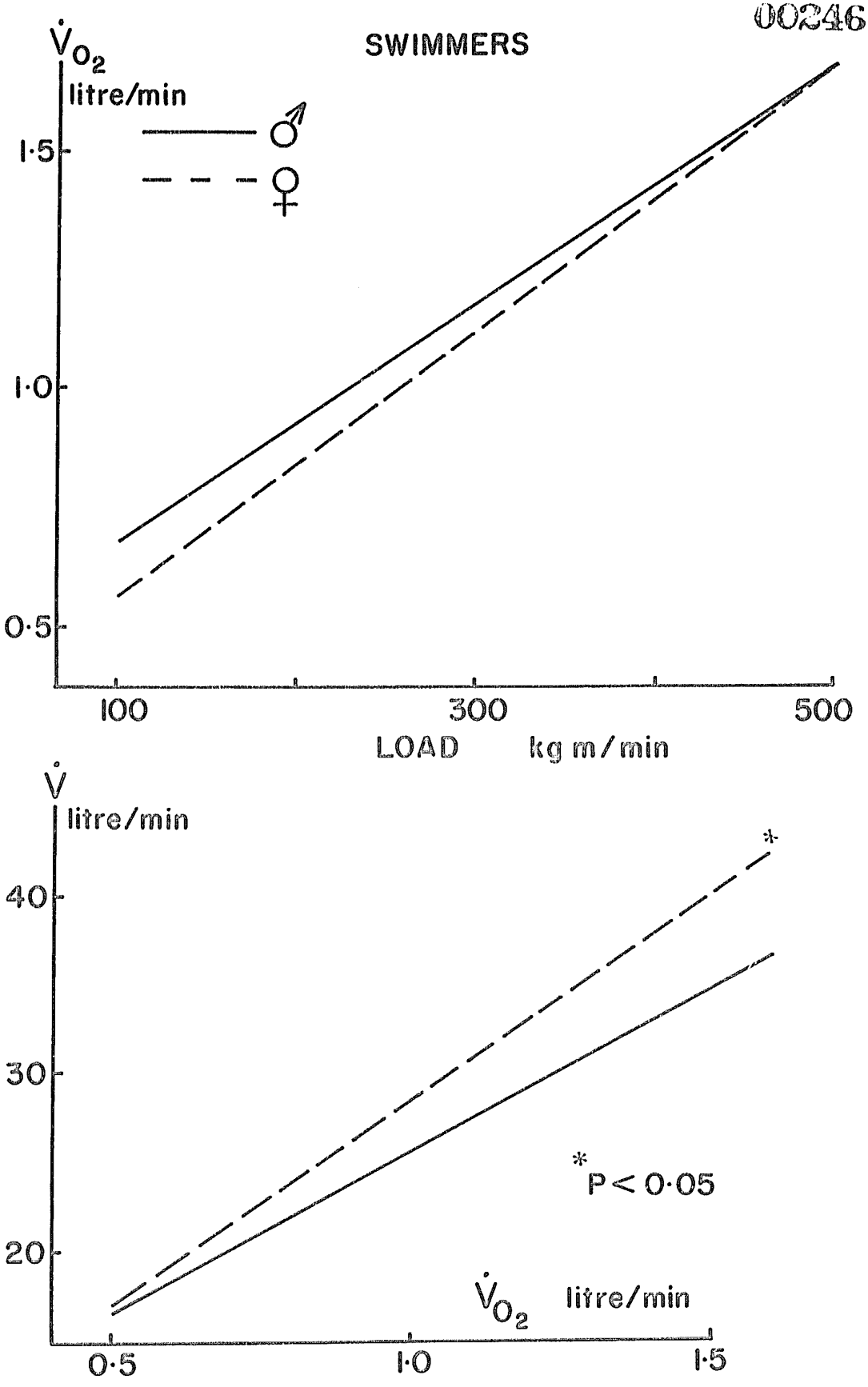


FIG. S_{22} - Sex comparison of swimmers in $\dot{V}o_2$ - work and $\dot{V}$ - $\dot{V}o_2$ relationships
(* indicate slope difference of regressions).

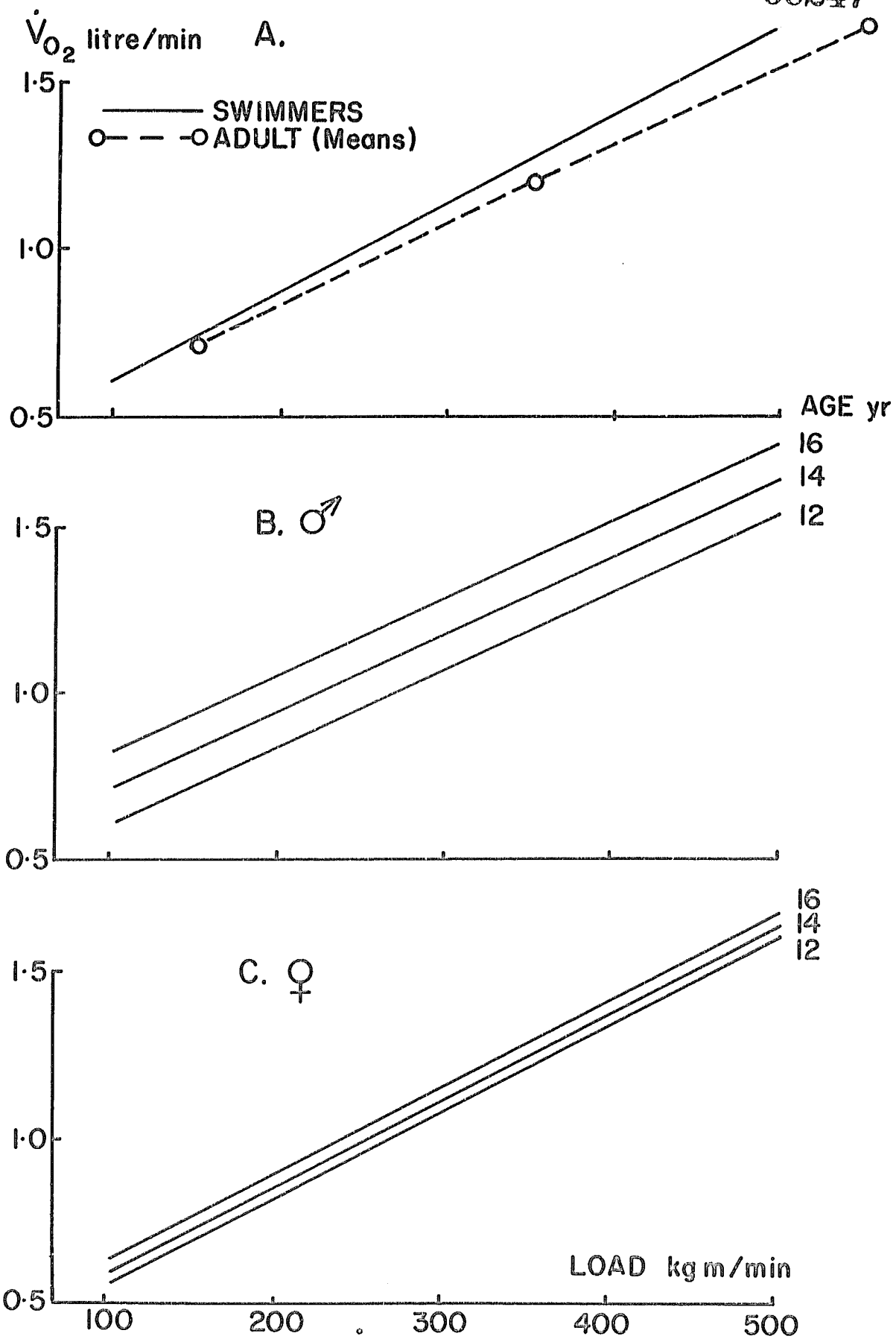


FIG. S_{23} - A. Relation of $\dot{V}o_2$ to work in swimmers and adults, (39) sexes combined.
B&C. Relation of $\dot{V}o_2$ to work in boy (B and girl (C) swimmers of different ages.

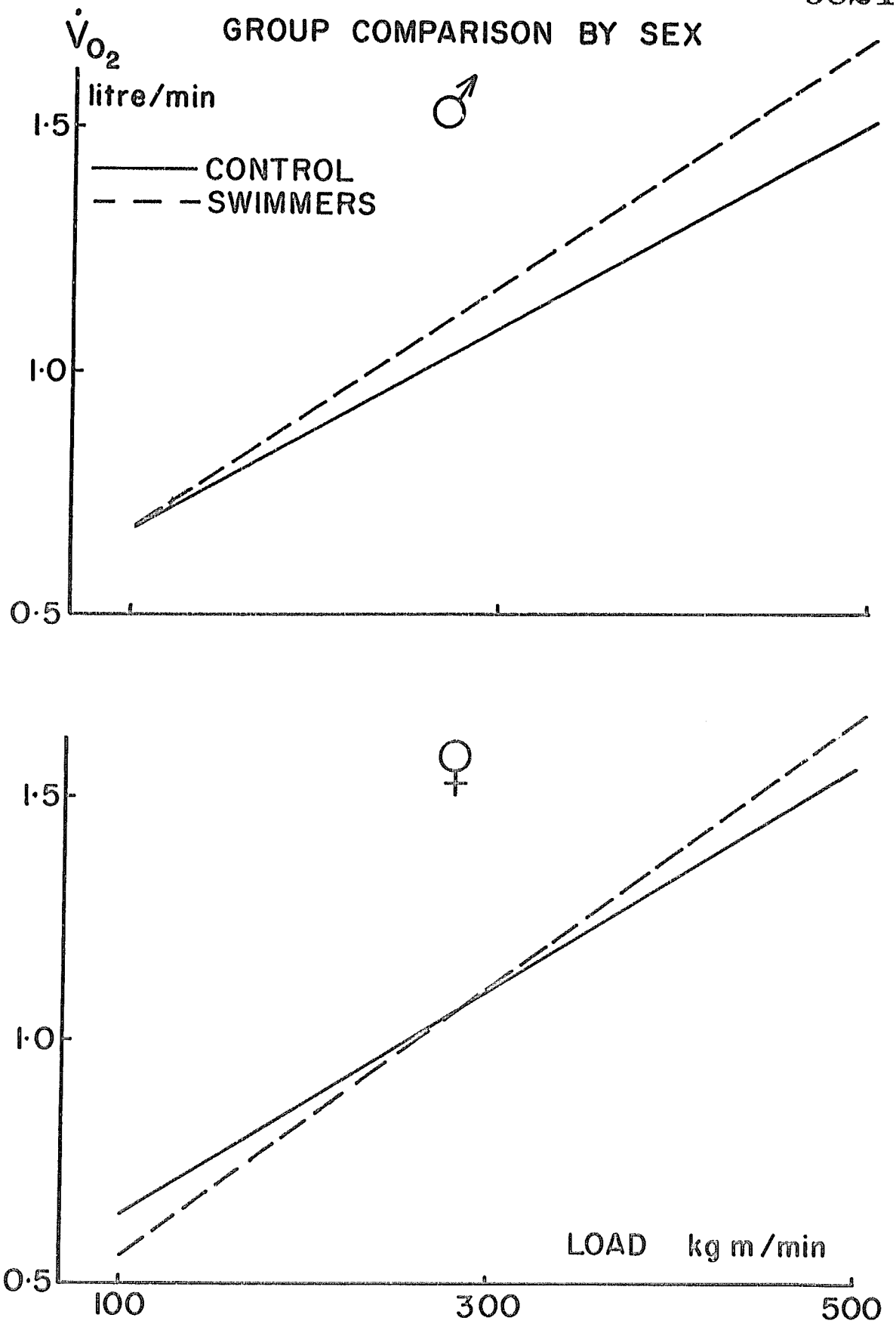


FIG. S_{24} - Comparisons of swimmers and Controls of regressions showing $\dot{V}o_2$ - work relationship.

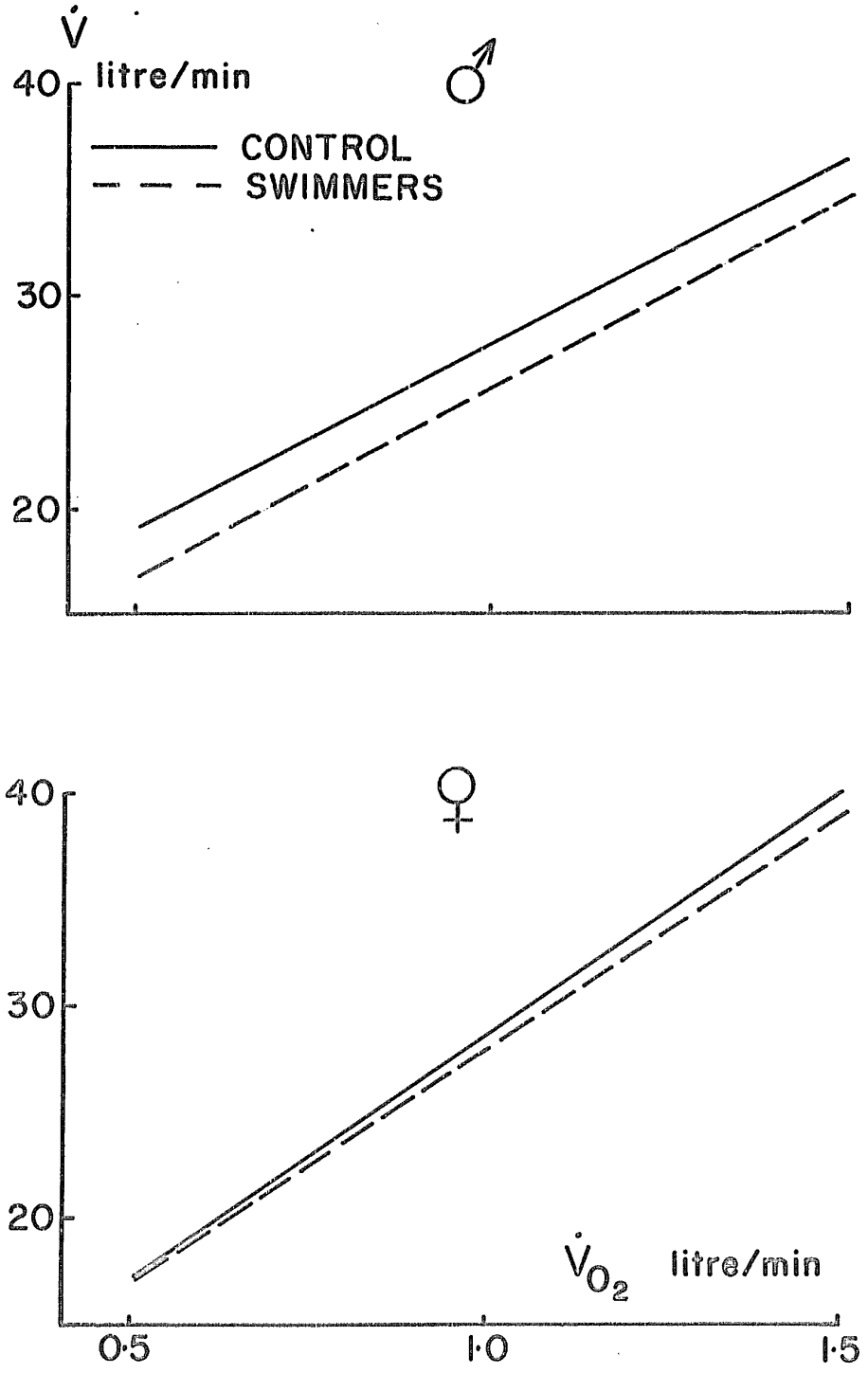


FIG. S_{25} - Regression comparison of Seminaw and Controls in respect to $\dot{V} - Vo_2$ relationship.

consequently ventilatory equivalent, was consistently less in male swimmers but not at the 5% level of significance.

Circulatory Results:

Fig.S26 shows results for $\dot{Q}c$ in relation to $\dot{V}_{O_2}$. In each sex the swimmers are shown to have a lower cardiac output than Controls for comparable $\dot{V}_{O_2}$. The difference is more marked in boys where the slopes of the regressions showing this relation are different ($P < .001$). However, when group comparison was made by height grouping, at few loads were these differences significar either in males, females or combined sexes.

The regressions showing group differences in heart rate as related to $\dot{V}_{O_2}$ are shown in Fig.S27 (boys) and Fig.S28 (girls). This comparison indicates generally lower values in Swimmers, except in the youngest (shortest). The group difference is more pronounced with age in both sexes and this difference is greater in boys than in girls. In males, at height 140-150 cms., for load 150 KgM/min., the difference was significicant (P .0320); with male swimmers of all heights combined, at load 150 the significance was high (P .0002). In no case were significant group differences in females found.

Stroke volume was shown to correlate highly with height ($r=.650$) in the swimmers (Table S10) and in both sexes the increase in SV with work was less in swimmers than Controls (Fig.S29 No consistent group difference in SV for boys was found (SV greater in swimmers at lower loads) but higher in Control boys

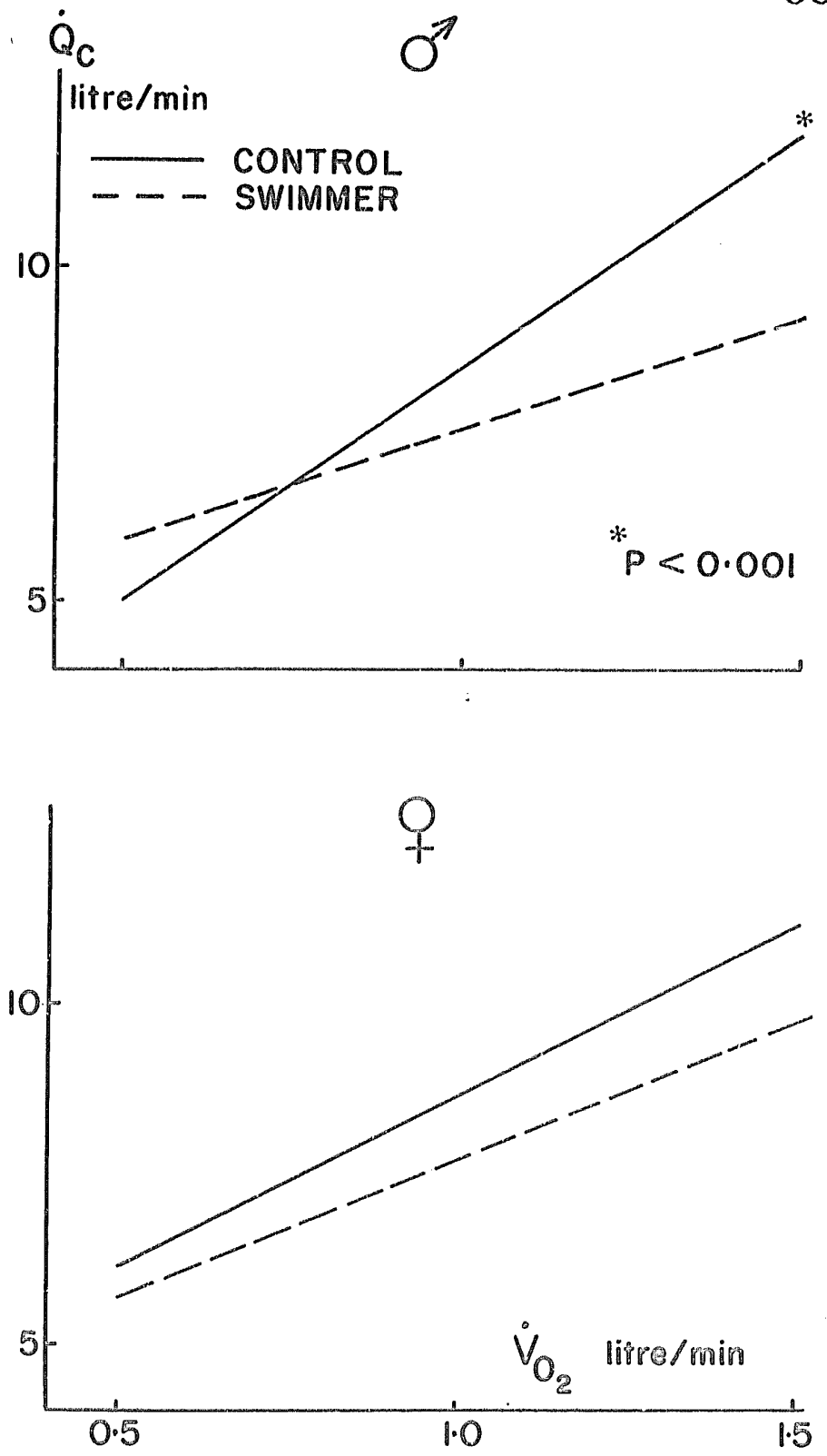


FIG. S_{26} - Regression comparison of swimmers and Controls in the $\dot{Q}_c$ - $\dot{V}o_2$ relationship
(*indicates slope difference in regression lines).

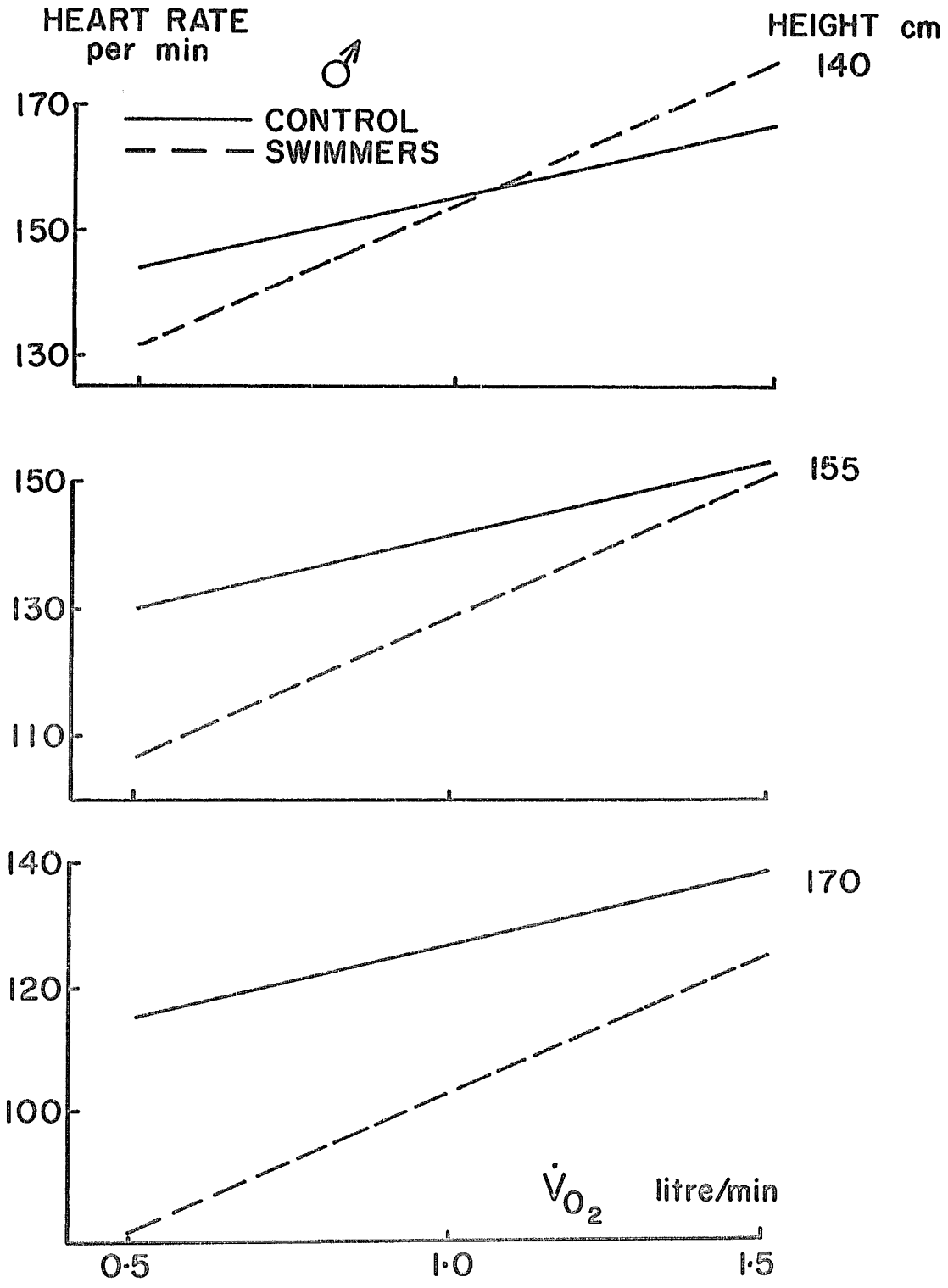


FIG. S_{27} - Heart rate - $\dot{V}o_2$ relationship comparing boy swimmers and Controls at different heights.

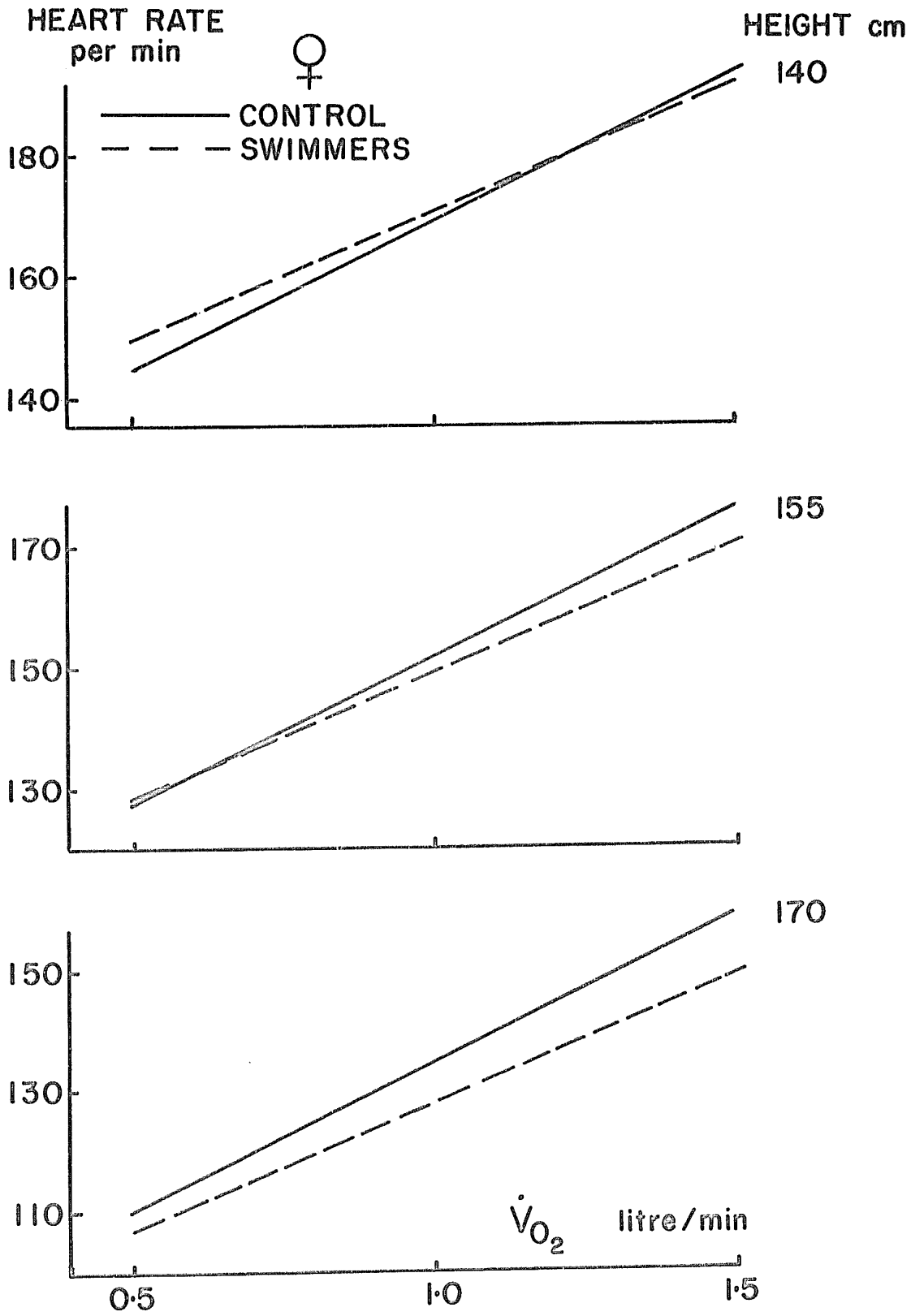


FIG. S_{28} - Heart rate - $\dot{V}o_2$ relationship comparing girl swimmers and Controls at different heights.

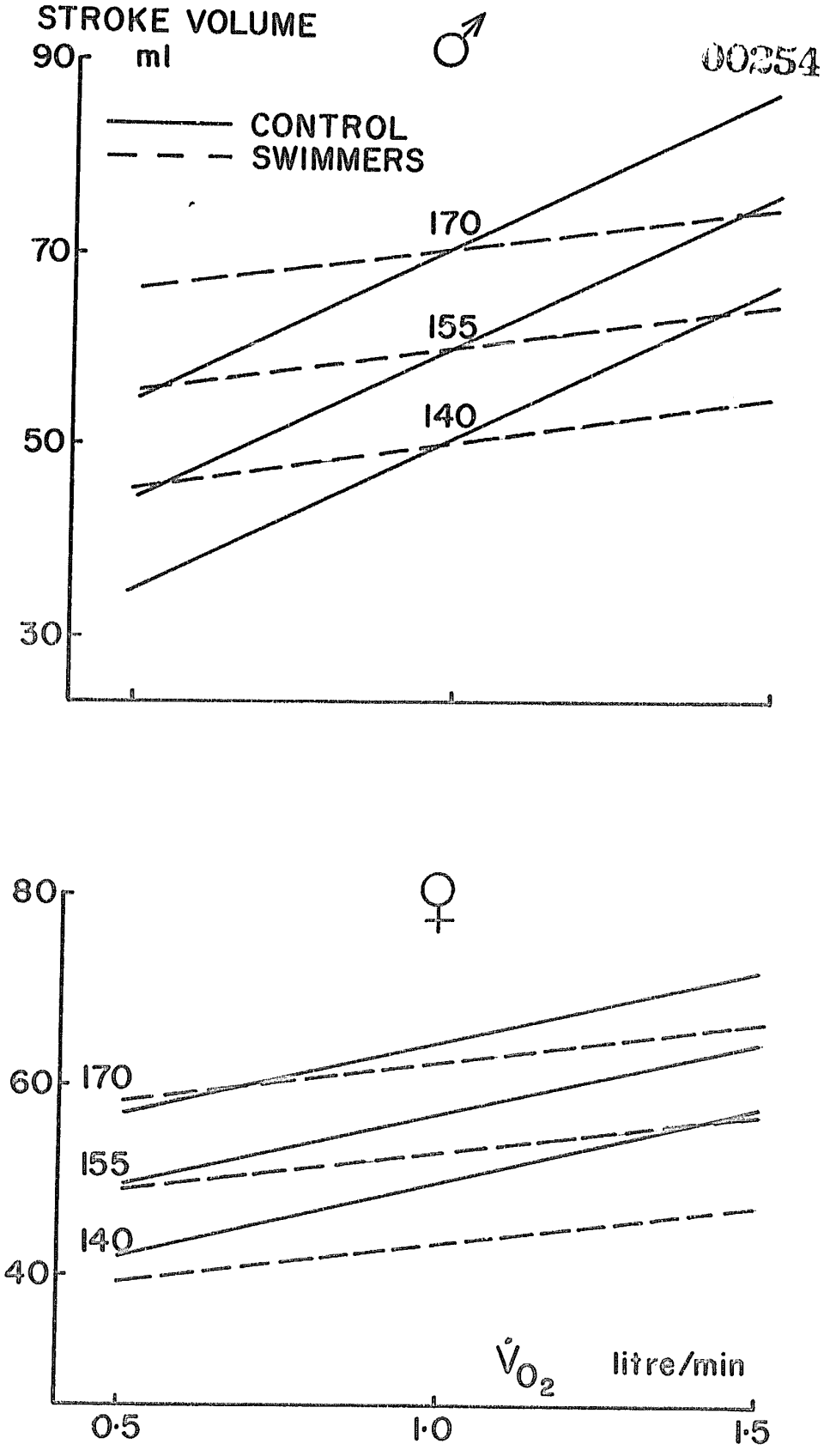


FIG. S_{29} - SV - $\dot{V}o_2$ relationship in Swimmer and Controls of of different heights.

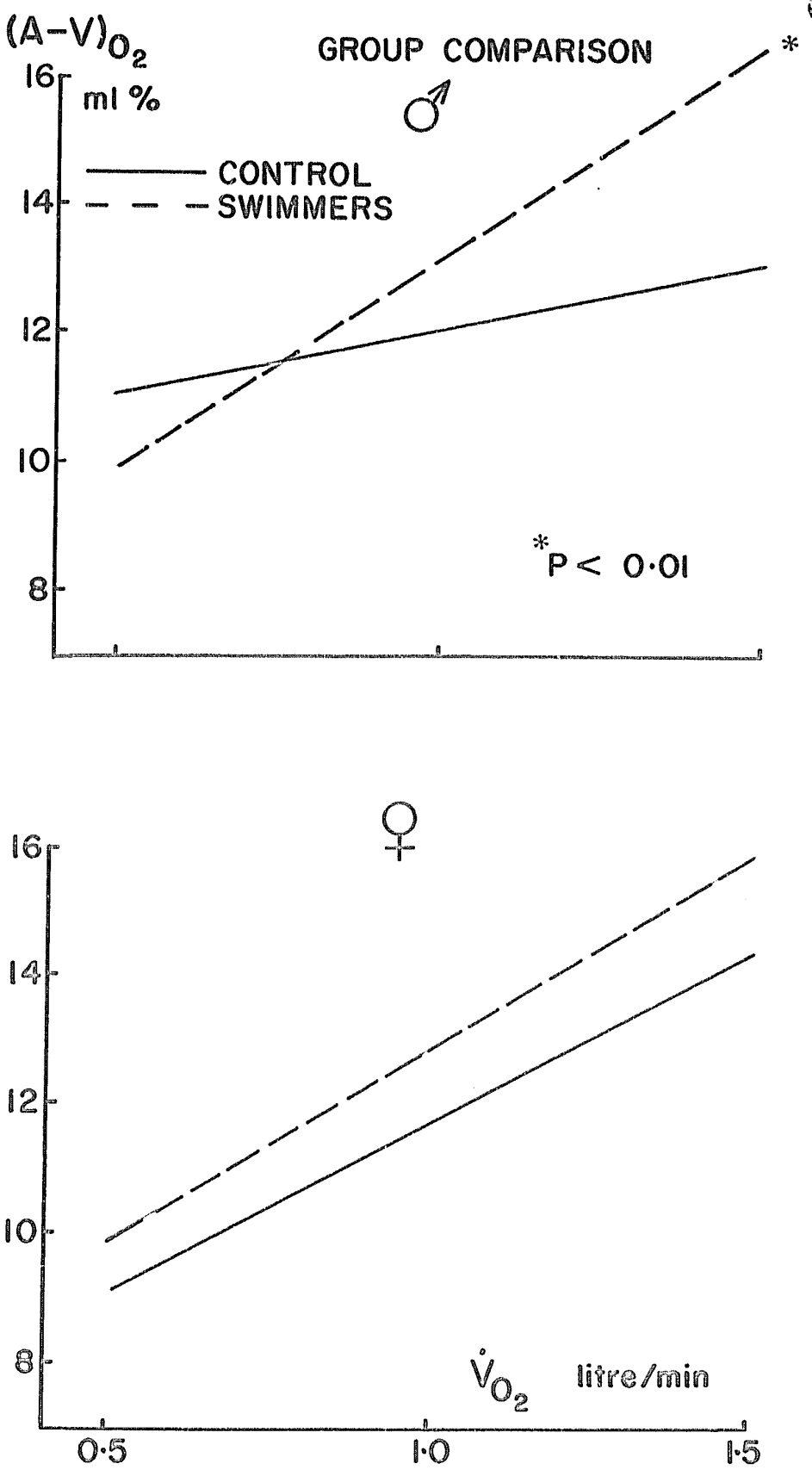


FIG. S_{30} - Relationship of $(A\text{-}V)_{O_2}$. Difference and $\dot{V}o_2$ in swimmers and Controls
(* indicates regression slope difference).

at higher workloads). Values in females swimmers were consistantly lower. A consequence of the lower $\dot{Q}c$ in swimmers, combined with only small group differences in $\dot{V}_{O_2}$, was the greater O_2 extraction (Fig.30) in swimmers. It was in this respect that group differences were most often significant.

Discussion:

The above results indicate clearly that exercise cardiac output for a given $\dot{V}O_2$ is lower in the trained swimmers. This difference is presumed attributable to the difference in level of training of the groups as indicated by their generally lower heart rate during exercise. As a consequence, it is also suggested that this reduction in $\dot{Q}c$, since it is associated with a greater O_2 extraction, probably represents an improved circulatory efficiency in that less work must be required of the heart for a given workload.

It is of interest that group differences in cardiac output, as for D_L, were generally more marked in male than female swimmers. It may be possible that organic differences in sexes could alter the training effects on adaptations to exercise. This might then imply a different mechanism responsible for initiating changes with training which seems unlikely. More probably, the difference may be attributable to greater 'contamination' of the female, than male, swimmers with more inferior performers.

Considering the well documented findings of a greater stroke volume in athletes than non-athletes for a given $\dot{V}O_2$ (57,109,312), it was surprising that a clear difference in this respect was not seen in this study on children. This suggests that the greater SV of the trained adult may be a result of his chronic, prolonged training and that this adaptation in training takes time to develop; endowment may then not be a major factor in this regard. In contrast, heart rate seems to be an early adaptation to training.

One wonders of the significance of the observed difference in efficiency, indicated by the $\dot{V}O_2$-work relationship, seen in the boys (Fig.S24). It seems unreasonable to expect a reduced efficiency in a subject conditioned to hard exercise, though perhaps this is possible when comparison is based on cycling efficiency, which may not be a type of exercise which is compatible with swim training. In a practical sense, swimmers generally avoid such exercise as running, cycling and skating during the swim season because of their tendency to develop 'hard' muscles in contrast with the characteristic 'soft' muscles which are said to characterize swimmers. Realizing the supportive role played by the leg muscles in such exercises, but not in swimming, this subjective description of muscle difference may be feasible and perhaps accounts for difference in efficiency. Alternatively, the difference may be due to a greater O_2 debt, not measured in this study, in Control boys. This seems unlikely in view of the modest test exercise loads employed.

PART IV

Chapter 8. Project Training

A. Effects of Training on Cardiac Functions

..subjects
..training program
..testing procedure and methods
..results
..discussion..ventilatory functions
..circulatory functions

B. Effects of Training on Exercise Diffusing Capacity

..subjects
..training program
..testing procedure and methods
..results
..discussion

PROJECT: TRAINING

From the above studies, in which group comparison was made between Controls and Swimmers in training, significantly higher values for exercise diffusing capacity were found in male, though not in female swimmers. The groups differed also in respect to exercise cardiac output where it was seen the trained swimmers had lower values in relation to $\dot{V}O_2$ than did Controls. This difference was not significant, though it was consistent.

Such group comparisons cannot define specifically the consequences of athletic training, although in the above discussions the slight but consistent group differences were assumed due solely to the swim training. The above studies suggested further that if there are differences in respect of D_L and $\dot{Q}_c$ effected by training they must be small differences which thus may easily be obscured by inter-individual variations which are known to be considerable in each of these measurements. For these reasons, a different experimental protocol was followed to study the effects of training on $\dot{Q}_c$ and D_L, whereby each individual could serve as his own control. This project consists of two parts..Cardiac Functions and Diffusing Capacity..which are presented below.

A. The Effects of Training on Cardiac Function:

The specific purpose of this study was to study the effects of seasonal training on cardiac output during exercise. Part of

this material has been previously published. (see attached)

Subjects:

In this study eight (8) individuals were studied. Four (4) were members of a senior Intercollegiate hockey team (designated here as Athletes) and four (4) were university student volunteers (designated as Freshman) who previously had not been engaged in any special training program.

Mean values and range of their physical chacteristics are as follows:

	Age (yrs.)	Height (cms.)	Weight (Kgs.)
Athletes	21 (19-23)	178 (175-180)	74 (71-79)
Freshman	18 (17-19)	179 (178-180)	67.9 (63.5-75.5)

Training Program:

The athletes, being hockeyists, participated in the regular training program as followed by the McGill University Senior Intercollegiate teams. As such, these were not champion calibre players as a team nor were these players individually of champion status. This point is irrelevant because of the protocol of the experiment. What is relevant however is that each has trained hard during the course of the hockey season. No individual record of the training time of each was kept. However, each did participate regularily in team practices which were held on an average of four (4) times weekly for a period of four (4) months, each session lasting 1½ hours. In addition,

they competed in at least one game weekly.

The training program of the Freshmen was less intense and of shorter duration than that of the athletes. The participants engaged in an exercise training program as a group, for a period of four (4) weeks. One hour daily sessions were held during the week-days under the supervision of a member of the McGill Athletics Department. Each was encouraged to continue individually the training during week-ends. Motivation to promote "all-out" training came from group, rather than individual, participation as well as from individual records of his daily performance.

Testing Procedure and Methods:

The athletes were studied either during the week prior to commencement, or in the first week of hockey training and the Freshmen were tested during the ten (10) day period preceeding training. Each group was retested again after completion of training, i.e. the athletes after 4 months, Freshmen after 4 weeks.

Each subject was tested at three (3) exercise loads during one visit on the same bicycle ergometer, the athletes at 550, 750 and 900 KgM/min, Freshmen at 350, 550 and 750 KgM/min. Each group thus performed two similar test exercise loads. Measurements were made of minute ventilation, oxygen consumption, heart rate and cardiac output. Stroke volume and A-V O_2 Difference were calculated. All calculations and statistics in this study were done manually.

Methods employed in the testing were similar to those

described in detail above. Cardiac output was calculated using a predicted dead space value (40).

Results:

Tables (1) and (2) show the individual pre-training values for each exercise load. Post-training values are presented as difference from the first measurement; (+) indicates an increase with training, (-) a decrease.

Table (3) is a summary table of these results, showing means, standard deviations for each exercise level as well as the levels of significance (P) of changes in the values with training. In addition, groups were combined and statistical analysis of all observations for each function was performed. These are shown at the bottom of this table.

Individual results are also plotted in Fig.(1), where before (Y axis) and after (X axis) training values are shown in relation to the 45^{o} line of identity. Thus, points falling on this line indicate no change with training, those above a decrease and below the line represents an increase. Since each performed three (3) test loads there are 3 points shown for each subject.

It is seen in Fig.(1B) that heart rate fell in all individuals at each exercise level, without exception. In the absence of an objective measure of work performed and improvement of performance with training, and accepting that reduction in heart rate is one of the more apparent consequences of training, (143, 322) this consistent

TABLE (1) INDIVIDUAL RESULTS - FRESHMEN

No.	Load KgM/min	$\dot{V}$ L/Min.	Δ	Resp.Freq.	Δ	$\dot{V}O_2$ L/Min.	Δ	$\dot{Q}c$ L/Min.	Δ	Heart Rate	Δ	S.V.cc/Beat	Δ	A-V O_2 Diff.	Δ
A.B.	350	30.2	+1.7	14	+2	1.24	± .20	9.75	-1.4	124	-12	78.5	+4.7	12.7	± 4.7
	550	43.6	-5.0	20	00	1.82	- .05	12.9	-3.5	150	-18	86.0	-15.0	14.1	± 4.7
	750	52.7	-4.3	22	00	2.26	± .01	13.2	-2.2	170	-20	77.4	-3.9	17.2	+3.4
D.F.	350	29.7	-2.2	20	-4	1.35	- .01	8.11	-0.02	126	-18	64.4	+10.5	16.6	00
	550	38.3	-2.9	17	00	1.69	± .07			128	-12				
	750	53.0	-0.4	18	+2	2.25	± .40	10.52	-0.3	144	-3	73.4	+3.2	21.4	+3.1
T.S.	350	41.9	-11.8	16	+4	1.23	± .14	11.8	-1.1	138	-12	85.5	-0.9	10.4	+2.5
	550	48.5	- 8.0	28	00	1.60	± .25	16.3	-2.0	168	-12	97.0	-5.4	9.8	+3.1
	750	82.5	-25.5	36	-6	2.35	_ .03	17.7	-1.0	190	-8	93.2	-1.5	13.3	+0.9
O.D.	350	25.9	-.560	11	00	1.33	- .11	10.35	-1.9	112	-8	92.5	-10.6	12.8	+1.5
	550	30.95	-1.8	12	+4	1.68	- .21	12.5	00	130	-8	93.5	+5.5	13.8	-1.7
	750	39.0	-5.9	15	+3	2.11	- .50	12.8	+0.4	156	-16	82.0	+12.6	16.5	-4.3

Δ - indicates change with training.

TABLE (2:) INDIVIDUAL RESULTS - ATHLETES

No.	Load KgM/min	$\dot{V}$ L/Min.	△	Resp.Freq.	△	$\dot{V}O_2$ L/min.	△	$\dot{Q}c$ L/Min.	△	Heart Rate	△	S.V·cc/Beat	△	A-V O_2 Diff.	△
B.H.	550	31.3	-1.1	1.55	-0.9	1.55	-0.69	13.75	-3.4	126	-12	109	-18	11.3	+1.5
	750	48.1	-16.3	16	+4	2.43	-0.60	16.2	-4.6	140	-20	116	-9.5	15.0	-5.3
	900	62.6	-20.6	24	-4	2.63	-0.20	16.9	-3.3	150	-10	113	-16.0	15.5	-5.8
D.C.	550	36.6	-4.4	16	-1	1.66	0.03	13.4	-3.5	156	-38	86.3	-1.8	12.3	-.04
	750	46.5	-3.6	20	0	1.70	+.67	15.2	-1.9	168	-42	90.4	15.6	11.2	+6.6
	900	55.9	-7.0	24	-2	2.33	+.15	14.7	-3.8	172	-24	85.5	11.5	15.8	+7.9
R.D.	550	35.5	-0.4	16	-1	1.63	+.11	11.5	- .9	130	-22	89.0	9.2	14.2	+2.2
	750	46.4	-4.2	18	-1	2.11	+.16	12.5	- .7	156	-24	80.0	9.4	16.8	+2.4
	900	52.6	-3.7	18	0	2.46	-.01	14.5	- .4	174	-30	83.5	14.5	17.0	+ .3
J.T.	550	32.3	-2.0	18	-4	1.60	.21	15.2	-3.7	138	-22	110	-11.0	10.5	+5.2
	750	47.0	-8.2	20	-4	2.38	-.01	16.4	-3.3	150	-12	109	-14	14.5	+3.1
	900	54.9	-10.7	28	-10	2.66	-.01	19.2	-3.0	168	-10	114	-12	13.8	+2.6

△ - indicates change with training.

TABLE (3) GROUP MEAN VALUES. ATHLETES AND FRESHMEN (NON-ATHLETES)

Cardiorespiratory measurements before training and changes after training

Group	Load, kg		V̇ BPTS		f		V̇O₂ STPD		Q̇c		Heart Rate		Stroke Vol.		(A−V)O₂ Difference	
			liter/min	Δ	breaths/min	Δ	liters/min	Δ	l/min	Δ	beats/min	Δ	ml	Δ	Vol %	Δ
Nonathletes	350	Mean	31.9	−3.2	15.3	+0.5	1.29	+0.06	10.0	−1.6	125.0	−12.5*	80.2	−1.4	13.1	+2.2
		± SD	9.1	5.9	3.3	3.5	0.06	0.14	1.5	0.8	10.6	4.1	12.9	8.9	2.6	2.0
	550	Mean	40.3	−4.4*	19.3	+1.0	1.70	+0.02	12.4	−1.0	134.0	−12.5*	84.4	−4.3	14.8	+0.9
		± SD	7.6	2.7	6.7	2.0	0.09	0.19	3.3	2.1	18.8	4.1	15.6	8.5	5.0	3.5
	750	Mean	56.8	−8.5	22.9	−0.3	2.24	−0.02	13.6	−0.9	165.0	−11.8	81.5	+2.6	17.1	+0.8
		± SD	18.3	11.5	9.3	4.0	0.10	0.04	3.0	1.0	19.8	7.7	8.5	7.3	3.3	3.6
Athletes	550	Mean	33.9	−2.0	16.6	−2.0	1.61	+0.06	13.5	−2.9*	137.5	−23.5*	98.6	−5.4	12.1	+2.1
		± SD	2.5	1.7	1.2	1.8	0.26	0.13	1.4	1.3	13.3	10.8	12.9	11.8	1.6	2.3
	750	Mean	47.0	−8.1	18.5	−0.3	2.16	+0.04	15.1	−2.6	154.0	−24.5	98.8	+0.4	14.4	+1.7
		± SD	0.8	5.8	1.7	3.3	0.33	0.60	1.8	1.7	11.7	12.7	16.4	14.0	2.3	1.3
	900	Mean	56.5	−10.5	23.5	−4.0	2.52	−0.02	16.3	−2.6*	166.0	−18.5	99.0	−6.2	15.5	+1.2
		± SD	4.3	7.3	4.1	4.2	0.15	0.14	2.2	1.5	10.9	10.1	16.7	14.0	1.3	5.6
Change after training (all observations)		Mean		−6.4		−0.8		+0.02		−1.8		−17.2		−2.39		+1.50
		± SD		6.4		3.4		0.26		1.6		9.5		10.3		3.5
		P		0.001		0.30		0.70		0.001		0.001		0.30		0.05

Δ = Change in measurement after training. * = Significantly different from 0 (0 = no change with training); i.e., $P < .05$ using Student's *t*-test.

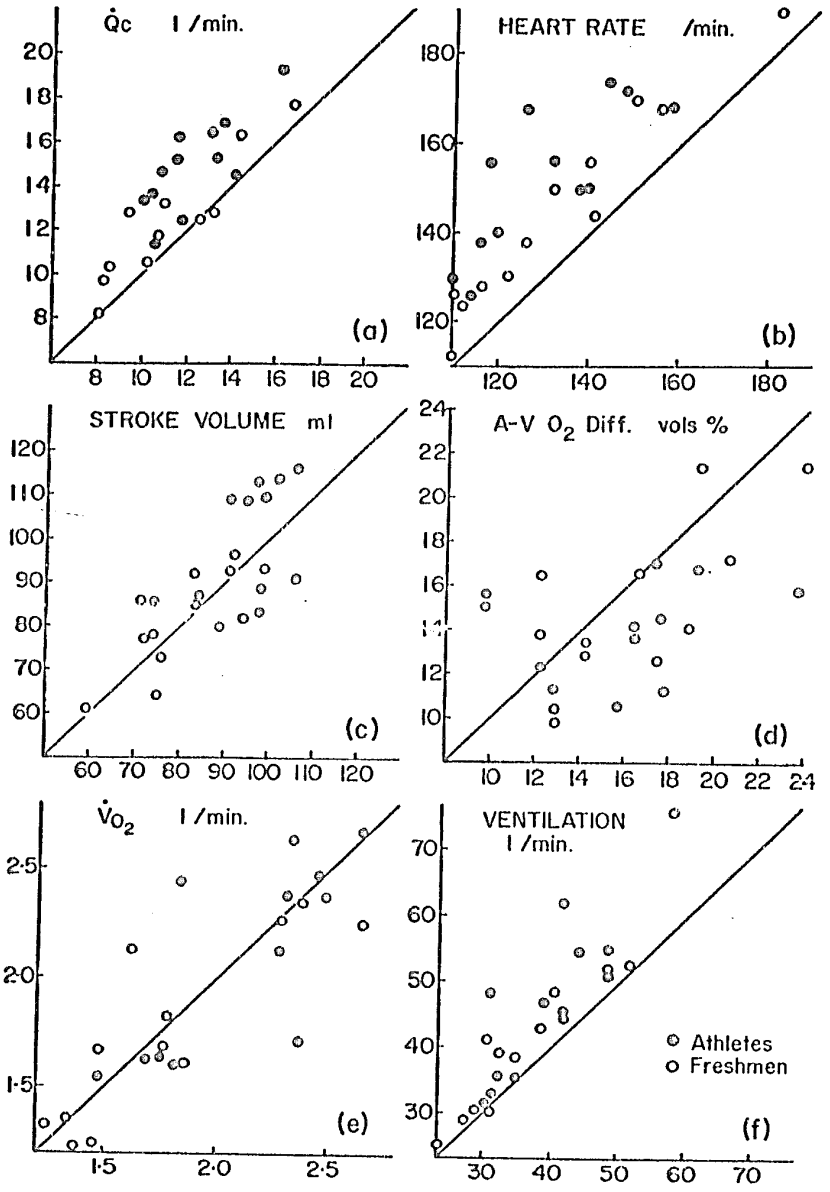


FIG. 1. Comparison of values for A: Qc; B: heart rate; C: stroke volume; D: $(A\text{-}V)O_2$ difference; E: $\dot{V}o_2$; and F: ventilation, after training (on the x axis) and before training (y axis). The 45° line indicates identity. Results are those of four athletes (filled circles) and four non-athletes (open circles), each studied at three exercise loads.

decrease can be interpreted as an indication that the subjects did in fact train. This decrease was highly significant ($P < .001$) in the combined analysis, though not always significant for each load in each group.

The drop in heart rate was associated with a concomitant fall, almost without exception (see Fig.1A), in cardiac output. Within groups, the decrease was significant only in the athletes at 2 exercise loads (550 and 900 KgM/min). When groups were combined, the mean change was significant at 1%. No consistent change was found in the calculated stroke volume, individual points falling for the most part close to the line of identity. (Fig.1c)

In respect to ventilatory functions, minute ventilation decreased in all but one subject at one load and the decrease was found significant in only the Freshmen group at the 550 KgM/min, exercise load. The combined group change was highly significant ($P < .001$). No change was seen in oxygen consumption and most points (see Fig.1E) fall closely about the line indicating no change. In this regard, there are 3 exceptions (subject O.D., B.H. & D.C.), each of which occurred at load 750. These may represent error although repeated analysis of the original tracings reveal no such evidence. The fall in $\dot{Q}c$, accompanied by no change in $\dot{V}O_2$, gave an increase in the calculated A-V O_2 Difference which was not significant in either groups at any exercise load; however, the combined group mean change was at the 5% level.

The decrease in $\dot{V}$, with no change in $\dot{V}O_2$, resulted in a lowered ventilatory equivalent ($\dot{V}/\dot{V}O_2$) with training in both groups ($P < .001$) (Since these data are inherent in the above tables, they are not shown). The relative hyperventilation in pre-trained also resulted in a decrease in respiratory quotient (R) with training in both groups ($P < .01$). Likewise, when alveolar ventilation ($\dot{V}_A$) was calculated using an assumed dead space,(9) there was a significant fall ($P < .001$) in both groups.

Group comparisons can also be seen from Table (3). Fig.(2) shows such comparison for athletes and Freshman in respect to $\dot{Q}c$, HR, $\dot{V}$ and $\dot{V}O_2$. No group difference, nor training effect, was found in $\dot{V}O_2$, as shown by Fig.(2C) where the lines joining mean group values are virtually coincident at the work loads which each group performed. $\dot{V}$ was higher initially in the freshmen and with training fell to the line representing the untrained athletes. The decrease in both groups with training was comparable in both groups.

In the untrained state, $\dot{Q}c$ was slightly higher in the Athletes (Fig.2A) but the fall with training was more marked in this group than in the Freshmen group. Likewise, with respect to HR, (Fig.2B) group differences were small in the untrained but the drop with training was greater in the Athletes. Stroke volume was greater in the Athletes.

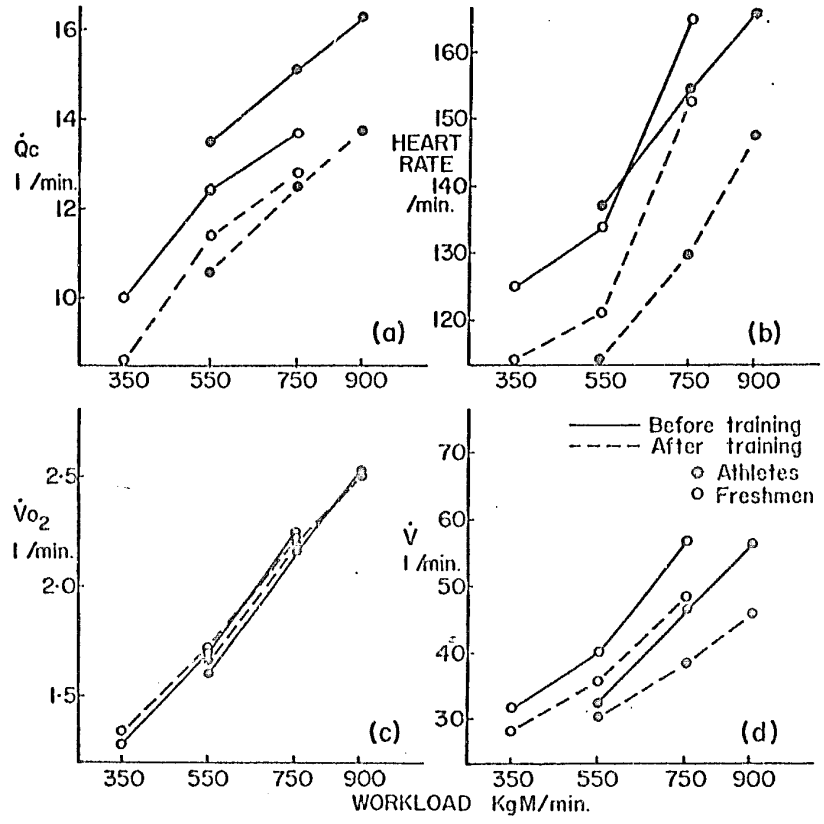


FIG. 2. Mean values for A: $\dot{Q}c$; B: heart rate; C: $\dot{V}o_2$; and D: $\dot{V}$, in athletes (filled circles) and nonathletes (open circles), plotted against external exercise load as the independent variable on the x axis.

DISCUSSION

Ventilatory Functions:

The findings in respect to $\dot{V}O_2$ (unchanged) and $\dot{V}$ (decreased) are in agreement with reports in the literature (114). This decreased ventilation can be regarded as a desirable feature in that the ventilatory equivalent fell, thereby lowering the O_2 cost of breathing. Admittedly, at moderate work levels this may not be a great advantage to the trained person but if corresponding decreases were found as maximal exercise levels are approached, the aerobic contribution to the energy producing system would be enhanced by training.

One wonders of the significance of the observed decrease in R with training, a finding observed early in the studies at the Harvard Fatigue Laboratory (44) when group comparison was made. At least two possibilities of explanation for this phenomenon are possible. If lactate production was greater in the pretrained, the greater ventilation could be in effect an attempt to maintain a normal blood pH by creating a respiratory alkalosis as compensation for the resultant metabolic acidosis in exercise. However, a significant change in lactate levels is doubted in our study, especially since the exercises were not severe. Nonetheless, this explanation may have merit, especially since it has been shown that lactate production for submaximal exercises decreases with training (300). Alternatively, training may effect a shift in 'perferred' metabolite from carbohydrates to fats; greater utilization of the latter would lower the CO_2

production. A contraindication of this is the report of Cobb and Johnson (92) who found no difference between trained and sedentary groups in the uptake of free fatty acids during exercise. The first possibility seems the more probable.

The decreased alveolar ventilation indicates an improved O_2-extraction at the lungs and these findings are in agreement with other reports (274).

Circulatory Functions:

The surprising finding of this study was the consistent lowering of exercise cardiac output with training. These results differ from those of Freedman (141) and Frick (143) who also made intra-individual comparisons, but is in partial agreement with Tabakin (340) who found lower values in exercise cardiac output at lower and moderate ($\dot{V}O_2 \leq 1.5L$), though not at higher, intensities of exercise. It is of interest that Varnauskas (349) observed changes with training in cardiac patients similar to our findings.

Our study contrasted with those of Freedman and Frick in that their studies were made with the subject supine, although training was done in the upright position. The hemodynamic changes known to be effected by study posture may have obscured the training effect in their studies. Freedman studied only 2 cross-country runners; the 'untrained' measurements were made after 3 months of detraining whereas Frick made measurements at only one mild (400 KgM/min) level of exercise. The more prolonged detraining period of our athletes (8 months) and the heavier

test exercises performed might also account for our different findings.

Tabakin was impressed that changes in cardio-respiratory variables were not more striking. These authors suggest, on the basis of the drop with training at low exercise levels only, that these changes "may represent an adaptation to a particular grade of work which the athlete performed daily during training" i.e. a sort of specificity of adaptation related to the particular level of training employed.

The possibility that difference in training methods may account in part for our different finding cannot be ruled out. Our subjects exercised frequently at or near maximal work levels for short periods (Cf. interval training plan in common use in athletic training) in contrast with the endurance type training of cross-country runners (141,340), and perhaps, with those in basic training in Finland (143). One also wonders, in view of the small change in heart rates with training, if the runners (140,340) really were 'unfit' in the untrained state.

The decrease in cardiac output was found to be due solely to a reduction in heart rate, there being no difference in the calculated stroke volume with training. Frick observed a significant increase in heart volume with training which was associated with a higher stroke index both at rest and in exercise. On the other hand, at the exercise levels in which a decreased $\dot{Q}c$ was found, Tabakin showed a decreased stroke volume.

Although our study was designed to permit intra-individual comparisons with training it is of interest to compare the groups (Athletes and Freshmen) in respect to exercise adaptation (see Fig.2). No difference was seen in efficiency since the $\dot{V}O_2$-work relationship between groups was not different. However, in the untrained state the Athletes had lower ventilation for the 2 comparable work loads performed by each group, and training had the effect of lowering the values in the Freshman to that of the untrained Athletes. This suggests that the athletes in the untrained condition were relatively more 'fit', although the untrained heart rates of the groups, which were not different, would not support this view. Alternatively, the difference in the untrained states might indicate a special endowment of the Athletes or possibly that the ventilatory effects of previous training may persist longer than do these effects on heart rate.

The untrained $\dot{Q}c$ of the Athletes was higher, though not at significant levels, than the Freshmen group, and the fall in this measurement, as well as in heart rate, was more marked in the Athletes. Presumably, this is a consequence of the much more extensive training program of the hockeyists. It has been seen from the literature review that numerous investigators (50, 92, 268, 312) found no group difference in $\dot{Q}c$ between the trained and the untrained. It is of interest to note that similar conclusions would have been made from the present study had each individual not served as his own control. In fact,

the only significant group difference (i.e. between untrained Freshmen and trained Athletes) would have been in respect of heart rate and ventilation. This supports our premise that the effects of training on parameters which have an accepted wide intra-individual variation can be studied only by repeat measurements on the same subject.

Finally, the higher values for stroke volume in our Athletes is in agreement with the well documented findings of other (57, 87, 312). Furthermore, this study would suggest that this feature of the Athletes, which must indicate a greater heart volume or greater systolic emptying, is a result of earlier intense training or endowment. Seasonal training seemingly had little effect on altering this dimension.

B. The Effects of Training on Exercise Diffusing Capacity:

The specific purpose of this study was to investigate differences in exercise diffusing capacity in subjects tested before and after a period on intensive swim training.

Subjects:

Six young adult subjects, all members of the McGill senior swim team, were studied. The physical characteristics of each is shown in Table (4). The best swimming event of each subject is also indicated here.

Training Program:

The training program for the group commenced in early October and terminated in late February of the following year. The first 10 days of training consisted of an on-land exercise program employing calisthenics, and weight lifting activities. Daily swim sessions (5/week) of about 11/2 hours were held for the following six weeks after which the number was reduced to 4/week. In addition, all subjects participated in periodic swim meets during the season.

Testing Procedure and Methods:

Each subject was tested before, and again after swim training. Three test exercise loads (see Table 5) were performed on the bicycle ergometer. Ventilation, oxygen consumption, and heart rate were measured for each load while diffusing capacity measurements were made for the two lower loads only.

Methods have been described previously. Correction for

TABLE (4) PHYSICAL CHARACTERISTICS - ADULT SWIMMERS

Name	Height (cms.)	Weight (Kgms)	Age (yrs)	Best Stroke and Distance
R.P.	185.5	80.0	22.1	Free Style ...100 M
R.T.	177.5	81.8	21.1	Breast ...100-200M
R.M.	176.5	70.5	19.3	Back only ..200 M
G.R.	181.5	88.7	20.3	Free Style ..50 M
E.H.	184.0	80.5	21.1	Breast..200 M
B.M.	176.5	66.5	19.4	Free Style ..50 M only
Means:	180.2	76.3	20.5	

ADULT SWIMMERS

Name	Load Kg/Min.	$\dot{V}$ l/min. Δ	$\dot{V}O_2$ l/min	Δ	Heart Rate /min	Δ	D_LCO ml/min/mmHg	Δ
R.P.	550	37.8	-2.6	1.89	-0.05	159	-26	47.1	+4.8
	750	43.1	+2.6	2.48	-0.06	168	-19	53.7	+2.1
	950	81.7	-24.8	2.78	-0.05	186	-19		
R.T.	550	32.4	+0.30	1.87	+0.09	148	-23	46.9	+5.4
	750	46.4	-4.8	2.57	-0.17	156	-16	53.2	+2.1
	950	74.4	-0.3	3.32	-0.23	186	-29		
R.M.	550	37.0	+0.8	2.12	-0.22	172	-24	45.4	-9.2
	750	51.0	+5.2	2.51	+0.03	186	-22	41.1	-0.7
	950	88.5	-18.8	3.43	-0.33	192	--		
G.R.	550	34.8	-1.7	2.08	-0.73	136	-10	41.1	-0.7
	750	43.1	-0.5	2.55	-0.28	150	- 8	48.1	-2.0
	950	51.0	+3.6	3.17	-0.27	172	-10		
E.H.	550	33.1	-4.1	1.84	-0.12	134	- 5	64.0	-2.5
	750	43.5	-8.8	2.40	-0.05	152	-10	64.6	+1.2
	950	41.8	+2.4	2.95	-0.11	172	- 4		
B.M.	550	36.2	+0.9	1.73	+0.45	184	-22	48.6	-1.4
	750	50.3	+3.1	2.15	+0.54	196	-16	52.6	-2.0
	950	68.4	+0.8	2.69	-0.17	205	-12		

Δ - indicates change with training.

TABLE (6) SEASONAL TRAINING EFFECTS - DIFFUSING CAPACITY

ADULT SWIMMERS

Load KgM/min.		Mean Ventilation ls/min.	△	Mean O_2 Consumption ls/min.	△	Mean Heart Rate /min.	△	Mean Diffusing Capacity ml/min/mmHg	△
550		35.2	-1.03	1.92	-0.09	155.5	-18.3	48.8	-0.6
	SD ±	3.7	1.41	.14	.25	14.1	8.6	7.8	3.1
	P		.20		--		.01 *		.60
750		46.2	0.50	2.44	----	168.0	-15.2	52.2	+0.1
	SD ±	3.6	2.80	.17	.19	19.2	5.3	5.9	0.6
	P		----		----		.0001 *		---
950		67.5	-7.80	3.06	-0.06	185.3	-12.3		
	SD ±	18.1	9.80		.03	12.2	10.5		
	P		0.10		---		0.05 *		
COMBINED:			-3.15		-0.05		-15.3		-0.25
	SD ±		6.65		0.19		8.3		2.48
	P		0.60		0.50		.0001 *		0.80

* significant level (P)

△ indicates change with training

COHb were made in DL calculations. All calculations were performed manually.

Results:

Individual results are given in Table 5; mean values for the group are presented in Table 6 and shown graphically in Fig.3. This figure clearly shows no training effects in respect to $\dot{V}$, $\dot{V}O_2$ and DL, although heart rate was significantly lower at each work level. This fall in heart rate was consistent in all individuals at all loads, except RM at load 950 where no change was found (see Table 5). Also shown on this figure is the predicted value (117) of DL for normals of similar age and at comparable levels of $\dot{V}O_2$. The mean values for the swimmers clearly lie above the confidence limits of the prediction equation. However, when individual untrained results are plotted (Fig.4) two of the swimmers lie below the line for normals, the others above, although only two of these are above the confidence limits. One of the present group had values comparable to the champion swimmers of Mostyn (266), shown as the dashed line.

Fig.5 shows the comparison of hockeyists and swimmers. Swimmers had higher values for heart rate, ventilation and oxygen uptake at each level of exercise in both the trained and untrained states and the decrease with training in heart rate and ventilation was less marked in the swimmers than in the hockeyists.

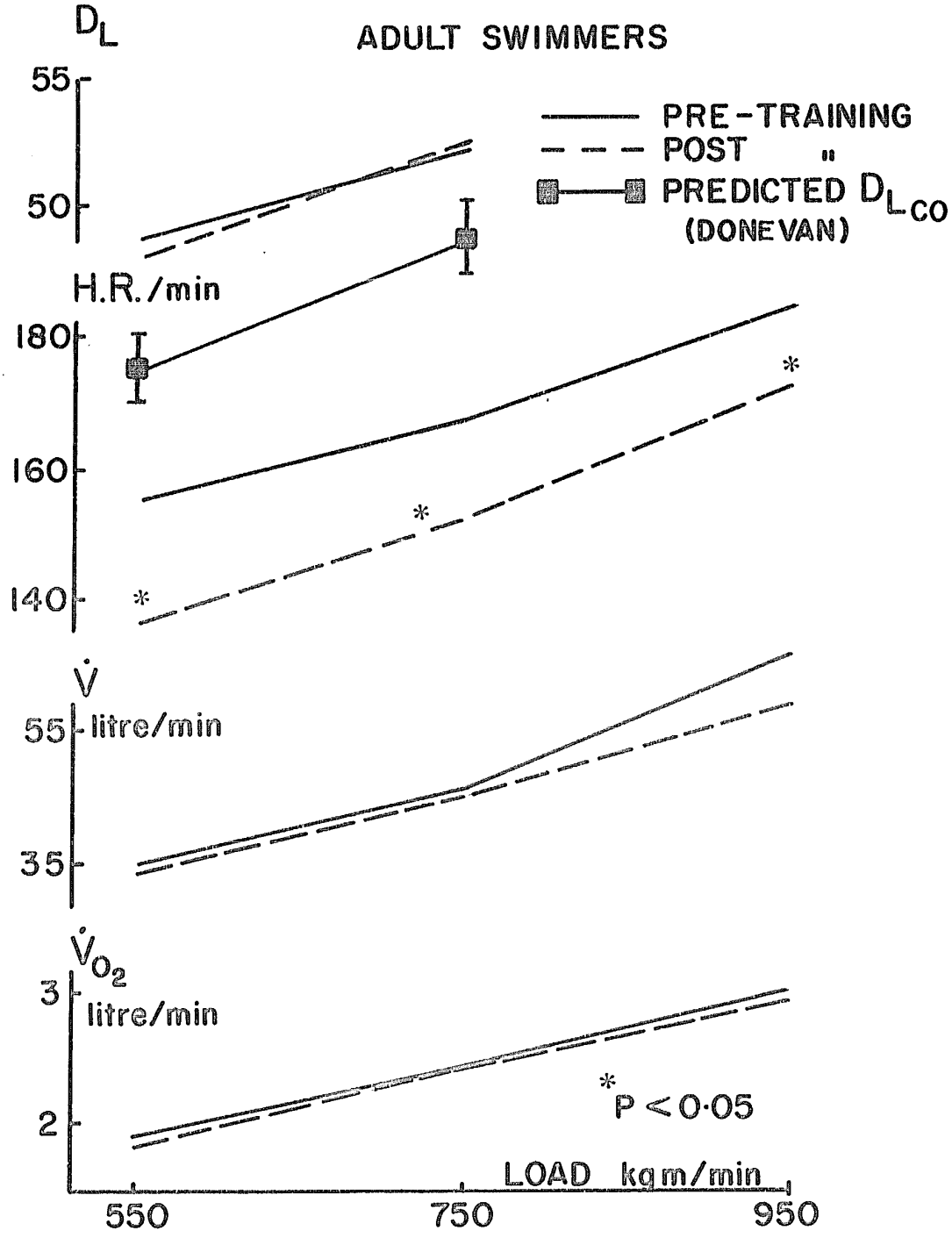


FIG. 3. Comparison of mean values pre- and post- training in adult swimmers of D_L, HR, $\dot{V}$ and $\dot{V}o_2$ in relation to workload. Regression (1 SD indicated) of D_L for adults (25 years) is shown.
(* indicate difference in mean values with training).

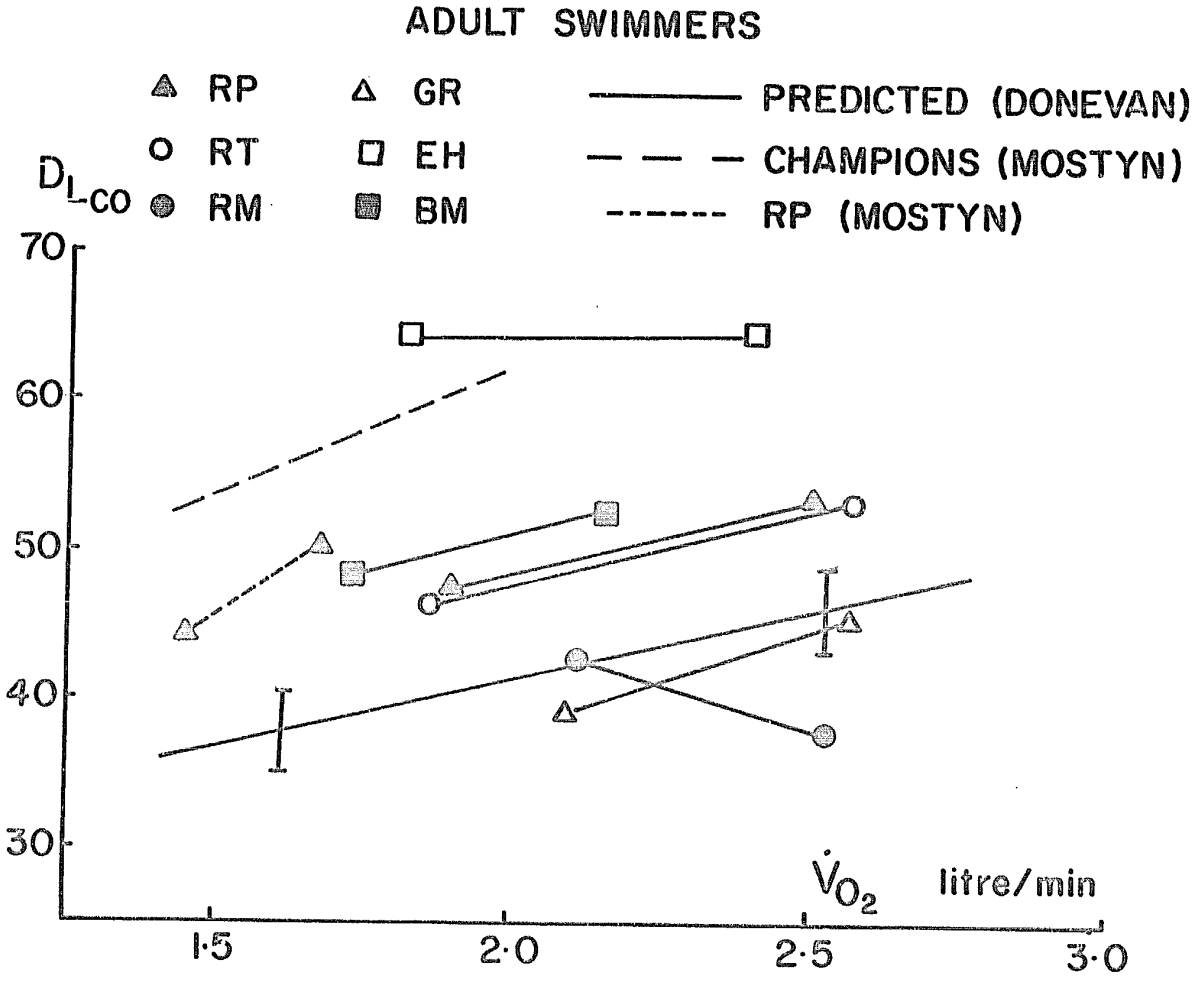


FIG. 4. Individual results showing D_L - $\dot{V}o_2$ relationship in adult swimmers (untrained) and in comparison with those predicted for adults (Donevan) and champion swimmers (Mostyn).

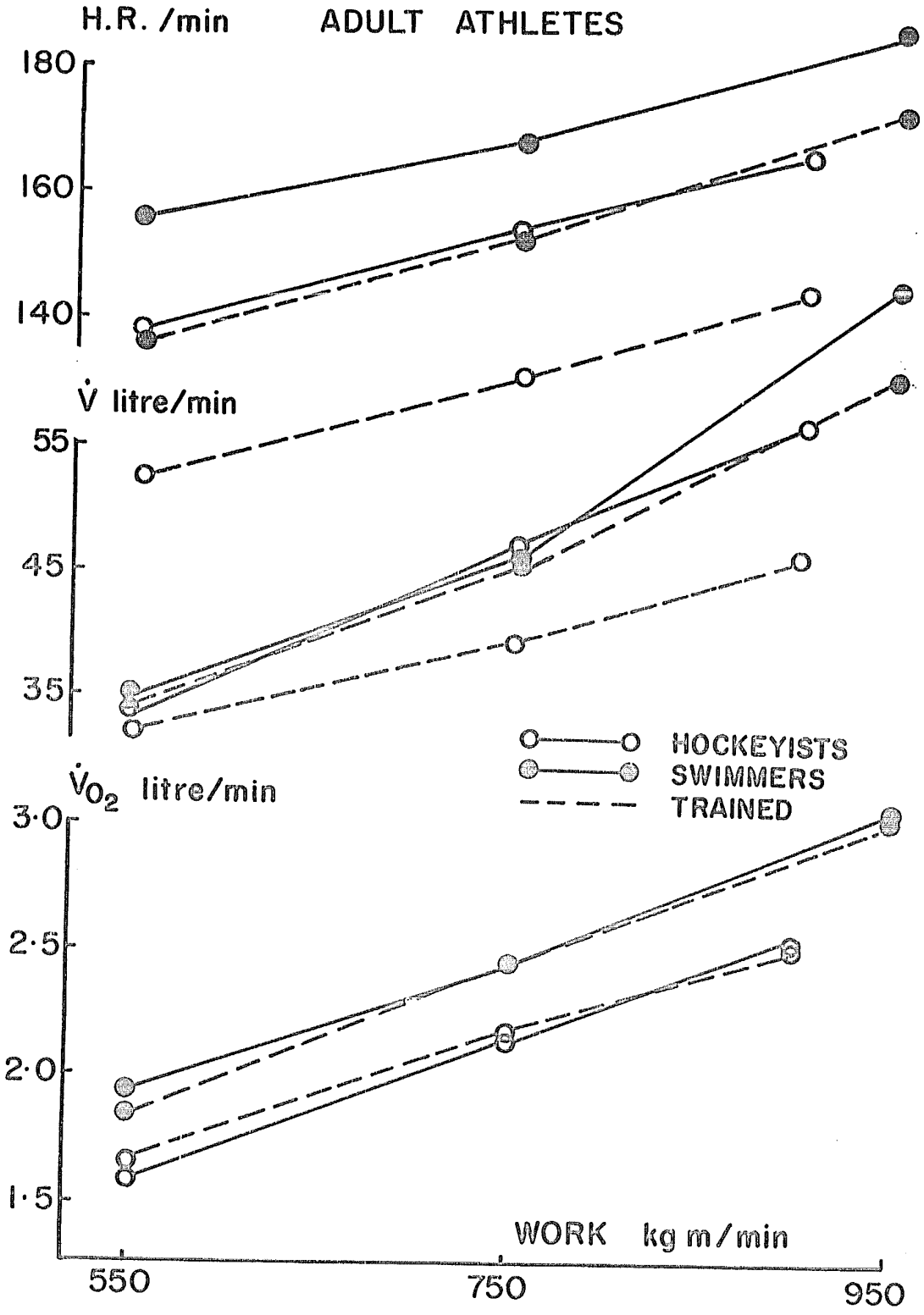


FIG. 5. Comparison of athletic groups (Hockeyists and swimmers) in pre- and post-trained states for HR, $\dot{V}$ and $\dot{V}o_2$ in relation to work.

DISCUSSION

D_L in competitive swimmers is not altered by five months of intensive training. However, these mean values for swimmers.. trained or untrained..are higher than predicted values for normal males of comparable age. In this respect, our findings agree with some investigators (88) who compared athletes and non-athletes, and others (91) who found no change with training. However, our results contrast with Newman's (274) in respect to training effects. She found training in one non-athletic subject decreased the $\dot{V}O_2$ requirement for a given load and since kCO was not altered, she concluded there was an increase in KCO, and therefore D_L, in relation to $\dot{V}O_2$ with training. Our study differed in that we studied althetes, rather than non-athletes, and this might account for the different findings. This suggest that if training increases D_L, this effect must persist in the athletes, whether he is trained or not.

Neither are our findings in group comparison in full agreement with Mostyn (266). These investigators found athletes, including average swimmers, did not differ from normals, although champion swimmers in their study did. We might thus conclude that our group included some champions who 'pulled' the group mean values up. This is in fact so, where it is seen (Fig.4) one Nationally rated swimmer (E.H.) clearly stood out in respect to D_L and whose results were similar to Mostyn's champion swimmers. One former

Olympic finalist (R.P.), in the champion group in Mostyn's study, was not significantly different from normals. A point of interest in respect to R.P. is the comparison with his D_L values of 3 years previous (Fig.4). Such comparison suggests this interval has decreased his D_L. Furthermore, at the time of our initial study he had not trained nor competed for 18 months prior to being tested; his slightly higher post-training values suggests that perhaps his subsequent training had some effect on improving D_L.

Additional points of interest arise from the studies on subjects R.M., G.R. and B.M. Subject R.M. was a proficient back stroke swimmer but did not perform nor train using other strokes requiring submersion. One wonders if this might relate to his low D_L results. A recent study (251) does indicate that back stroke swimmers differ from other swimmers. Subject G.R. was highly rated as a 50 yard free-style swimmer but his performance was surprisingly inferior in longer distances, whereas B.M., a mediocre performer, could not swim events longer than 50 yards. An explanation for the latter is probably his low maximal aerobic capacity which likely was reached in his highest exercise load ($\dot{V}O_2$ of 2.69 ls., at heart rate of 204). Perhaps a low D_L limited the performance in endurance events in subject G.R.

Finally, it is of interest to compare groups of athletes who follow different training plans. This comparison (see Fig.5) is

surprising in that not only do swimmers have greater heart rate and ventilation for a given exercise load, but they are less efficient in cycling than are hockeyists. The explanation for these differences is not clear. The higher heart rate and ventilation suggest the swimmers were initially less fit than the hockeyists; this does not seem feasible since one would expect swimmers to be more active in their sport during the summer holidays. The more probable explanation might be that there is a specificity to task which accompanies the training process and the fact that hockey skill is more similar to that of cycling than is swimming. These findings, also suggested in the children's study, indicate that cycling may not be a compatible exercise with swimming and perhaps is not a suitable test exercise for laboratory studies on these athletes.

PART V

GENERAL DISCUSSION AND SUMMARY

Contents

GENERAL DISCUSSION

The principal purpose of this thesis was to investigate some of the physiological changes (particularily in exercise D_L and $\dot{Q}c$) produced by athletic training. Observations have been made on young adults before and after seasonal training, and in young child swimmers as they developed.

Results of the present study suggest that the effects of training can be divided into two groups:

1) those which can be effected by seasonal, short term training (eg.HR, $\dot{Q}c$) and 2) those which may result from chronic strenuous training (eg.SV). This indicates the importance of experimental design if one wishes to separate these effects of training from each other and from other factors such as endowment. Accordingly, when the effects of training are small, quickly acquired and interindividual variability of a measurement is wide, it is essential to study the same individual in the untrained and trained states. Our study on the hockeyists and Freshmen in respect to $\dot{Q}c$ clearly indicates this conclusion. However, this experimental approach can be affected by subject selection and by duration of seasonal training. For example, it is readily accepted that athletes as a group, even out of training, are more active than non-athletes; thus, to observe the greatest effects of seasonal training, subjects must initially be as detrained as possible. Likewise, there is great inhomogeneity within groups of athletes; this was found by Åstrand (20) even when champion swimmers were carefully selected. The only way to

minimize this effect on results is to use each individual as his own control.

By contrast with the above approach, which can define the effects of seasonal training, the effects of chronic, long term training can only be determined by a longitudinal study on developing athletes. Whereas the many group-comparison studies reported (182,268) have clearly shown that there are marked dimensional differences between trained and untrained subjects (eg.higher SV, lung volumes,heart volume etc.,in the trained), this comparison does not specifically define whether these differences are genetically inherited or due to training. Furthermore, since it is accepted that the development of an athlete is a process usually commenced in early childhood and since many of the training effects may persist even in detraining, to best show the effects of chronic training, as distinct from endowment, children, rather than untrained adults, should be studied. Our findings on the effects of training during growth (eg.VC and flow rate changes, see Figs.S9-10,S13-14) would support this conclusion.

The most interesting consequence of training as observed in the present study was the consistent and significant decrease in cardiac output. One can only guess at present as to whether the decrease was general, thereby affecting all tissues equally, or was regional. A regional redistribution of blood flow with training would imply changes in vaso-regulatory mechanisms. There is good evidence that redistribution plays a part in the

adaptation to exercise (eg.reduced renal (350) and hepatic flow (307)); perhaps training does alter these mechanisms making possible a maintenance of normal, or even higher, flow to exercising muscle in the trained, but reduced flow to other areas. On the other hand, if the decrease was a general one, affecting flow to muscle as well as other tissues, this would seem an embarassing state in which to place the exercising muscles. On the basis of present reports, it is not yet clear which of these two mechanisms predominates. The plethysmographic studies (302) on change in exercise blood flow in the forearm showed increased flow with swim training; the Xenon clearance technique employed by Grimby (157) on the other hand showed a lower flow/unit of tissue in athletes for a given level of exercise. Our preliminary studies (215), in which regional forearm blood flow was measured directly using dye dilution, strongly suggest lower flow in trained athletes during exercise (especially athletes in whom the forearm muscle groups are extensively used in their performance eg.paddlers). This, and the wider (A-V) O_2 difference, suggest the decrease in $\dot{Q}c$ with training is a general one.

It has been reported that trained athletes have greater maximal cardiac output (17,155) and that this is one of the factors accounting for the athletes superior performance. However, a recent study by Douglas (119) does not support this view. In his study the same subjects were studied before and after training; during submaximal work he found a reduction in cardiac output, in agreement with our findings, but no change in maximal values were found. In view of the higher aerobic capacity of the trained person

(20,78,186), it can only be concluded that the trained must have a greater maximal ability for O_2 extraction (a point of which there is good agreement (17,158,268)) and this, rather than a higher maximal $\dot{Q}c$, is responsible for his greater working capacity. Indeed, our findings would suggest that there is a greater reserve of function on the part of the heart at sub-maximal levels, seemingly an obvious advantage, particularily if the cardiac output is a limiting factor in work performance.

The improved extraction ability of trained subjects must involve local changes at cellular level. One favourable adaptation in muscles with training would be increased capillarity, which should facilitate diffusion processes at the cells. A.Krogh showed in 1919 (220) that the number of capillaries in muscle was a function of intensity of metabolism in animals; Petren's early observations (285) show the same effect with training. Such increased capillarity in itself could result in greater extraction for a given flow. In addition, there now seems little doubt that there are significant enzyme changes in muscle cells, at least in rats, with training. Hearn reported recently (167) an increase in the cytochrome enzymatic activity; these alterations were found to persist during detraining. In addition, the more recent study by Holloszy (177) showed a marked increased ability for O_2 uptake by mitochondria extracted from the exercised (trained) muscle cells of rats in comparison with mitochondria of sedentary cells. Thus, if the chief site of limitation in the energy producing systems is in respect to the aerobic system

involving internal respiration, as in fact is indicated by lactate production, then these adaptations within the cells can account for the greater aerobic capacity in the trained. These findings support our results and suggest that perhaps the reduction in cardiac output can be directly attributable to changes in the cells. On the basis of these findings, it would seem that Bock's statement (57) of 1928 is being supported.

> "..we believe that the capacity for exercise is bound up with changes in the oxidative processes within the cells (and) ..the secret of such efficiency.. appears to lie in the muscle cells themselves".

Indeed, it is logical to expect these findings, since when one works or trains, it is the skeletal muscles which is the primary system; this should then be the system most affected by training. One is even tempted to suggest that the changes with training occuring in other systems(eg.respiratory,and circulatory system) are the consequence of cellular alterations in skeletal muscle. This strongly suggests that ultimately the important consequence of training is the enhanced ability of acceptance of O_2; perhaps the greater overall dimensions of the O_2 transport system are of secondary importance.

The comparative study made on children revealed that swimmers had larger lung volumes (as a result of a greater VC), higher flow rates, slightly higher exercise D_L in boys and lower cardiac output in boys and girls. In general, these differences were more marked in boy than girl swimmers.

In view of the finding of a reduced $\dot{Q}c$ with training in the adults, it is presumed that the lower value in the child swimmers,

for a given $\dot{V}O_2$, is a result of their strenuous exercise program. This suggests that training has the same effect, at least in this respect, in children as in adults. Surprisingly, SV differences in the groups of children were not observed, although the previously well documented lower heart rate in the trained person was evident in the trained child. Considering the lack of seasonal training on SV in our adults, one wonders at what stage in development this larger dimension (SV) does appear. The present studies suggest that it is not an endowment. Perhaps it appears with training during the immediate, post-pubertal years at which time growth of many other aspects are most marked. Such a postulate is logical if one considers the changes in attitudes and way of life which often are seen in children of this age. For example, younger children, whether engaged in organized sports activities or not, tend to be active. However, the onset of puberty often is associated with decreased play activity, and increased inhibition (or self-consciousness) which causes the less skilled child to cease participation in games and sports. To some extent, the same phenomenon can be seen among athletes whereby the less proficient often discontinues the sport at puberty while the good performer continues to train.

The greater VC would seem a natural ensuant of strenuous training, where hypertrophy of accessory respiratory muscles, in particular, could be expected because of their repeated subjection to heavy work. Since the difference is not always apparent in other, older athletic groups (153), one might conclude the

difference is attributable to the added work of breathing imposed by the water pressure on the thorax or perhaps due to training during growth. The higher flow rates in swimmers may be a consequence of the change in lung volume, affecting only the upper portion of the forced expiration curves. This is indicated by the fact that flow rates at lower lung volumes are dependant not on motivation and muscle power (33) but on the intrinsic properties of the lungs and thorax (241), which properties are probably unaffected by training. The advantages of higher lung volumes and flow rates as suggested above (see discussion), are apparent for swimmers and probably these changes among athletes are unique to aquatic performers. In respect to D_L, the study on adults showed no change with seasonal training. However, mean values of these few subjects was greater than predicted, mainly because of high values in a few persons in the group. We cannot be sure on the effects of training on D_L in childhood. It was observed that values were higher in boy, though not in girl, swimmers. If training was responsible for the higher values in boys, it was surprising that comparable changes were not seen in girl swimmers who followed an equally strenuous training program. In view of the above findings in adult swimmers (i.e.higher values in some) it is probable that the higher values in boy swimmers as a group is likewise due to high values in a few subjects; perhaps the girl swimmers included fewer potential champions than the boys group, thereby normalizing the results. In the light of Mostyn's findings, and our observations, it is suggested that the high

values are an endowment rather than a result of prolonged strenuous training. On the other hand, the longitudinal study on the swimmers strongly suggests that dimensional differences in lung volume and flow rates are chiefly due to training. Indeed, there is little to suggest from our study (except for D_L possibly) that the observed group differences are due to endowment. In respect to such dimensions, in so far as athletes differ from non-athletes, it seems that an athlete is made, not born.

In conclusion, one wonders as to the primary underlying mechanism(s) responsible for changes with training. In many respects, the larger dimensions of the overall O_2 transport system of the trained may be thought analogous to hypertrophy of muscles and perhaps this also accounts for greater lung and heart volumes. Undoubtedly, hypertrophy is one of the more important changes due to training, though this phenomenon is not well understood. It has been suggested that hypoxia may be the essential mechanism in training; this is indicated by Lamb (227) who points out that many of the effects of detraining can be off-set by low-oxygen breathing. In many respects, the heavy work regime followed by athletes in training must simulate hypoxia conditions, especially at cellular level, and perhaps this is a primary mechanism.

SUMMARY

The effects of athletic training on resting lung volumes and expiratory flow rates, and cardio-respiratory functions in exercise have been studied on 69 children over three consecutive years of swim training and in 14 young adults before and after seasonal training. These functions were also measured on 83 normal children who served as a basis for comparison with the child swimmers.

Findings from the study on children indicate:

1) Total lung volumes were greater in swimmers, as a result of a larger vital capacity. No differences in respect to other subdivisions of lung volumes were seen.

2) Swimmers had higher expiratory flow rates and this difference became more marked with training during growth.

3) No difference was found in ventilatory equivalent.

4) Exercise diffusing capacity was higher in boy, but not in girl swimmers. When the better girl swimmers were compared with other swimmers and Controls, at comparable levels of oxygen consumption, these selected girl swimmers had generally higher values.

5) Exercise cardiac output for comparable exercise levels was lower in the swimmers, chiefly as a consequence of a lower heart rate.

From the studies made on young adults, it was found that:

1) Training decreased the exercise cardiac output and this was a result of a lowered heart rate. Seasonal training had no

effect on stroke volume.

2) Exercise diffusing capacity was higher in swimmers than normals, but seasonal training had no effect on this measurement.

The changes in vital capacity in the child swimmers were due to athletic training, presumably the consequence of hypertrophy of muscles of the shoulder girdle; the higher vital capacity of child swimmers can account for their higher flow rates. The group differences in diffusing capacity are a result of high values in some swimmers, and it is suggested this is due to endowment, since no evidence of a training effect was found in child or adult swimmers.

The lower exercise cardiac output and heart rate in both the trained child and trained adults was the consequence of their athletic training. Since stroke volume was not changed by training in adults, and no difference was observed between the groups of children, it is suggested the larger stroke volume, which characterizes the adult athlete, is developed in the post-pubertal period of growth. The lower cardiac output was made possible by an improved oxygen extraction since oxygen consumption, and hence efficiency, was not altered with training.

BIBLIOGRAPHY

1. Adams, F.H., E. Bengtsson, H. Berven and C. Wegelius
The Physical Working Capacity of Normal School Children: II Swedish City and Country. Ped. 28, 243, 1961.

2. Adams, F.H., L.M. Linde and H. Miyake
The Physical Working Capacity of Normal School Children: I. California Ped. 28, 55, 1961.

3. Andrew, G.M.
The Effect of Training on Cardiovascular Dynamics. M.Sc. Thesis, Faculty of Graduate Studies, McGill University, 1963.

4. Apthorp, G.H. and R. Marshall
Pulmonary Diffusing Capacity: A Comparison of Breathholding and Steady State Methods using Carbon Monoxide. J. Clin. Invest. 40, 1775, 1961.

5. Asmussen, E and O. Bøje
Body Temperature and Capacity for Work. Acta Physiol. Scand. 10, 1, 1945.

6. Asmussen, E and M. Nielsen
The Cardiac Output in Rest and Work Determined Simultaneously by the Acetylene and Dye Injection Methods. Acta Physiol. Scand. 27, 217, 1953.

7. Asmussen E., and M. Nielsen
Studies on the Initial Changes in Respiration at the Transition from Rest to Work and from Work to Rest. Acta Physiol. Scand. 16, 270, 1948.

8. Asmussen E., and M. Nielsen
Cardiac Output during Muscular Work and its Regulation. Physiol. Rev. 35, 778, 1955.

9. Asmussen E., and M. Nielsen
Physiological Dead Space and Alveolar Gas Pressures at Rest and during Muscular Exercise. Acta Physiol. Scand. 38, 1, 1956.

10. Åstrand I.
Capacity for Oxygen Consumption and Related Functions during Cycling in Women. Acta Physiol. Scand. 49, Supp 169, 11, 1960.

11. Åstrand I., P.-O. Åstrand, E.H. Christensen and R. Hedman
Circulatory and Respiratory Adaptation to Severe Muscular Work. Acta Physiol. Scand. 50, 254, 1960.

12. Åstrand I., P.-O.Astrand and K. Rodahl
Maximal Heart Rate during Work in Older Men. J.Appl. Physiol. 14, 562, 1959.

13. Åstrand P.-O.
Experimental Studies on Physical Working Capacity in Relation to Sex and Age. Ejnar Munksgaard, Copenhagen, 1952.

14. Åstrand,P.-O.
A Study of Capacity for hard Muscular Work of 17 to 19 Year-Old Male Youths. Arb.Physiol.15, 251,1953

15. Åstrand, P.-O.
New Records in Human Power. Nature, 176, 922,1955.

16. Åstrand, P.-O.
Human Physical Fitness with Special Reference to Sex and Age. Physiol.Rev. 36, 307,1956.

17. Åstrand, P.-O.
Proc.Int.Symp. Physical Activity and Cardiovascular Health. Toronto, 1966. Canada M.A.J. 96, 760,1967.

18. Åstrand, P.-O., and E.H.Christensen
The Hyperpnoea of Exercise. The Proc.J.S.Haldane Centenary Symp., from 'The Regulation of Human Respiration', Ed. D.J.C.Cunningham and B.B.Lloyd, Blackwell Scient.Prod.,1963.

19. Åstrand, P.-O., T.E.Cuddy, B.Saltin and J.Stenberg
Cardiac Output during Submaximal and Maximal Work. J.Appl.Physiol. 19, 268,1964.

20. Åstrand, P.-O., L.Engstrom, B.O.Eriksson, P.Karlberg, I.Nylander, B.Saltin and C.Thoren. Girl Swimmers,with special reference to Respiratory and Circulatory Adaptation and Gynaecological and Psychiatric Aspects. Acta Paediat. Supp.147, 1963.

21. Åstrand, P.-O and I. Ryhming
A Nomogram for Calculation of Aerobic Capacity (Physical Fitness) from Pulse Rate during Submaximal Work. J.Appl. Physiol. 7, 218, 1954.

22. Åstrand, P.-O and B.Saltin
Oxygen Uptake during the first 5 minutes of Heavy Muscular Exercise. J.Appl.Physiol. 16, 971, 1961.

23. Åstrand, P.-O and B.Saltin
Maximal Oxygen Uptake and Heart Rate in Various Types of Muscular Exercise. J.Appl.Physiol. 16, 977,1961.

24. Åstrand P.-O and B.Saltin
Plasma and Red Cell Volume after Prolonged Severe Exercise. J.Appl.Physiol. 19, 829,1964.

25. Bainbridge, F.A.
The Physiology of Muscular Exercise. 3rd Edition, rewritten by A.V.Bock and D.B.Dill, Langmans, Green & Co, London, 1931.

26. Baldwin, E.deF., A.Cournand and D.W.Richards,Jr.
Pulmonary Insufficiency: I. Physiological Classification, Clinical Methods of Analysis, Standard Values in Normal Subjects. Medicine 27, 243, 1948.

27. Bannister, R.G., J.E.Coates, R.S.Jones and F.Meade
Pulmonary Diffusing Capacity on Exercise in Athletes and Non-Athletic Subjects. J.Physiol (London), 152, 66P,1960.

28. Barach,A.L.
Physiological Methods in the Diagnosis and Treatment of Asthma and Emphysema. Ann.Int.Med. 12, 454, 1938.

29. Barcroft, J.
Features in the Architecture of Physiological Function. Cambridge Univ.Press. London, 1938.

30. Bates, D.V.
The Uptake of Carbon Monoxide in Health and in Emphysema. Clin.Sci. 11, 21, 1952.

31. Bates, D.V.
The Measurement of Pulmonary Diffusing Capacity in the Presence of Lung Disease. J.Clin.Invest.37, 591, 1958.

32. Bates, D.V., N.G.Boucot and A.E.Dormer
The Pulmonary Diffusing Capacity in Man. J.Physiol.(London) 129, 237, 1955.

33. Bates, D.V., and R.V.Christie
Respiratory Function in Disease. W.B.Saunders Co., Philadelphia and London, 1964.

34. Bates, D.V., J.B.L.Gee, L.G.Bentivoglio and E.M.Mostyn
Diffusion as a Limiting Factor in Oxygen Transport across the lung. Proc.Int.Symp. Cardiovasc.Respir.Effects Hypoxia, Kingston, 1965, Karger, Basel/New York, 1966.

35. Bates, D.V., and J.F.Pearce
The Pulmonary Diffusing Capacity; a Comparison of Methods of Measurement and a Study of the Effect of Body Position. J.Physiol. (London) 132, 232, 1956.

36. Bates, D.V., C.J.Varvis, R.E.Donevan and R.V.Christie
Variations in Pulmonary Capillary Blood Volume and Membrane Diffusion Component in Health and Disease. J.Clin.Invest. 39, 1401, 1960.

37. Bates, D.V., C.R.Woolf and G.I.Paul
Chronic Bronchitis. Med.Serv.J.Canada. 18, 211, 1962

38. Beaudry, P.
Unpub.data, Joint Card.Resp.Centre, McGill Univ. and Montreal Children's Hospital.

39. Becklake, M.R., H.Frank, G.R.Dagenais, G.L.Ostiguy and C.A.Guzman. Influence of Age and Sex on Exercise Cardiac Output. J.Appl.Physiol. 20, 938, 1965.

40. Becklake, M.R., C.J.Varvis, L.D.Pengelly, S.Kenning, M.McGregor and D.V.Bates. Measurement of Pulmonary Blood Flow during Exercise using Nitrous Oxide. J.Appl.Physiol. 17, 579, 1962.

41. Bedell, G.N., and R.W.Adams
Pulmonary Diffusing Capacity during Rest and Exercise. A Study of Normal Persons and Persons with Atrial Septal Defect, Pregnancy and Pulmonary Disease. J.Clin.Invest. 41,1908,1962.

42. Bengtsson,E.
The Working Capacity in Normal Children, Evaluated by Submaximal Exercise on the Bicycle Ergometer and Compared with Adults. Acta Med.Scand. 154, 91,1956.

43. Berggren, G.,and E.H.Christensen
Heart Rate and Body Temperature as Indices of Metabolic Rate during Work. Arb.Physiol. 14, 255, 1950.

44. Berglund,E., G.Birath, J.Bjure, G.Grimby, I.Kjellmer, L.Sandqvist and B.Söderholm. Spirometric Studies in Normal Subjects: I. Forced Exspirograms in Subjects Between 7 and 70 years of Age. Acta Med.Scand.173, 185,1963.

45. Bernstein, I.L., R.G.Fragge, M.Gueron, L.Kriendler and J.E.Ghory. Pulmonary Function in Children: I.Determination of Norms. J.of Allergy. 30,514,1959.

46. Bernstein, I.L., and D.Mendel
The Accuracy of Respirographic Recording at High Respiratory Rates. Thorax 6, 297, 1951.

47. Berven, H.
The Physical Working Capacity of Healthy Children. Seasonal Variations and Effect of Ultraviolet Radiation. Acta.Paediat.Supp. 148, 1963.

48. Bevegård, S., U.Freyschuss and T.Strandell
Circulatory Adaptation to Arm and Leg Exercise in Supine and Sitting Position. J.Appl.Physiol. 21, 36, 1966.

49. Bevegård, S., A.Holmgren and B.Jonsson
The Effect of Body Position on the Circulation at Rest and during Exercise with Special Reference to the Influence on the Stroke Volume. Acta Physiol. Scand. 49, 279, 1960.

50. Bevegård, S., A.Holmgren and B.Jonsson
Circulatory Studies in Well Trained Athletes at Rest and during Heavy Exercise with Special Reference to Stroke Volume and the Influence of Body Position. Acta.Physiol. Scand. 57, 26, 1963.

51. Bevegård, S., and J.T.Shepherd
Reaction in Man of Resistance and Capacity Vessels in Forearm and Hand to Leg Exercise. J.Appl.Physiol. 21,123, 1966.

52. Bevegård, B.S., and J.T.Shepherd
Regulation of the Circulation during Exercise in Man. Physiol. Rev. 47, 178, 1967.

53. Birath, G., I.Kjellmer and L.Sandqvist.
Spirometric Studies in Normal Subjects: II. Ventilatory Capacity Tests in Adults. Acta Med.Scand.173, 193, 1963.

54. Bjure, J.
Spirometric Studies in Normal Subjects: IV. Ventilatory Capacities in Healthy Children 7 to 17 years of Age. Acta.Paediat. 52, 232, 1963.

55. Bjure, J.
Pulmonary Diffusing Capacity for Carbon Monoxide in Relation to Cardiac Output in Man. Scand. J.Clin. and Lab. Invest. 17, Supp. 81,1,1965.

56. Bock,A.V., D.B.Dill and J.H.Talbott
Studies in Muscular Activity: I.Determination of the Rate of Circulation of Blood in Man at Work. J.Physiol.(London), 66, 121,1928.

57. Bock, A.V., C.Vancoulaert, D.B.Dill, A.Fölling and L.M.Hurxthal
Studies in Muscular Activity: III. Dynamical Changes Occurring in Man at Work. J.Physiol.(London) 66,136,1928.

58. Bohr,C.
Über die Spezifische Tätigkeit der Lungen bei der respiratorischen Gasaufnahme und ihr Verhaltzen zu der durch die alveolarwand stattfindenden Gasdiffusion. Skand.Arch. Physiol.22, 221,1909.

59. Bøje, O.
Über die Größe de Lungendiffusion der Menschen während Ruhe und körperlichen Arbeit. Arb.Physiol.7. 157,1934.

60. Bornstein A.
Eine Methode zur vergleichenden Messung des Herzschlag-volumens beim Menschen. Pflüg.Arch.Physiol.132,307,1910.

61. Brandi, G., and I.Brambilla
Arterio-venous Difference of Oxygen, Cardiac Output and Stroke Volume in Function of the Energy Consumption. Arb.Physiol. 19, 130, 1961.

62. Brashear, R.E., J.C.Ross and W.J.Daly
Pulmonary Diffusion and Capillary Blood Volume in Dogs at Rest and with Exercise. J.Appl.Physiol. 21,516,1966.

63. Briggs, H.
Fitness and Breathing during Exertion. J.Physiol.(London), 53, 37P, 1918.

64. Briggs, H.
Physical Exertion, Fitness and Breathing. J.Physiol.(London) 54, 292, 1920.

65. Brody,A.W.
Tests of Ventilatory Strength and Mechanics. Graphs of Normal Values. Am.Rev.Resp.Dis. 89, 270, 1964.

66. Broman, B., G.Dahlberg and A.Lichtenstein
Height and Weight during Growth. Acta.Paediat.30, 1, 1942.

67. Bryan, A.C., L.G.Bentivoglio, F.Beerel, H.MacLeish, A.Zidulka and D.V.Bates. Factors Affecting Regional Distribution of Ventilation and Perfusion in the Lung. J.Appl.Physiol. 19, 395, 1964.

68. Bryan A.C., J.Milic-Emili and D.Pengelly
Effect of Gravity on the Distribution of Pulmonary Ventilation. J.Appl.Physiol. 21, 778, 1966.

69. Bucci, G., and C.D.Cook
Studies of Respiratory Physiology in Children: VI. Lung Diffusing Capacity, Diffusing Capacity of the Pulmonary Membrane and Pulmonary Capillary Blood Volume in Congenital Heart Disease. J.Clin.Invest. 40, 1431,1961.

70. Bucci,G., C.D.Cook and H.Barrie
Studies of Respiratory Physiology in Children: V.Total Lung Diffusion, Diffusing Capacity of Pulmonary Membrane and Pulmonary Capillary Blood Volume in Normal Subjects from 7 to 40 years of Age. J.Paediat.58, 820,1961.

71. Buskirk, E.R., P.F.Iampietro and D.E.Bass
Work Performance after Dehydration: Effects of Physical Conditioning and Heat Acclimatization. J.Appl.Physiol. 12,189,1958.

72. Buskirk, E.R., and H.G.Taylor
Relationships between Maximal Oyxgen Intake and Components of Body Composition. Fed.Proc. 13, 12, 1954.

73. Campbell, E.J.M., E.K.Westlake and R.M.Cherniack
Simple Method of Estimating Oxygen Consumption and Efficiency of the Muscles of Breathing. J.Appl.Physiol. 11, 303, 1957.

74. Carlson, L.A., and B.Pernox
Oxygen Utilization and Lactic Acid Formation in the Legs at rest and during Exercise in Normal Subjects and in Patients with Arteriolsclerosis Obliterans. Acta.Med. Scand. 164, 39, 1959.

75. Cayler, G.G., A.M.Rudolph and A.S.Nador
Systemic Blood Flow in Infants and Children with and without Heart Disease. Ped.32, 186, 1963.

76. Cerretelli, P., and R.Margaria
Maximum Oxygen Consumption at Altitude. Arb.Physiol.18, 460, 1961.

77. Cerretelli, P., J.Piiper, F.Mangili and B.Ricci
Aerobic and Anaerobic Metabolism in Exercising Dogs. J.Appl.Physiol. 19, 25, 1964.

78. Cerretelli, P., and P.Radovani
Il Massimo consumo di O_2 in Athleti Olimpionici diVarie Specialita. Boll.Soc.Ital.Biol.Sper. 36, 1871,1960.

79. Cerretelli, P., R.Sikand and L.E.Farhi
Readjustment in Cardiac Output and Gas Exchange during Onset of Exercise and Recovery. J.Appl.Physiol. 21, 1345, 1966.

80. Chapman, C.B.(ed)
Physiology of Muscular Exercise. Circ.Res.20,Supp.1,1967.

81. Chapman, C.B., J.N.Fisher and B.Sproule
Behavior of Stroke Volume at Rest and during Exercise in Human Beings. J.Clin.Invest.39, 1208, 1960.

82. Chapman, C.B., and J.H.Mitchell
The Physiology of Exercise. Sc.Am.212, 88, 1965.

83. Cherniack, R.M.
Ventilatory Function in Normal Children. Canada M.A.J.87, 80, 1962.

84. Cherniack,R.M.
Oxygen Cost of Breathing as a Limiting Factor in Physical Performance. Proc.Int.Symp.Cardiovasc.Respir. Effects Hypoxia, Kingston,1965. Karger,Basel/New York,1966.

85. Chevalier, R.B., J.A.Bowers, S.Bondurant and J.C.Ross
Circulatory and Ventilatory Effects of Exercise in Smokers and Non-Smokers. J.Appl.Physiol.18, 357,1963.

86. Christie, R.V.
The Lung Volume and Its' Subdivisions: I.Methods of Measurement. J.Clin.Invest.11, 1099,1932.

87. Christensen, E.H., and P.Högberg
The Physiology of Skiing. Arb.Physiol. 14, 292,1950.

88. Christensen, J., G.G.Douglas and J.S.Haldane
The Absorption and Dissociation of Carbon Dioxide by Human Blood. J.Physiol.(London), 48,244,1914.

89. Cinkotai,F.F., M.L.Thomson and A.R.Guyatt
Effect of Apprehension on Pulmonary Diffusing Capacity in Man. J.Appl.Physiol. 21, 534,1966.

90. Coates, J.E., J.Drummond, F.Meade and C.Yandle
The Energy Requirement of Treadmill Walking in Relation to Sex and Athletic Training. J.Physiol.(London), 153, 60P,1960.

91. Coates,J.E.,and F.Meade
Physical Training in Relation to the Energy Expenditure of Walking, and to Factors Controlling Respiration during Exercise. Ergonomics 2, 195, 1959.

92. Cobb,L.A., and W.P.Johnson
Hemodynamic Relationships of Anaerobic Metabolism and Plasma Free Fatty Acids during Prolonged Strenuous Exercise in Trained and Untrained Subjects. J.Clin.Invest.42, 800,1963.

93. Cohn,J.E., D.G.Carroll,B.W.Armstrong, R.H.Shepard and R.L.Riley. Maximal Diffusing Capacity of the Lung in Normal Male Subjects of Different Ages. J.Appl.Physiol. 6, 588,1954.

94. Collet,M.E., and G.Liljestrand
The Minute Volume of the Heart in Man during some Different Types of Exercise. Skand.Arch.f.Physiol.45, 29,1924.

95. Comroe,J.H.Jr., R.E.Forster II., A.B.DuBois, W.A.Briscoe and E.Carlson. 'The Lung': Clinical Physiology and Pulmonary Function Tests. 2nd Ed.Chicago, Year Book Medical Publishers, 1962.

96. Cook,C.D., and J.F.Hamann
Relation of Lung Volumes to Height in Healthy Persons between the Ages of 5 and 38 Years. J.Ped.59, 710,1961.

97. Craig,F.N., and E.G.Cummings
Dehydration and Muscular Work. J.Appl.Physiol. 21,670,1966.

98. Cumming G.R., and P.M.Cumming
Working Capacity of Normal Children Tested on a Bicycle Ergometer. Canada M.A.J. 88,351,1963.

99. Cumming,G.R., and R.Danzinger
Bicycle Ergometer Studies in Children - Correlation of Pulse Rate with Oyxgen Consumption. Ped.32, 202,1963.

100. Cureton, T.K.
Res.Quart. 7,80,1934.

101. Daly,W.J., S.T.Giammona, J.C.Ross and H.Feigenbaum
Effects of Pulmonary Vascular Conjestion on the Postural Changes in the Perfusion and Filling of the Pulmonary Vascular Bed. J.Clin.Invest. 43, 68,1964.

102. Damoiseau,J., R.Deroanne and J.M.Petit
Consommation Maximale d'oxygène aux Différents Ergometres J.Physiol.(Paris) 55, 235, 1963.

103. Danzinger,R.G., and G.R.Cumming
Effects of Chlorothiazide on Working Capacity on Normal Subjects. J.Appl.Physiol. 19, 636,1964.

104. Davy,H. (J.Davy ed.)
Researches, Chiefly concerning Nitrous Oxide, Collected Papers Volume 3, London, Smith Elder 1839.

105. Dejours, P.
La Regulation de la ventilation au cours de l'exercise musculaire chez l'homme. J.Physiol.(Paris) 51,163,1959.

106. Dejours,P., J.C.Mithoefer and Y.Labrousse
Influence of Local Chemical Change on Ventilatory Stimulus from the Legs during Exercise. J.Appl.Physiol.10, 372,1957.

107. Demuth,G.R.,W.F.Howatt and B.M.Hill
The Growth of Lung Function. Ped.35,Supp.,161-218,1965.

108. Dexter,L., J.L.Whittenberger, F.W.Haynes, W.T.Goodale, R.Gorlin and C.G.Sawyer. Effect of Exercise on Circulatory Dynamics of Normal Individuals. J.Appl.Physiol.3, 439,1951.

109. Dill, D.B., and C.F.Consolazio
Responses to Exercise as related to Age and Environmental Temperature. J.Appl.Physiol. 17, 645, 1962.

110. Dill,D.B., H.T. Edwards, E.V.Newman and R.Margaria
Analysis of Recovery from Anaerobic Work. Arb.Physiol.9, 299,1937.

111. Dill,D.B., S.M.Horvath and F.N.Craig
Responses to Exercise as Related to Age.
J.Appl.Physiol. 12, 195,1958.

112. Dill,D.B., L.G.Myhre, E.E.Phillips Jr., and D.K.Brown
Work Capacity in Acute Exposure to Altitude.
J.Appl.Physiol. 21, 1168,1966.

113. Dill,D.B., S.Robinson, B.Balke and J.L.Newton
Work Torerence: Age and Altitude.
J.Appl.Physiol. 19, 483,1964.

114. Dill,D.B., J.H.Talbott and H.T.Edwards
Responses of Several Individuals to a Fixed Task.
J.Physiol.(London) 69, 267, 1930.

115. Dollery, C.T., N.A.Dyson and J.D.Sinclair
Regional Variations in Uptake of Radioactive CO in the Normal Lung. J.Appl.Physiol. 15,411, 1960.

116. Donald, K.W., J.M.Bishop, G.Cumming and O.L.Wade
The Effect of Exercise on the Cardiac Cutput and Circulatory Dynamics of Normal Subjects.
Clin.Sc. 14, 37, 1955.

117. Donevan,R.E.,W.H.Palmer, C.J.Varvis and D.V.Bates
Influence of Age on Pulmonary Diffusing Capacity.
J.Appl.Physiol. 14, 483, 1959.

118. Douglas,C.G., and J.S.Haldane
The Capacity of the Air Passages under Varying Physiological Conditions. J.Physiol.(London), 45,235,1912.

119. Douglas,F.G.
Effects of Training on Cardiorespiratory Performance during Maximal Physical Effort.
M.Sc.Thesis, Faculty of Graduate Studies,McGill University, submitted summer 1967.

120. Dunhill, M.S.
Postnatal Growth of the Lung. Thorax 17, 329,1962.

121. Edwards,H.T., M.I.Cohen, D.B.Dill and A.Thorndike Jr.
Renal Function in Exercise. Arb.Physiol. 9, 610, 1937.

122. Ekelund,L.G., and A.Holmgren
Circulatory and Respiratory Adaptation during Long Term, Non-Steady State Exercise in the Sitting Position.
Acta Physiol.Scand. 62, 240, 1964.

123. Elsner, R.W., and Carlson,L.D.
Post-exercise Hyperemia in Trained and Untrained Subjects.
J.Appl.Physiol. 17, 436, 1962.

124. Emerson, P.W., and H.Green
Vital Capacity of the Lungs of Children.
Am.J.Dis.Child 22, 202, 1921.

125. Emery, J.L., and A.Mithal
The Number of Alveoli in the Terminal Respiratory Unit of Man during Late Intrauterine Life and Childhood. Arch.Dis.Childhood 35, 544, 1960.

126. Engel, S.
The Childs' Lung: Developmental Anatomy, Physiology and Pathology. Arnold, London, 1947.

127. Englert, M.
L'influence de l'age sur la capacité de diffusion pulmonaire chez l'homme normal. Med.Thorax 21, 1, 1964.

128. Engström, I., P.Karlberg and S.Kraepelien
Respiratory Studies in Children: I. Lung Volumes in Healthy Children 6 to 14 years of Age.
Acta Paediat. 45, 277, 1956.

129. Engström, I., P.Karlberg and C.L.Swarts
Respiratory Studies in Children: IX. Relationships between Mechanical Properties of the Lungs, Lung Volume and Ventilatory Capacity in Healthy Children 7 to 15 years of Age. Acta Paediat. 51, 68, 1962.

130. Erikson, H.
The Respiratory Gaseous Exchange after a Short Burst of Exercise. Acta Physiol. Scand. 40, 182, 1957.

131. Erikson, L., E.Simonson, H.L.Taylor, H.Alexander and A.Keys. Energy Cost of Horizontal and Grade Walking. Am.J.Physiol. 145, 391, 1946.

132. Federation of American Societies for Experimental Biology: Standardization of Definitions and Symbols in Respiratory Physiology. Fed.Proc. 9, 602, 1950.

133. Ferrer, M.I., R.M.Harvey, R.T.Cathcart, A.Cournand and D.W.Richards, Jr. Hemodynamic Studies in Rheumatic Heart Disease. Circulation 6, 688, 1952.

134. Ferris, B.G.Jr., J.L.Whittenberger and J.R.Gallagher
Maximum Breathing Capacity and Vital Capacity of Male Children and Adolescents. Ped. 9, 659, 1952.

135. Filley, G.F., D.J.MacIntosh and G.W.Wright
Carbon Monoxide Uptake and Pulmonary Diffusing Capacity in Normal Subjects at Rest and during Exercise.
J.Clin.Invest. 33, 530, 1954.

136. Forssmann, W.
Die Sondierung des Rechten Herzens. Klin.Wochenschrift 8, 2085, 1929.

137. Forster,R.E.
Exchange of Gases between Alveolar Air and Pulmonary Capillary Blood: Pulmonary Diffusing Capacity. Physiol.Rev. 37,391,1957.

138. Forster, R.E., W.S.Fowler, D.V.Bates and B.VanLingen
The absorption of Carbon Monoxide by the Lungs during Breathholding. J.Clin.Invest. 33, 1135, 1954.

139. Forster,R.E., F.J.W.Roughton, L.Cander, W.A.Briscoe and F.Kreuzer. Apparent Pulmonary Diffusing Capacity for CO at Varying Alveolar O_2 Tensions. J.Appl.Physiol.11, 277,1957.

140. Fowler, W.S.
Lung Function Studies: II. The Respiratory Dead Space. Am.J.Physiol. 154, 405, 1948.

141. Freedman,M.E., G.L.Snider, P.Brostoff, S.Kimelblot and L.N.Katz. Effects of Training on Response of Cardiac Output to Muscular Exercise in Athletes. J.Appl.Physiol. 8, 37, 1955.

142. Freyser,R., J.C.Ross, H.S.Levin, J.V.Messer and J.Pines
Effect of Increasing Environment Temperature on Pulmonary Diffusing Capacity. J.Appl.Physiol. 21, 147, 1966.

143. Frick,M.H., A.Konttinen and H.S.S.Sarajas
Effects of Physical Training on Circulation at Rest and during Exercise. Am.J.Cardiol. 12, 142, 1963.

144. Gandevia, B.
Normal Standards for Single Breath Tests of Ventilatory Capacity in Children. Arch.Dis.Children.35,236,1960.

145. Gandevia,B., and P.Hugh-Jones.
Terminology for Measurement of Ventilatory Capacity. Thorax 12, 290, 1957.

146. Gemmill,C., W.Booth and B.Pacock
Muscular Training: I. The Physiological Effect of Daily Repetition on the Same Amount of Light Muscular Work. Am.J.Physiol. 92, 253, 1930.

147. Giammona,S.T.J., and W.J.Daly
Pulmonary Diffusing Capacity in Normal Children Ages 4 to 13. Am.J.Dis.Child.110, 144,1965.

148. Glassford,R.G., G.H.Y.Baycroft, A.W.Sedgwick and R.B.J.McNab
Comparison of Maximal Oxygen Uptake Values Determined by Predicted and Actual Methods. J.Appl.Physiol.20,509,1965.

149. Goff,L.G., and R.G.Bartlett
Elevated end-tidal CO_2 in Trained Underwater Swimmers. J.Appl.Physiol. 10,203,1957.

150. Goldberg,S.J. R.Weiss and F.H.Adams
A Comparison of the Maximal Endurance on Normal Children and Patients with Congenital Cardiac Disease. J.Ped. 69, 46, 1966.

151. Goldberg,S.J., R.Weiss, E.Kaplan and F.H.Adams
Comparison of Work Required by Normal Children and those with Congenital Heart Disease to Participate in Childhood Activities. J.Ped. 69, 56, 1966.

152. Goldman,H.I. and M.R.Becklake
Respiratory Function Tests: Normal Values at Median Altitudes and the Prediction of Normal Results. Am.Rev.Tuberc. 79, 457,1959.

153. Gordon,B.,S.A.Levine and A.Wilmaers
Observations on a Group of Marathon Runners. Arch. Int.Med. 33,425,1924.

154. Granath,A., B.Jonsson and T.Strandell
Studies on the Central Circulation at Rest and during Exercise in the Supine and Sitting Body Position in Old Men. Acta Med.Scand. 176, 425, 1964.

155. Grande,F and H.L.Taylor
Adaptive Changes in the Heart, Vessels and Patterns of Control under Chronically High Loads. Handbook of Physiology: Circulation, Sec.2,3, 2615, 1965 ed. W.F. Hamilton and P.Dow, Am.Physiol.Soc., Wash.,D.C.

156. Gray,J.S., F.S.Grodins and E.T.Carter
Alveolar and Total Ventilation and the Dead Space Problem. J.Appl.Physiol. 9, 307, 1956.

157. Grimby,G., E.Häggendal and B.Saltin
Local Xenon^{133} Clearance from the Quadriceps Muscle during Exercise in Man. J.Appl.Physiol.22, 305,1967.

158. Grimby,G., N.J.Nilsson and B.Saltin
Cardiac Output during Submaximal and Maximal Exercise in Active Middle Age Athletes. J.Appl.Physiol.21,1150,1966.

159. Grimby,G., and B.Saltin
Physiological Analysis of Physically Well Trained Middle Aged and Old Athletes. Acta Med.Scand. 179,513,1966.

160. Grimby,G., and B.Söderholm
Spirometric Studies in Normal Subjects: III.Static Lung Volumes and Maximum Voluntary Ventilation in Adults with a Note on Physical Fitness. Acta.Med.Scand. 173,199,1963.

161. Grollman,A.
The Measurement of the Circulation Rate in Man by the Acetylene Method. J.Physiol.(London), 70, 39, 1930.

162. Guyatt,A.R.,F.Newman, F.F.Cinkotai, J.I.Palmer and M.L.Thomson. Pulmonary Diffusing Capacity in Man during Immersion in Water. J.Appl.Physiol.20,878,1965.

163. Haldane J.S., and J.G.Priestley
Respiration, 2nd ed, New Haven, Yale University Press, 1935.

164. Hamilton, W.F., J.W.Moore, J.M.Kinsman and R.C.Spurling
Studies on the Circulation: IV. Further Analysis of the Injection Method and of Changes in Hemodynamics under Physiological and Pathological Conditions.
Am.J.Physiol. 99, 534, 1932.

165. Hanson, J.S., and B.S.Tabakin
Comparison of the Circulatory Response to Upright Exercise in 25 Normal Men and 9 Distance Runners. Br.Heart J.27, 211,1965.

166. Hart,M.C., M.M.Orzalesi and C.D.Cook
Relation between Anatomic Respiratory Dead Space and Body Size and Lung Volume. J.Appl.Physiol. 18, 519, 1963.

167. Hearn,G.R.
The Effects of Terminating and Detraining on Enzyme Activity of Heart and Skeletal Muscle of Trained Rats.
Int.Z.angew Physiol. 21, 190, 1965.

168. Heese, H.deV.
Quantitative Investigations of the Forced Vital Spirogram in Healthy Children. Br.J.Dis.Chest, 55,131,1961.

169. Heinecker,A., K-E.Zipf and H.W.Lösch
Über den Einfluss körperlichen Trainings auf Kreislauf und Atmung. Z.Kreisl.-Forsch 49, 913, 1960.

170. Heinonen,A.O., M.J.Karvonen and R.Ruosteenoja
Pulmonary Diffusing Capacity at Rest and Physical Fitness.
J.Physiol.(London), 142, 54P, 1958.

171. Helliesen,P.J., C.D.Cook, L.Friedlander and S.Agathon
Studies of Respiratory Physiology in Children: I.Mechanics of Respiration and Lung Volumes in 85 Normal Children 5 to 17 years of Age. Ped.22, 80, 1958.

172. Henderson,M., and G.H.Apthorp.
A Rapid Method for Estimation of Carbon Monoxide in Blood.
Br.Med.J. 2,1853,1960.

173. Hermannsen,J.
Untersuchungen uber die Maximalle Ventilations-grosse (Atemgrenzwert) Z.ges.Experimentalle Med.90, 30, 1933.

174. Hermansen,L. and K.L.Anderson
Aerobic Work Capacity in Young Norwegian Men and Women.
J.Appl.Physiol. 20, 425, 1965.

175. Hickman, J.B., and W.H.Cargill
Effect of Exercise on Cardiac Output and Pulmonary Arterial Pressure in Normal Persons and in Patients with Cardio-Vascular Disease and Pulmonary Emphysema. J.Clin.Invest. 27, 10,1948.

176. Hill,A.V., and H.Lupton
Muscular Exercise, Lactic Acid and the Supply and Utilization of Oxygen. Quart.J.Med.16,135,1923.

177. Holloszy,J.D.
Biochemical Adaptations in Muscle. Effect of Exercise on Mitochondrial Oxygen Uptake and Respiratory Enzymes Activity in Skeletal Muscle. J.Biol.Chem.242,2278,1967.

178. Holmgren,A.
On the Reproducability of Steady State D_LCO Measurements during Exercise in Man. Scand.J.Clin.& Lab.Invest.17,110,1965.

179. Holmgren,A.
On the Significance of Pulmonary Mean Capillary CO Back Pressure Corrections for Repeated Measurements of D_LCO during Exercise in Man. Scand.J.Clin. & Lab.Invest.17, 117,1965.

180. Holmgren,A.
On the Reproducability of D_LCO with Increasing Oxygen Uptake during Exercise in Healthy Trained Young Men and Women. Acta Physiol.Scand. 65, 207, 1965.

181. Holmgren,A.
The 'Oxygen Conduction Line' of the Human Body. Proc.int. Symp.cardiovasc.respir.effects Hypoxia, Kingston, Ont.1965. Karger, Basel/New York,1966.

182. Holmgren,A., and P.-O.Åstrand
D_L and the Dimensions and Functional Capacities of the O_2 Transport System in Humans. J.Appl.Physiol.21,1463,1966.

183. Holmgren,A.,B.Jonsson and T.Sjostrand
Circulatory Data in Normal Subjects at Rest and during Exercise in Recumbent Position, with Special Reference to the Stroke Volume at Different Work Intensities. Acta Physiol.Scand. 49, 343,1960.

184. Holmgren,A., B.Jonsson, M.Lavender, H.Linderholm, F.Mossfeldt, T.Sjostrand and G.Ström. Physical Training of Patients with Vasoregulatory Asthenia. Acta Med.Scand. 158, 437, 1957.

185. Holmgren,A., and M.B.McIlroy
Effect of Temperature on Arterial Blood Gas Tensions and pH during Exercise. J.Appl.Physiol. 19, 243,1964.

186. Holmgren,A., F.Mossfeldt, T.Sjostrand and G.Ström
Effect of Training on Work Capacity, Total Hemoglobin Blood Volume, Heart Volume, and Pulse Rate in Recumbent and Upright Positions. Acta Physiol.Scand. 50, 72, 1960.

187. Holmgren,A.,and C.O.Ovenfors
Heart Volume at Rest and during Muscular Work in the Supine and in the Sitting Position. Acta Med.Scand.167, 267,1960.

188. Holmgren,A., and G.Ström
Vasoregulatory Asthenia in a Female Athlete and DaCosta's Syndrome in the Male Athlete Successfully Treated by Physical Training. Acta Med.Scand.164, 113, 1959.

189. Hoogerwerf,S.
Electrolcardiographische Untersuchungen der Amsterdamer Olympiadekämpfer. Arb.Physiol. 2, 61, 1929.

190. Hornbein,T.F., and A.Roos
Effect of Polycythemia on Respiration. J.Appl.Physiol.12, 86,1958.

191. Howell,M.L., A.P.Bakogeorge and B.A.Kerr
Progressive Treadmill Test Norms for College Males. Res.Quart. 35, 322, 1964.

192. Huckabee,W.E.
Relationships of Pyruvate and Lactate during Anaerobic Metabolism: II. Exercise and Formation of O_2 Debt. J.Clin.Invest. 37, 255, 1958.

193. Huckabee,W.E.
The Role of Anaerobic Metabolism in the Performance of Mild Muscular Work: II. The Effect of Asymtomatic Heart Disease. J.Clin.Invest.37, 1593, 1958.

194. Hurtado,A., and C.Boller
Studies of Total Pulmonary Capacity and its' Subdivisions. J.Clin.Invest. 12, 793, 1933.

195. Hutchinson,J.
On Capacity of the Lungs and on the Respiratory Movements with the View of Establishing a Precise and Easy Method of Detecting Disease by the Spirometer. Lancet 1, 630,1846.

196. Jegier,W., P.Sekelj, H.T.Davenport and M.McGregor
Cardiac Output and Related Hemodynamic Data in Normal Children and Adults. Canda.J.Biochem.and Physiol.39, 1747,1961.

197. Johnson,R.L.Jr., W.S.Spicer, J.M.Bishop and R.E.Forster
Pulmonary Capillary Blood Volume, Flow and Diffusing Capacity during Exercise. J.Appl.Physiol.15, 893, 1960.

198. Johnson,R.L.Jr., H.F.Taylor and W.H.Lawson Jr.
Maximal Diffusing Capacity on the Lung for Carbon Monoxide. J.Clin.Invest. 44, 349, 1965.

199. Kagan,E.M.,and P.M.Kaplan
Untersuchung der dosierten und maximalen Arbeit bei Personen von verschiedener physischer Leistungsfähigkeit. Arb.Physiol. 3, 61, 1927.

200. Kaltreider,N.L., W.W.Fray and H.V.Hyde
The Effect of Age on the Total Pulmonary Capacity and its' Subdivisions. Am.Rev.Tuberc. 37, 662, 1938

201. Kanagami,H., K.Baba, T.Katsura and K.Shiroishi
Studies on the Pulmonary Function during Exercise in Normal Subjects. On the Comparison of Three Different Exercise Tests. Resp. & Circ. 9, 188,1961.

202. Kaneko,K., J.Milic-Emili, M.B.Dolovich, A.Dawson and D.V.Bates
Regional Distribution of Ventilation and Perfusion as a Function of Body Position. J.Appl.Physiol. 21, 767,1966.

203. Karpovich, P.V.
Physiology of Muscular Activity. 6th ed.W.B.Saunders Co, Philadelphia,1965.

204. Kauf.E.
Ueber die Einwirkung von Atropin und Adrenalin auf das Herz Sporttreibender. Wien.Klin.Wochenschr. 39, 212,1926.

205. Keen,E.N., and A.W.Sloan
Observations on the Harvard Step Test. J.Appl.Physiol.13, 241,1958.

206. Kelly,H.G.
A Study of Individual Differences in Breathing Capacity in Relation to Some Physical Characteristics. Univ.of Iowa Studies, Studies in Child Wlefare 7,1933.

207. Kennedy, M.S.C.
A Practical Measure of Maximum Ventilatory Capacity in Health and Disease. Thorax 8, 73, 1953.

208. Kennedy,M.S.C., D.C.Thursby-Pelham and P.D.Oldham
Pulmonary Function Studies in Normal Boys. Arch Dis. Chilh. 32, 347,1957.

209. Kety,S.S.
The Theory and Applications of the Exchange of Inert Gas at the Lungs and Tissues. Pharm.Rev. 3, 1,1951.

210. Kety,S.S., M.H.Harmel, H.T.Broomell and C.B.Rhode
The Solubility of Nitrous Oxide in Blood and Brain. J.Biol.Chem. 173, 487,1948.

211. Kilburn,K.H., H.A.Miller, J.E.Burton and R.Rhodes.
Effects of Altering Ventilation on Steady State Diffusing Capacity for Carbon Monoxide. J.Appl.Physiol.18,89,1963

212. Kjellberg,S.R., U.Rudhe and T.Sjostrand
Increase of the Amount of Hemoglobin and Blood Volume in Connection with Physical Training. Acta Physiol.Scand. 19, 146,1949.

213. Kjellberg,S.R., and U.Rudhe
The Amount of Hemoglobin (Blood Volume) in Relation to the Pulse Rate and Heart Volume during Work. Acta Physiol. Scand. 19,152,1949.

214. Kjellmer,I.
The Effect of Exercise on the Vascular Bed of Skeletal Muscle. Acta Physiol.Scand. 62, 18, 1964.

215. Klassen,G., and G.M.Andrew
Unpublished Data. Royal Victoria Hospital, Montreal,Canada.

216. Knehr,C.A., D.B.Dill and W.Neufeld
Training and its' Effects on Man at Rest and at Work. Am.J.Physiol. 136, 148, 1942.

217. Knuttgen,H.G.
Oxygen Debt, Lactate, Pyruvate, and Excess Lactate after Muscular Work. J.Appl.Physiol. 17, 639, 1962

218. Knuttgen, H.G.
Aerobic Capacity of Adolescents. J.Appl.Physiol.22,655,1967.

219. Krahl,V.E.
Anatomy of the Mammalial Lung. Handbook of Physiology Respiration Sec.3,1, 213, 1964.

220. Krogh,A.
The Number and Distribution of Capillaries in Muscle with Calculations of the Oxygen Pressure Head Necessary for Supplying the Tissue. J.Physiol.(London) 52,409,1919.

221. Krogh,A., and M.Krogh
On the Rate of Diffusion of Carbonic Oxide into the Lungs of Man. Scand.Arch.Physiol.23,236,1910.

222. Krogh,A.,and J.Lindhard
Measurements of the Blood Flow through the Lungs of Man. Skand.Arch.Physiol. 27, 100, 1912.

223. Krogh,A., and J.Lindhard
The Volume of the "Dead Space" in Breathing. J.Physiol.(London 47, 30, 1913.

224. Krogh,A., and J.Lindhard
The Regulation of Respiration and Circulation during the Initial Stages of Muscular Work. J.Physiol.(London), 47, 112, 1913.

225. Krogh,M.
The Diffusion of Gases through the Lungs of Man. J.Physiol.(London) 49, 271, 1915.

226. Lagerlöf, H., and L. Werkö
Normal Values for Cardiac Output and Pressure in the Right Auricle, Right Ventricle and Pulmonary Artery. Acta Physiol.Scand. 16, 75, 1948.

227. Lamb,L.E.
Hypoxia - An Anti-Deconditioning Factor for Manned Space Flight. Aerospace Med. 36, 97, 1965.

228. Larsson,Y., B.Persson, G.Sterky and C.Thorén
Functional Adaptation to Rigorous Training and Exercise in Diabetic and Non-Diabetic Adolescents. J.Appl.Physiol. 19, 629, 1964.

229. LeBlanc,J.A.
Use of Heart Rate as an Index of Work Output. J.Appl.Physiol. 10, 275, 1957.

230. Leuallen,E.C., and W.S.Fowler
Maximal Mid-Expiratory Flow. Am.Rev.Tuberc. 72, 783, 1955.

231. Lewis,B.M., R.E.Forster and E.L.Beckman
Effect of Inflation of Pressure Suit on Pulmonary Diffusing Capacity in Man. J.Appl.Physiol. 12, 57, 1958.

232. Lewis,B.M., W.T.McElroy, E.J.Hayford-Welsing and L.C.Samberg
The Effects of Body Position, Ganglionic Blockade and Norepinephrine on the Pulmonary Capillary Bed. J.Clin.Invest. 39, 1345, 1960.

233. Lewis,B.M., T-H.Lin, F.E.Noe, and E.J.Hayford-Welsing
Measurement of Diffusing Capacity by Rebreathing. J.Clin.Invest. 38, 2073, 1959.

234. Lilienthal,J.L.Jr., R.L.Riley, D.D.Proemmel and R.E.Franke
An Experimental Analysis in Man of the Oxygen Pressure Gradient from Alveolar Air to Arterial Blood during Rest and Exercise at Sea Level and at Altitude. Am.J.Physiol. 147, 199, 1946.

235. Linderholm,H.
On the Significance of CO Tension in Pulmonary Capillary Blood for Determination of Pulmonary Diffusing Capacity with the Steady State CO Method. Acta.Med.Scand.156, 413, 1957.

236. Linderholm,H.
Diffusing Capacity of the Lungs as a Limiting Factor for Physical Working Capacity. Acta Med.Scand.163,61,1959.

237. Lindhard,J.
Über das Minutenvolum des Herzens bei Ruhe und bei Muskelarbeit. Pflügers'Arch für Physiol. 161, 233, 1915.

238. Loewry,A.
Ueber die Bestimmung der Grösse der "Schadlichen Luftrammes" im Thorax und der alveolaren Sauerstoffspannung Pflügers'Arch.für Physiol. 58, 416, 1894.

239. Lyons,H.A., and R.W.Tanner
Total Lung Volume and its' Subdivision in Children: Normal Standards. J.Appl.Physiol. 17, 601, 1962.

240. Lyons,H.A., R.W.Tanner and T.Picco
Pulmonary Function Studies in Children. Am.J.Dis.Child, 100, 196, 1960.

241. Macklem,P.T., and J.Mead
The Physiological Basis of Common Pulmonary Function Tests. Arch.Environ.Health. 14, 5, 1967.

242. MacNamara,J., F.J.Prime and J.D.Sinclair
An Assessment of the Steady-State Carbon Monoxide Method of Estimating Pulmonary Diffusing Capacity. Thorax 14, 166, 1959.

243. MacNamara,J., F.J.Prime and J.D.Sinclair
The Increase in Diffusing Capacity of the Lung on Exercise. Lancet 1, 404, 1960.

244. McGregor,M.
The Value of an Index of Maximal Expiratory Force in the Interpretation of Tests of Maximal Ventilatory Capacity. Am.Rev.Tuberc. 78, 692, 1958.

245. McGregor,M., W.Adam and P.Sekelj
Influence of Posture on Cardiac Output and Minute Ventilation during Exercise. Circ.Res.9, 1089, 1961.

246. McGregor,M., R.E.Donevan and N.M.Anderson
Influence of CO_2 and Hyperventilation on Cardiac Output in Man. J.Appl. Physiol. 17, 933, 1962.

247. McIlroy, M.B.
The Respiratory Response to Exercise. Pediatrics 32 (supp), 680, 1963.

248. McKerrow,C.B., and A.B.Otis
Oxygen Cost of Hyperventilation. J.Appl.Physiol. 9,375,1956.

249. McMichael,J.
A Rapid Method of Determining Lung Capacity.
Clin.Sc.4,167,1939.

250. McNeill,R.S., J.Rankin and R.E.Forster
The Diffusing Capacity of the Pulmonary Membrane and the Pulmonary Capillary Blood Volume in Cardio-Respiratory Disease. Clin.Sc. 17, 465, 1958.

251. Magel,J.R., and J.A.Faulkner
Maximum Oxygen Uptakes of College Swimmers. J.Appl. Physiol. 22, 928, 1967.

252. Margaria,R.
A Historical Review of the Physiology of Oxygen Debt and Steady State in Relation to Lactic Acid Formation and Removal. Med.dello Sport 3, 637, 1963.

253. Margaria,R., P.Cerretelli, S.Marchi and L.Rossi
Maximum Exercise in Oxygen. Arb.Physiol. 18, 465,1961.

254. Margaria,R., P.Cerretelli and F.Mangili
Balance and Kinetics of Anaerobic Energy Release during Strenuous Exercise in Man. J.Appl.Physiol.19, 623, 1964.

255. Margaria,R., H.T.Edwards and D.B.Dill
The Possible Mechanisms of Contracting and paying the Oxygen Debt and the Role of Lactic Acid in Muscular Contracti
Am.J.Physiol. 106, 689, 1933.

256. Metheny,E., L.Brouha, R.E.Johnson and W.H.Forbes
Some Physiological Responses of Women and Men to Moderate and Strenuous Exercise: A Comparative Study.
Am.J.Physiol. 137, 318,1942.

257. Milic-Emili,G.
Heart Rate and Ventilation during Recovery from Heavy Exercise in Trained and Untrained Individuals.
Arb.Physiol. 17, 455, 1959.

258. Milic-Emili,G., J.M.Petit and R.Deroanne
Mechanical Work of Breathing during Exercise in Trained and Untrained Subjects. J.Appl.Physiol.17, 43, 1962.

259. Milic-Emili,G., P.Cerretelli, J.M.Petit and C.Falconi
La consommation d'oxygène en fonction de l'intensité de l'exercise musculaire. Arch.Int.Physiol. et Biochem. 67, 10, 1959.

260. Milic-Emili,G.,J.A.M.Henderson, M.B.Dolovich, D.Trop and K.Kaneko. Regional Distribution of Inspired Gas in the Lung. J.Appl.Physiol. 21, 749, 1966.

261. Milic-Emili,G., and J.M.Petit
Mechanical Efficiency of Breathing. J.Appl.Physiol.15, 359, 1960.

262. Mitchell,J.H., B.J.Sproule and C.B.Chapman
The Physiological Meaning of the Maximal Oxygen Intake Test. J.Clin.Invest. 37, 533, 1958.

262a. Montoye,H.J., W.D.Collings and G.C.Stauffer
Effects of Conditioning on the Ballistocardiogram of College Basketball Players. J.Appl.Physiol.15,449,1960.

263. Moore,R., and E.R.Buskirk
Exercise and Body Fluids. Science and Med.of Exercise and Sports. W.R.Johnson, ed. Harper and Rowe, 1960.

264. Morse,M., F.W.Schlutz and D.E.Cassels
The Lung Volumes and its' Subdivisions in Normal Boys 10 to 17 years of Age. J.Clin.Invest.31, 330,1952

265. Morse,M., F.W.Schlutz and D.E.Cassels
Relation of Age to Physiological Responses of the Older Boys(10 to 17 Years) to Exercise. J.Appl.Physiol.1,683, 1948.

266. Mostyn,E.M., S.Helle, G.B.L.Gee, L.G.Bentivoglio and D.V.Bates. The Pulmonary Diffusing Capacity of Athletes. J.Appl.Physiol. 18, 687, 1963

267. Murray,A.B., and C.D.Cook
Measurements of Peak Expiratory Flow Rates in 220 Normal Children from 4, 5 to 18.5 Years of Age. J.Ped.62,186,1963.

268. Musshoff,K., H.Reindell and H.Klepzig
Stroke Volume, Arterio-Venous Difference, Cardiac Output and Physical Working Capacity and their Relationship to Heart Volume. Acta Cardiol (Brux) 14, 427, 1959.

269. Nairn,J.R., A.J.Bennet, J.D.Andrew and P.MacArthur
A Study of Respiratory Function in Normal School Children. The Peak Flow Rate. Arch.Dis.Child 36, 253, 1961.

270. Needham,C.D., M.C.Rogan and I. MacDonald
Normal Standards for Lung Volumes, Intrapulmonary Gas-mixing, and Maximum Breathing Capacity. Thorax 9,313,1954.

271. Newman,F.
The Effect of Change in Posture on Alveolar-Capillary Diffusion and Capillary Blood Volume in the Human Lung. J.Physiol.(London),162, 29P,1962.

272. Newman,F., B.F.Smalley and M.L.Thomson
A Comparison between Athletes and Non-Athletes in Oxygen Consumption and Pulmonary Diffusion at Near Maximal Exercise. J.Physiol.(London), 156, 7P,1961.

273. Newman,F., B.F.Smalley and M.L.Thomson
A Comparison between Body Size and Lung Function of Swimmers and Normal School Children. J.Physiol.(London) 156, 9P, 1961.

274. Newman,F., B.F.Smalley and M.L.Thomson
Effect of Exercise, Body and Lung Size on D_LCO in Athletes and Non-Athletes. J.Appl.Physiol. 17, 649, 1962.

275. Newman,F., and M.L.Thomson
The Effect of the Inverted Position on Alveolar-Capillary Diffusion and Volumes of the Human Lung. J.Physiol.(London) 153, 71P, 1960.

276. Newton,J.L.
The Assessment of Maximal Oxygen Intake.
J.Sports Med. 3, 164, 1963.

277. Ogilvie,C.M., R.E.Forster, W.S.Blakemore and J.W.Morton
A Standardized Breath Holding Technique for the Clinical Measurement of the Diffusing Capacity of the Lung for Carbon Monoxide. J.Clin.Invest. 36, 1,1957.

278. Ostiguy,G.L.
Measurement of Cardiac Output by the Foreign Gas Method using Nitrous Oxide. M.Sc.Thesis, Faculty of Graduate Studies, McGill University, July 1964.

279. Otis,A.B.
The Work of Breathing. Physiol.Rev.34, 449,1954.

280. Ouellet,Y.
Cardiac Output during Maximal Exercise.
M.Sc.Thesis, Faculty Graduate Studies, McGill University, August 1966.

281. Pace,N., W.V.Consolazio, W.A.White Jr., and A.R.Behnke
Formulation of the Principal Factors Affecting the Rate of Uptake of Carbon Monoxide by Man. Am.J.Physiol.147,352,1946.

282. Palmer, D.M.
The Lungs of a Human Foetus of 170mm. Am.J.Anat. 58,59,1936.

283. Pembrey,M.S., and A.H.Todd
The Influence of Exercise upon the Pulse and Blood Pressure.
J.Physiol.(London) 37, 66P,1908.

284. Pengelly,L.D.
Cardiac Dye Injector Synchronizer.
Trans.Bio-Med.Electron,BME. 8,113,1961.

285. Fetren,T.,T.Sjostrand and B.Sylven
Der Einflus des Training auf die Häufigkeit der Capillaren in Hertz und Skeletmusculatur. Arb.Physiol.9, 376,1936.

286. Piiper,J., P.Cerretelli, F.Cultica and F.Mangili
Energy Metabolism and Circulation in Dogs Exercising in Hypoxia. J.Appl.Physiol. 21,1143,1966.

287. Pugh,L.G.C.E.
Cardiac Output in Muscular Exercise at 5800M (19000Ft.) J.Appl.Physiol. 19, 441,1964.

288. Pugh,L.G.C.E., M.B.Gill, S.Lahiri, J.S.Milledge, M.P.Ward and J.B.West. Muscular Exercise at Great Altitudes. J.Appl.Physiol. 19, 431,1964.

289. Püschel,E.
Über die Spirometrie und ihre Ergebnisse in Kindesalter. Erg.Inn Med. 61, 786, 1942.

290. Rahn,H.
A Concept of Mean Alveolar Air and the Ventilation-Blood Flow Relationships during Pulmonary Gas Exchange. Am.J.Physiol.158, 21,1949.

291 Reddan,W., J.Burpee, P.Reuschlein, J.B.Gee and J.Rankin
Pulmonary Adaptations to Strenuous Training in Competitive Swimming. Fed.Proc. 25, 325, 1966.

292. Reeves,J.T., R.F.Grover, S.G.Blount Jr., and G.F.Filley
Cardiac Output Response to Standing and Treadmill Walking. J.Appl.Physiol. 16, 283, 1961.

293. Reeves,J.T., R.F.Grover, G.F.Filley and S.G.Blount Jr.
Cardiac Output in Normal Resting Man. J.Appl.Physiol.16, 276, 1961.

294. Riley,R.L., and A.Cournand
"Ideal" Alveolar Air and the Analysis of Ventilation-Perfusion Relationships in the Lung. J.Appl.Physiol.1, 825, 1949.

295. Riley,R.L., A.Himmelstein, H.L.Motley, H.M.Weiner and A.Cournand. Studies of the Pulmonary Circulation at Rest and during Exercise in Normal Individuals and in Patients with Chronic Pulmonary Disease. Am.J.Physiol. 152,372,1948.

296. Riley,R.L., R.H.Shepard, J.E.Cohn, D.G.Carroll and B.W.Armstrong. Maximal Diffusing Capacity of the Lungs. J.Appl.Physiol. 6, 573, 1954.

297. Robinson,B.F.,S.E.Epstein, R.L.Kehler and E.Braunwald Circulatory Effects of Acute Expansion of Blood Volume Studies during Maximal Exercise and at Rest. Circ.Res.19, 26, 1966.

298. Robinson,S. Experimental Studies of Physical Fitness in Relation to Age. Arb.Physiol. 10, 251,1938.

299. Robinson,S., H.T.Edwards and D.B.Dill New Records in Human Power. Science 85, 409,1937

300. Robinson,S., and P.M.Harmon Lactic Acid Mechanisms and Blood Changes in Training. Am.J.Physiol. 132, 757, 1941.

301. Robinson,S., D.L.Robinson, R.J.Mountjoy and R.W.Bullard Influence of Fatigue on the Efficiency of Men during Exhausting Runs. J.Appl.Physiol. 12, 197,1958.

302. Rohter,F.D., R.H.Rochelle and C.Hyman Exercise Blood Flow Changes in the Human Forearm during Physical Training. J.Appl.Physiol. 18, 789, 1963.

303. Rosenberg,E. Effects of Physical Training on Single Breath Diffusing Capacity Measured at Rest. Submitted June,1967, Int. Z.eit für angewardte Physiol.

304. Ross,J.C., R.Frayser and J.B.Hickam A Study of the means by which Exercise Increases the Pulmonary Diffusing Capacity for Carbon Monoxide. J.Clin.Invest. 37, 926, 1958.

305. Roughton,F.J.W. The Average Time Spent by the Blood in the Human Lung Capillary and its' Relation to the Rates of CO Uptake and Elimination in Man. Am.J.Physiol. 143, 621, 1945.

306. Roughton,F.J.W., and R.E.Forster Relative Importance of Diffusion and Chemical Reaction Rates in Determining Rate of Exchange of Gases in the Human Lung, with Special Reference to true Diffusing Capacity of Pulmonary Membrane and Volume of Blood in the Lung Capillaries. J.Appl.Physiol. 11, 290, 1957.

307. Rowell,L.B., J.R.Blackmon and R.A.Bruce Indocyanine Green Clearance and Estimated Hepatic Blood Flow during mild to Maximal Exercise in Upright Man. J.Clin.Invest. 43, 1677,1964.

308. Rowell,L.B., H.L.Taylor, Y.Wang and W.S.Carlson
Saturation of Arterial Blood with Oxygen during Maximal Exercise. J.Appl.Physiol. 19, 284, 1964.

309. Rushmer,R.F., and O.A.Smith,Jr.
Cardiac Control. Physiol.Rev. 39, 41, 1959.

310. Rushmer,R.F., O.A.Smith,Jr., and E.P.Lasher
Neural Mechanisms of Cardiac Control during Exercise. Physiol. Rev. 40, Supp.4, 27,1960.

311. Saltin,B., and J.Stenberg
Circulatory Response to Prolonged Severe Exercise. J.Appl.Physiol. 19, 833, 1964.

312. Schneider,E.C., and C.B.Crampton
A Comparison of Some Respiratory and Circulatory Reactions of Athletes and Non-Athletes. Am.J.Physiol.129, 165,1940.

313. Schwartz,L., R.H.Britten and L.R.Thompson
Studies in Physical Development and Posture: I. The Effect of Exercise on the Physical Condition and Development of Adolescent Boys. Pub.Health Bull #179, 1928.

314. Shapiro,W., C.E.Johnston, R.A.Dameron Jr., and J.L.Patterson, Jr. Maximal Ventilatory Performance and its' Limiting Factors. J.Appl.Physiol. 19, 199,1964.

315. Shaw,D.B., F.Cinkotai and M.L.Thomson
Syncope Induced by Application of Negative Pressure to the Lower Body and its' Effect on Lung CO Diffusing Capacity. Aerospace Med. 37, 154, 1966.

316. Shephard,R.H., E.Varnauskas, H.B.Martin, H.A.White, S.Permutt, J.E.Coates and R.L.Riley. Relationship between Cardiac Output and Apparent Diffusing Capacity of the Lung in Normal Men. J.Appl.Physiol.13,205,1958.

317. Shephard,R.J.
The Development of Cardio-Respiratory Fitness. Med.Serv.J.Canada. 21, 533, 1965.

318. Simonson,E.
Physical Fitness and Working Capacity of Older Men. Geriatrics 2, 110, 1947.

319. Simonson,E., and O.Riesser
Zur Physiologie des Energieumsatzes Beim Menschen: IV. Mittlg.zur Physiologie der Atmung. Pflügers Arch.für Physiol. 215, 743, 1927.

320. Skubic,V., and J.Hilgendorf
Anticipatory Exercise and Recovery Heart Rate of Girls as Affected by Four Running Events. J.Appl.Physiol.19, 853,1964.

321. Sloan,A.W.
Effect of Training on Physical Fitness of Women Students. J.Appl.Physiol. 16, 167, 1961.

322. Sloan,A.W., and E.N.Keen
Physical Fitness of Oarsmen and Rugby Players before and after Training. J.Appl.Physiol. 14, 635, 1959.

323. Slonim,N.B., D.G.Gillespie and W.H.Harold
Peak Oxygen Uptake of Healthy Young Men as Determined by a Treadmill Method. J.Appl.Physiol. 10, 401, 1957.

324. Stahlman,M.T.
Pulmonary Ventilation and Diffusion in the Human Newborn Infant. J.Clin.Invest. 36, 1081,1957.

325. Stead,E.A.,J.V.Warren, A.J.Merrill and E.S.Brannon
The Cardiac Output in Male Subjects as Measured by the Technique of Right Atrial Catheterization. Normal Values with Observations of the Effects of Anxiety and Tilting. J.Clin.Invest. 24, 326, 1945.

326. Steinhaus,A.H.
Chronic Effects of Exercise. Physiol.Rev.13, 103,1933.

327. Stenberg,J., P.-O.Åstrand, B.Ekblom, J.Royce and B.Saltin
Hemodynamic Response to work with Different Muscle Groups, Sitting and Supine. J.Appl.Physiol.22, 61,1967.

328. Sterky,G.
Physical Working Capacity in Diabetic School Children. Acta.Paediat. 52, 1, 1963.

329. Stewart,C.A.
The Vital Capacity of the Lungs of Children in Health and Disease. Am.J.Dis.Child. 24, 451,1922.

330. Stewart,G.N.
Researches on the Circulation Time and on the Influences which Affect it: IV. The Output of the Heart. J.Physiol.(London) 22,159,1897.

331. Strandell,T.
Circulatory Studies on Healthy Old Men with Special Reference to the Limitations of the Maximal Physical Working Capacity. Acta.Med.Scand. 175, Supp.414, 1964.

332. Strang,L.B.
The Ventilatory Capacity of Normal Children.
Thorax 14, 305, 1959.

333. Strang,L.B.
Measurement of Pulmonary Diffusing Capacity in Children.
Arch.Dis.Childh. 35, 232, 1960.

334. Strydom,N.B., C.H.Wyndham, C.G.Williams, J.M.Morrison, G.A.G.Bredell, A.J.S.Benade, and M.Von Ramden.
Acclimatization to Humid Heat and the Role of Physical Conditioning. J.Appl.Physiol. 21, 636, 1966.

335. Stuart,D.G., and W.D.Collings
Comparison of Vital Capacity and Maximal Breathing Capacity of Athletes and Non-Athletes. J.Appl.Physiol.14, 507, 1959.

336. Stuart,H.C., and H.V.Meredith
Use of Body Measurement in the School Health Program.
Am.J.Pub.Health 36, 1365, 1946.

337. Suggs,C.W., and W.E.Splinter
Some Physiological Responses of Man to Workload and Environment. J.Appl.Physiol.16, 413, 1961.

338. Summers,E., C.A.Guzman and M.R.Becklake
Unpublished Data, Royal Victoria Hospital, Montreal 1966.

339. Tabakin,B.S., J.S.Hanson,T.W.Merriam,Jr.,and E.J.Caldwell
Hemodynamic Response of Normal Men to Graded Treadmill Exercise. J.Appl.Physiol. 19, 457,1964.

340. Tabakin,B.S., J.S.Hanson and A.M.Levy
Effect of Physical Training on the Cardiovascular and Respiratory Response to Graded Upright Exercise in Distance Runners. Br.Heart J. 27, 205, 1965.

341. Taylor,H.L., E.Buskirk and A.Henschel
Maximan Oyxgen Intake as an Objective Measure of Cardio-Respiratory Performance. J.Appl.Physiol. 8, 73, 1955.

342. Taylor,H.L., A.Henschel, J.Brozek and A.Keys
Effects of Bed Rest on Cardiovascular Function and Work Performance. J.Appl.Physiol. 2, 223,1949.

343. Taylor, H.L., Y.Wang, L.Rowell and G.Blomqvist
The Standardization and Interpretation of Submaximal and Maximal Tests of Working Capacity. Pediatrics 32,703,1963 (Sup

344. Thomas,H.D., B.Boshell, C.Gaos and T.J.Reeves
Cardiac Output during Exercise and Anaerobic Metabolism in Man. J.Appl.Physiol. 19, 839, 1964.

345. Torelli,G., and G.Brandi
Regulation of the Ventilation at the beginning of Muscular Exercise. Int.Z.angew.Physiol. 19,134,1961.

346. Turino,G.M., M.Brandfonbrener and A.P.Fishman
Determinants of Pulmonary Diffusing Capacity. J.Clin.Invest. 38, 1186,1959.

347. Turner, J.A., and R.L.McLean
Spirometric Measurements of Lung Function in Healthy Children. Pediatrics,7,360,1951.

348. Van Slyke,D.D., and C.A.L.Binger
The Determination of Lung Volume without Forced Breathing. J.Exp.Med. 37, 457,1923.

349. Varnauskas,E., H.Bergman, P.Houk and P.Bjorntorp
Hemodynamic Effects of Physical Training in Coronary Patients. Lancet ii, 8, 1966.

350. Wade,O.L., and J.M.Bishop
Cardiac Output and Regional Blood Flow. Blackwell Scientific Publications, Oxford 1962.

351. Wahlund,H.
Determination of the Physical Working Capacity. Acta.Med.Scand. Supp. 215, 1,1948.

352. Wang,Y., R.J.Marshall and J.T.Shepherd
The Effects of Changes in Posture and of Graded Exercise on Stroke Volume in Man. J.Clin.Invest. 39, 1051,1960.

353. Wang,Y., J.T.Shepherd, R.J.Marshall, L.Rowell and H.L.Taylor
Cardiac Response to Exercise in Unconditioned Young Men and in Athletes. Circulation 24, 1064,1961 (abstract, 34th Scientific sessions).

354. Wasserman,K., A.L.VanKessel and G.G.Burton
Interaction of Physiological Mechanisms during Exercise. J.Appl.Physiol. 22, 71, 1967.

355. Weibel,E.R.
Morphology of the Human Lung. Academic Press Inc,N.Y.,1963.

356. Wells,J.G., B.Balke and D.D.VanFossan
Lactic Acid Accumulation during Work. A Suggested Standardization of Work Classification. J.Appl.Physiol.10, 51,1957.

357. West,J.B.
Diffusing Capacity of the Lung for Carbon Monoxide at High Altitude. J.Appl.Physiol. 17, 421, 1962.

358. West,J.B., and C.T.Dollery
Distribution of Blood Flow and Ventilation-Perfusion Ratio in the Lung measured with Radioactive CO_2.
J.Appl.Physiol. 15, 405, 1960.

359. West,J.B., S.Lahiri, M.G.Gill, J.S.Milledge, L.G.C.E.Pugh and M.P.Ward. Arterial Oxygen Saturation during Exercise at High Altitude. J.Appl.Physiol. 17, 617, 1962.

360. Whitfield,A.G.W., J.A.H.Waterhouse and W.M.Arnott
The Total Lung Volume and its' Subdivisons. A Study in Physiological Norms: II. The Effect of Posture.
Br.J.Soc.Med. 4, 86,1950.

361. Williams,C.G., G.A.G.Bredell, C.H.Wyndham, N.B.Strydom, J.F.Morrison,J.Peter, P.W.Flemming and J.S.Ward.
Circulatory and Metabolic Reactions to Work in Heat.
J.Appl.Physiol. 17, 625, 1962.

362. Wilson,M.G., and D.J.Edwards
The Vital Capacity of the Lungs and its' Relation to Exercise Tolerance in Children with Heart Disease, Standards for Normal Vital Capacity for Children: the Lung Capacity in Certain Intrathoracic Conditions.
Am.J.Dis.Child. 22, 443, 1921.

363. Wyndham,C.H., N.B.Strydom, J.S.Maritz, J.F.Morrison, J.Peter and Z.V.Potgieter. Maximum Oxygen Intake and Maximum Heart Rate during Strenuous Work. J.Appl.Physiol. 14, 927, 1959.

364. Wyndham,C.H., N.B.Strydom, J.F.Morrison, J.Peter, C.G.Williams, G.A.G.Bredell and A.Joffe.
Differences between Ethnic Groups in Physical Working Capacity. J.Appl.Physiol. 18, 361, 1963.

365. Wyndham,C.H., and J.S.Ward.
An Assessment of the Exercise Capacity of Cardiac Patients.
Circulation 16, 384, 1957.

366. Young,A.C.
Dead Space at Rest and during Exercise.
J.Appl.Physiol. 8, 91,1955.

367. Zechman,F.W., F.S.Musgrave, R.C.Mains and J.E.Cohn
Respiratory Mechanics and Pulmonary Diffusing Capacity with Lower Body Negative Pressure. J.Appl.Physiol.22,247,1967.

368. Zuntz,N., and D.Hagemann
Stoffwecksel des Pferdes bei Ruhe und Arbeit.
Landwirtschaftliche Jahrbucher 27, 371,1898.

369. Zwi,S., J.C.Theron, M.McGregor and M.R.Becklake
The Influence of Instrumental Resistance on the Maximal Breathing Capacity. Dis.Chest 36, 361, 1959.

ACKNOWLEDGEMENTS

It is inevitable that a project of this nature required the assistance of many whom I wish to acknowledge. During the four years of this study, several technicians have been involved in making measurements; these include the Misses M.Schmidt, J.Clarke, B.Wright, J.Dryberg, L.Hutton, ~~and~~ Mrs. E.Summers, ~~and~~ Mr.G.Dupras, and J.Nowaczek, whose help has been appreciated. Additional assistance and support were given by Doctors C.Guzman and J.S.Guleria. Mr.L.D.Pengally designed and built most of the testing circuits used in the study and he along with his assistants, J.Pinto, M.Ballantyne and J.Ghose, gave invaluable technical support throughout. I am indebted to Mr.L.Bartlett, not only for his help as Chief Technician, but also for his artististic aid in preparing the figures. Mr. A.Greenberg is acknowledged for his help in data processing; he was responsible for writing most of the computer programs.

Doctor M.Becklake acted as my supervisor. She was a constant source for support and guidance and helped immeasurably, through her constructive advice and criticism, in the interpretation and presentation of results. I am deeply appreciative also for the support of Doctor D.V.Bates for his direction during the study. Furthermore, I acknowledge that without his interest, enthusiasm and backing it might not have been possible for me to persue this program at the Joint Cardio-Respiratory Service of the Royal Victoria Hospital and McGill University, Montreal.

The author is indebted for financial support, through Doctor Bates, to the John Hartford Foundation and the National Fitness Council of Canada.

Finally, I would be remiss for failing to acknowledge the support of my wife and children who shared in the problems and pleasures of this endeavour.

Diffusing Capacity (D_L)	- the rate of gas transfer through a membrane in relation to a constant pressure difference across it. Units are ml/min/mmHg. A subscript indicates the gas used (eg. D_{CO}, D_{O_2}).
$\dot{V}O_2$	- minute uptake of oxygen expressed at standard conditions (ie. STPD). Subscript MAX indicates maximal value attainable in exercise.
Cardiac Output ($\dot{Q}c$)	- minute output of blood by the heart. In health, except in transitory conditions, the flow through the pulmonary capillaries and into the aorta are virtually the same, and the two are considered synonymous here.
$(A-V)\ O_2$ Difference	- difference in O_2 constent (ml.O_2 /100 ml) between arterial and mixed venous blood. (referred to as O_2 extraction as well).

JOINT CARDIO-RESPIRATORY SERVICE
McGILL UNIVERSITY
and
ROYAL VICTORIA HOSPITAL

1st July, 1965

Dear Parent,

Through the kind co-operation and permission of the Parks and Playgrounds Commission of the City of Montreal, we are conducting a series of tests on children enrolled in their summer program at our exercise laboratories. Because of the age group of the children concerned (8 to 15 years) it is necessary to gain consent of the parent (or guardian) before doing the test.

The purpose of the study is to collect information on lung and heart function during rest and exercise, on normal healthy children. Similar information has just been obtained on the older age groups 20 - 70 years and these tests will provide complete data for all age groups. As you may then realize, this study is designed to help gain a better understanding of how we "grow old", which of course is necessary if we wish to learn how to "stay young".

The tests are COMPLETELY without danger and discomfort and the following points should eliminate all doubts you may have regarding your child's participation.

1. No needles or drugs are required.
2. Physical examination is given prior to test.
3. Tests require pedalling on a stationary bicycle.
4. Transportation to and from the park areas concerned is provided by an authorized school bus.
5. Total testing time is about 1 hour. Since the children will be transported in groups of 3 - 5, this means each child will be required to be away from the park for about 3 hours.
6. Close medical supervision is provided at all times.

PARENT'S CONSENT FORM

I, the parent or guardian of .....
Print child's name

do hereby consent to participation by my child in the Research Study mentioned in the attached letter, and absolve any individual, institution or Boards of Directors involved of all legal liability.

.....
Signature (parent or guardian)

DATE: .....

ADDRESS.....

.....

PHONE: HOME ..... BUSINESS .....

CHILD's STATISTICS (to be completed by parent)

BIRTHDAY .... SEX .....
Date Month Year

HEIGHT ..... WEIGHT .....

LAST MEDICAL CHECK-UP - DATE (approx) .....

HAS YOUR CHILD 1. Ever been advised against exercise? .....

2. Ever had any heart disease? .....

3. Ever had any lung disease? .....

(FOR MEDICAL EXAMINERS USE ONLY)

CHEST .....

HEART: SOUNDS ..... RATE (sitting) .....

B.P. .....

OTHER .....

COMMENTS:

Signature of Examiner

The tests are being made on July 12 - 16 and 19 - 23. In all, eighty children will be tested and this group will include an equal number of each sex, 10 in each age group.

You may well understand that not all children have the appropriate temperament for such tests. Your child has been selected as a suitable subject and we would therefore appreciate your completing, signing and returning to the Park Monitor, the enclosed form. Thank you for your anticipated co-operation, without which this study cannot be made.

Yours truly,

George M. Andrew, B.Sc.(P.E.) M.Sc.
Lecturer, McGill University.
Research Fellow, Royal Victoria Hospital.

PHONE: 842-1251 Local 795.

TESTING SCHEDULE..CONTROLS

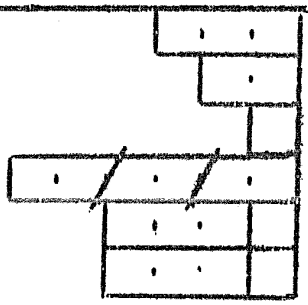
*

STATION	PHASE NUMBER											
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
Records, Examination		A	C		D					B		
Flow Rates	ABCD											
Lung Volumes		B	B	C	C	D	D	A	A			
DL &VO_2 (1)		CD	A	B								
VO_2 (2)			D	A	B	C						
VO_2 (3)				D	A	B	C					
Qc (1)							B	D	C	A		
Qc (2)								B	D	C	A	
Qc (3)									B	D	C	A
Wait						A	A	C			D	

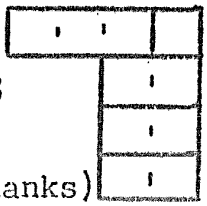
* Each phase required about 15 minutes.

CARDIORESPIRATORY SERVICE EXERCISE $\dot{Q}_c$ MEASUREMENT

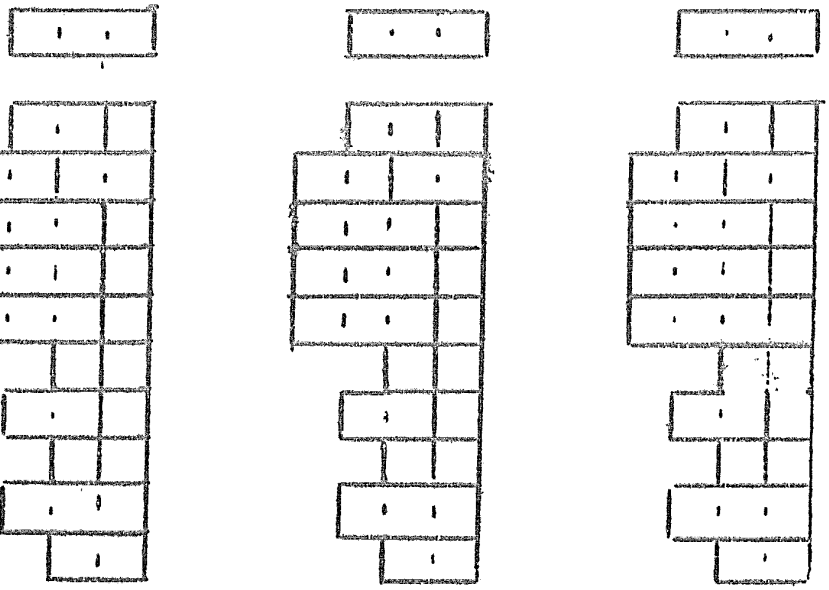
IBM PUNCH CARD CODING FORM



NAME
AGE
SEX
DATE(d,mo,yr)
HEIGHT
WEIGHT

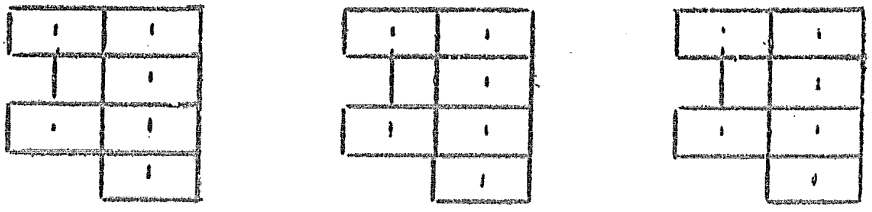


BAROMETRIC PRESSURE
WATER VAPOUR PRESSURE
ROOM TEMP
(punch blanks)



LOAD

VOLUME
TIME FOR VOLUME
F_I N_2O
F_E N_2O
F_A N_2O
$F_{A'}$ N_2O
N_2O RISE
N_2 RISE
PULSE RATE /min
RESP FREQ (N_2O)



F_E O_2
F_E CO_2
VOLUME INSPIRED
RESP FREQ (O_2)

Reprinted from JOURNAL OF APPLIED PHYSIOLOGY
Vol. 21, No. 2, March, 1966
Printed in U.S.A.

Effect of athletic training on exercise cardiac output[1,2]

GEORGE M. ANDREW, CAROLE A. GUZMAN, AND MARGARET R. BECKLAKE
Cardiorespiratory Service, Royal Victoria Hospital, McGill University, Montreal, Canada

ANDREW, GEORGE M., CAROLE A. GUZMAN, AND MARGARET R. BECKLAKE. *Effect of athletic training on exercise cardiac output.* J. Appl. Physiol. 21(2): 603–608. 1966.—In four college athletes and four nonathletic freshmen measurements were made of ventilation, O_2 consumption, cardiac output, and heart rate at three submaximal levels of exercise before, and again after, a period of athletic training. In both groups there was a decrease in heart rate, cardiac output, and minute ventilation at any given work load. Oxygen consumption was unaffected and therefore the arterial-venous O_2 difference was increased. Before training, the athletes differed from the nonathletes in having a lower minute ventilation, a larger stroke volume at the two external work loads studied, and a slower heart rate at the higher load. These differences persisted after training, when it was found also that the athletes had lower values for cardiac output at equal exercise loads.

cardiorespiratory effects of athletic training

THE CARDIORESPIRATORY CONSEQUENCES of athletic training have been the subject of numerous reports (1, 3, 9, 11-13, 15, 18, 20, 21, 24). Studies made on individuals before and after a period of training have consistently shown that this causes a reduction in heart rate (3, 11, 12, 15, 24) and minute ventilation (11, 15, 24) for any given exercise load. By contrast, studies of cardiac output have yielded conflicting results, suggesting that training may cause a higher (1, 8), lower (3, 15, 26), or unchanged cardiac output (3, 13, 20) for a given work load or O_2 consumption. However; most of these studies have been comparisons of groups of subjects who, it was hoped, differed only in respect to degree of training.

The present study was designed to ascertain the effects of training on exercise cardiac output in athletes and nonathletes, using each subject as his own control.

MATERIALS AND METHODS

Eight subjects were studied. Four were athletes (members of the university ice-hockey team); they were studied during the 1st week of training and 4 months later after they had trained for 6–8 hr weekly and played at least one game weekly. Four were nonathletes (university freshmen), who were studied before and after a 4-week training period in which they spent an hour daily, 5 days/week, on running, bench-jumping, and rope-climbing exercises, each performed to the maximum of their ability. Physical characteristics of both groups are given in Table 1.

The subjects were studied during exercise on a bicycle ergometer (Elema-Schönander, Stockholm) while seated in the normal cycling position.[3] Minute ventilation ($\dot{V}_I$) and O_2 consumption ($\dot{V}_{O_2}$) were recorded on a circuit previously described from this laboratory (19), the former on dry gas meter (Parkinson and Cowan, type C dry gas meter) on the inspired-air line and the latter calculated from $F_{E_{CO_2}}$ and $F_{E_{O_2}}$, which were sampled continuously from a mixing chamber in the expired-air line (Beckman F_3 industrial paramagnetic O_2 analyzer; Cambridge thermal-conductance CO_2 analyzer). Heart rate was recorded throughout the procedure by an infrared-sensitive photocell on the ear (22), but in a few instances it had to be counted by palpation of the radial pulse.

Cardiac output ($\dot{Q}_C$) was measured by an indirect Fick method using N_2O, previously described in detail (5). The absence of blood sampling makes this method particularly suitable for repeated use in the exercising normal subject. The calculation was made according to the formula

$$\dot{Q}_c = \frac{[\dot{V}_I - n(V_D + V_D')][F_{I_{N_2O}} - F_{A_{N_2O}}]60/t}{0.474[F_{A_{N_2O}} - F_{A'_{N_2O}}](PB - W/760)}$$

Received for publication 3 May 1965.
[1] This study was supported by The John A. Hartford Foundation (USA), the Medical Research Council of Canada, and Physical Fitness Research Programme of the Department of National Health and Welfare, Canada.

[2] Part of this material was included in the thesis of G. M. Andrew for the Master of Science degree in Physiology at McGill University.

[3] Subjects were seated upright with legs down, in contrast to the armchair-type bicycle used in some studies.

where

t	= time period in seconds over which N_2O uptake was measured
$\dot{V}_I$	= sum of inspired tidal volumes (BTPD) in liters during time t
V_D	= subject's anatomical dead space, predicted from the mean tidal volume over time t, using the formula of Asmussen and Nielsen (2)
V_D'	= 0.210 liter, the apparatus dead space
n	= number of breaths in time t
F_{IN_2O} and F_{AN_2O}	= concentration of N_2O in inspired and end-tidal air, respectively; values derived from the continuous record of N_2O concentration of respired gas on an N_2O meter (Hilger—IRD, London, England) inserted between the mouthpiece and breathing valve.
F'_{AN_2O}	= the meter reading of F_{AN_2O} on air breathing before the experiment commenced; this included a correction for existing low levels of N_2O in blood, because of immediately preceding experiments
0.474	= solubility coefficient of N_2O in blood, i.e., milliliters of N_2O at 37 C which will dissolve in 1 ml blood when equilibrated at 760 mm at 37 C

The uptake of N_2O was monitored during a period of steady-state breathing, after the replacement of alveolar air by test gas and before its reappearance in pulmonary arterial blood. We have shown that no significant error will occur from alveolar gas replacement or from recirculation in normal subjects in the period 15–30 sec after commencing to breathe test gas (5); thus, measurement of $\dot{V}_{N_2O}$ was confined to this period.

Procedure. On arrival at the laboratory the subject underwent a physical examination. After this he exercised on a bicycle ergometer[3] at the first exercise load while O_2 uptake ($\dot{V}_{O_2}$) was recorded (19). Measurements were continued for about 5 min, by which time $\dot{V}_{O_2}$ had remained steady for 2–3 min, as evidenced by steady values for V_I, $F_{E_{CO_2}}$ and $F_{E_{O_2}}$. While exercise continued, the subject was connected to the circuit for measurement of $\dot{Q}_c$ as described above, a further 1–2 min being required to complete this. After a rest period of at least 15 min, the whole procedure was repeated at two higher exercise loads. The three exercise loads for athletes were 550, 750, and 900 kg/min, and for nonathletes were 350, 550, and 750 kg/min. Stroke volume was calculated as $\dot{Q}_c$/heart rate, and arterial-venous O_2 difference as $\dot{V}_{O_2}/\dot{Q}_c$.

RESULTS

The relationship between the results obtained before and after training is shown in Fig. 1. It can be seen that after training the heart rate fell in all subjects at all loads, although these differences were significant in only three comparisons—nonathletes at 350 and 550 kg/min and athletes at 550 kg/min (Table 2). The $\dot{Q}_c$ decreased in most studies (Fig. 1), the fall being significant in the athletes at only two work loads (550 and 900 kg/min). When all data were combined the group mean changes in heart rate and $\dot{Q}_c$ were significant at the 1 % level (Table 2). Stroke volume did not show any consistent change (Fig. 1*C*, *E*). Similarly, $\dot{V}_{O_2}$ showed no consistent change, so that the (A-V)O_2 difference (a computed value) increased in most instances (Fig. 1*D*). The minute volume ($\dot{V}_I$) decreased in all but one study (Fig. 1*F*), though the fall was significant only for the nonathletes at the 550 kg/min load; however, the mean change for the combined groups was significant at the 1 % level (Table 2). In the athletes the fall in ventilation was accompanied by a fall in respiratory frequency (Table 2), a measurement which did not change in the nonathletes. Since $\dot{V}_{O_2}$ showed no consistent change, the ventilatory equivalent for O_2 decreased. Thus, the effects of training were in general similar in athletes and nonathletes, but differed in degree, being more marked in the athletes. (It will be recalled that the athletes trained for 4 months and the nonathletes for 4 weeks.)

Comparison of athletes and nonathletes, in the untrained and in the trained state, is given in Fig. 2, in which group mean values for $\dot{Q}_c$, heart rate, $\dot{V}_{O_2}$, and ventilation are plotted against external work load. The $\dot{V}_{O_2}$ in relation to external work load is similar in athletes and nonathletes both in the untrained and in the trained states.[4] In the untrained state the two groups were similar also in respect to heart rate in relation to external work load, but the athletes had a lower ventilation and higher cardiac output (Fig. 2 and Table 2). However, these differences were not significant (P 0.4–0.3). In the trained state, $\dot{Q}_c$, heart rate, and ventilation were lower in the athletes, but again none of these differences was significant at the 5% level. Ventilation in the nonathletes after training was comparable to that in athletes before training.

TABLE 1. *Physical characteristics of subjects: mean values*

	Age, yr	Height, cm	Weight, kg
Athletes	21 (19–23)	178 (175–180)	74.0 (71–79)
Nonathletes	18 (17–19)	179 (178–180)	67.9 (63.5–75.5)

Range in parentheses.

DISCUSSION

Potential method errors. Before consideration of these results it is important to exclude sources of method error which might have accounted for our findings. The measurement of pulmonary blood flow by indirect Fick methods is subject to error from two sources in particular: overestimation occurring from incomplete replacement of alveolar gas by the test gas before measurement of gas uptake ($\dot{V}_{N_2O}$), and underestimation due to recirculation of test gas while $\dot{V}_{N_2O}$ is being measured. An important

[4] The absolute values for $\dot{V}_{O_2}$ in relation to external work load are somewhat higher than those reported by others (7) and probably are the consequence of calibration differences in the bicycle. However, since the same bicycle was used for the pre- and post-training measurements there is no reason why our conclusions about the effects of training should not be valid.

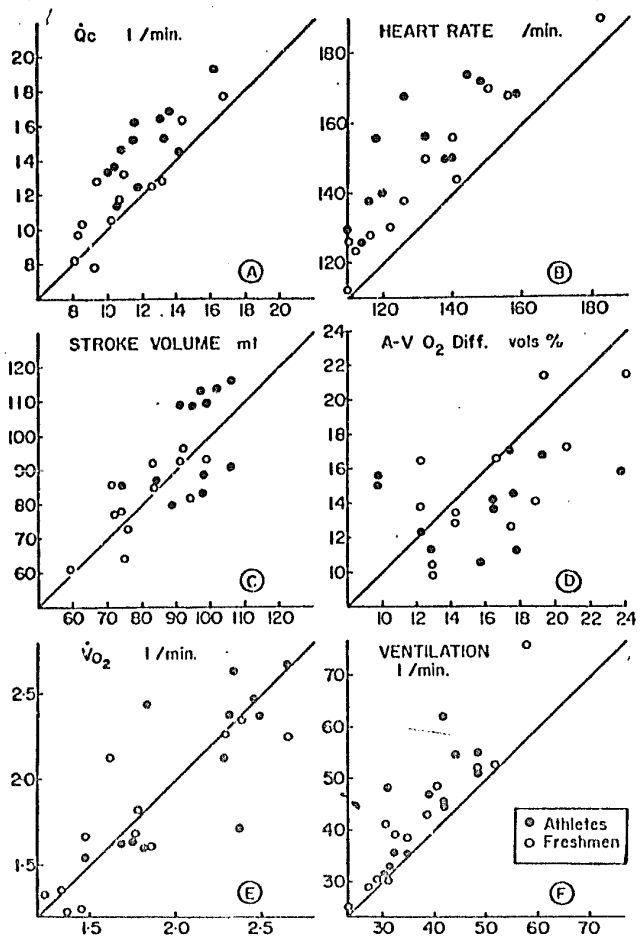


FIG. 1. Comparison of values for *A*: $\dot{Q}c$; *B*: heart rate; *C*: stroke volume; *D*: (A-V)O_2 difference; *E*: $\dot{V}O_2$; and *F*: ventilation, after training (on the *x* axis) and before training (*y* axis). The 45° line indicates identity. Results are those of four athletes (filled circles) and four nonathletes (open circles), each studied at three exercise loads.

advantage of the present method is that the first of these errors can be assessed from the fall in $F_{E_{N_2}}$ and the second from the rise in $F_{A_{N_2O}}$ during the time period of $\dot{V}_{N_2O}$ measurement (5). From the data shown in Table 3 it may be concluded that the consistent finding of a lower $\dot{Q}_c$ after training could not be attributed either to slower alveolar washout in the pretraining studies or to faster "recirculation" after training.

Another possible source of error is the use of a predicted value of V_D to compute $F_{A_{N_2O}}$; however, by analogy to West's conclusions concerning D_{LCO} similarly calculated, the computed $\dot{Q}c$ is relatively insensitive to the value of V_D used (28). In the present study there can be little doubt that the assumed value for V_D was too high (and consequently the absolute value of $\dot{Q}c$ too low) in certain experiments in which high values were obtained for the computed (A-V)O_2 differences (Table 2 and Fig. 1). However, there is no reason to doubt the validity of the change in $\dot{Q}c$ in any individual before and after training.

Comparison with data published previously. The present study shows that athletic training had no influence on the mechanical efficiency of cycling in either group. Apart from studies in which the form of training has been identical or similar to the test exercise performed (8, 15, 23), this finding is consistent with other reports (3). Likewise, the reduction in minute ventilation and heart rate is in agreement with previous observations (3). The latter finding can be taken also as evidence that the subjects were relatively out of training when first studied.

Our findings differ from many published previously (1, 3, 8, 13, 20) in that we observed a fall in $\dot{Q}c$ for a given work load (or $\dot{V}O_2$) after training, with consequent greater posttraining values for the computed (A-V)O_2 difference ($\dot{V}O_2/\dot{Q}c$). It should be noted that in most previous studies the experimental design involved comparison of groups of subjects (athletes and nonathletes), and often the number of subjects was small. In the earlier studies (1, 8, 16), differences in athletic training were thought to account for intersubject variation, because at the time there were relatively few reported measurements of exercise cardiac output and the range of variation in normal subjects (5) was not appreciated. In more recent studies involving larger numbers of subjects (6, 7, 20) it is possible that intersubject variation may have obscured small differences between group mean values. Another decisive factor in comparative studies is the selection of nonathletic controls. On the basis of a slower exercise heart rate in relation to O_2 consumption, we suggested previously that the general level of physical activity in the control group of Swedes studied by Bevegård and associates (6, 7) may have been higher than in a North American control group studied by ourselves (4). This may account for their finding comparable values for exercise $\dot{Q}c$ in athletes and nonathletes. Alternatively, it is possible also that the cardiorespiratory adjustment of those trained in endurance sports—such as the cyclists studied by Bevegård and associates—may differ from that of ice-hockey players, who are required to reach what must be nearly maximal performance rapidly but for shorter periods.

Only two other reports were traced in which the experimental plan was directly comparable to our own, i.e., the subject acted as his own control (13, 26). In the more recent of these (26), a study of nine cross-country runners before and after 3 months' training, the results were in agreement with our own, and showed a fall in $\dot{Q}c$ for a given $\dot{V}O_2$. In the other (13), two cross-country runners were studied supine by the direct Fick method before and after training; one showed a small fall in $\dot{Q}_c$ for a given $\dot{V}O_2$ and one a small rise. In both, however, the relationship of $\dot{Q}_c$ to $\dot{V}O_2$ was well within the reported normal range on both occasions. There are three reasons that may explain why these two men did not show the consistent trends demonstrated in our subjects. First, the runners were trained for an upright task, but they were studied while supine, when cardiovascular adaptation is known to be different (6, 17). Second, a training effect may have persisted despite the 3-month detraining period

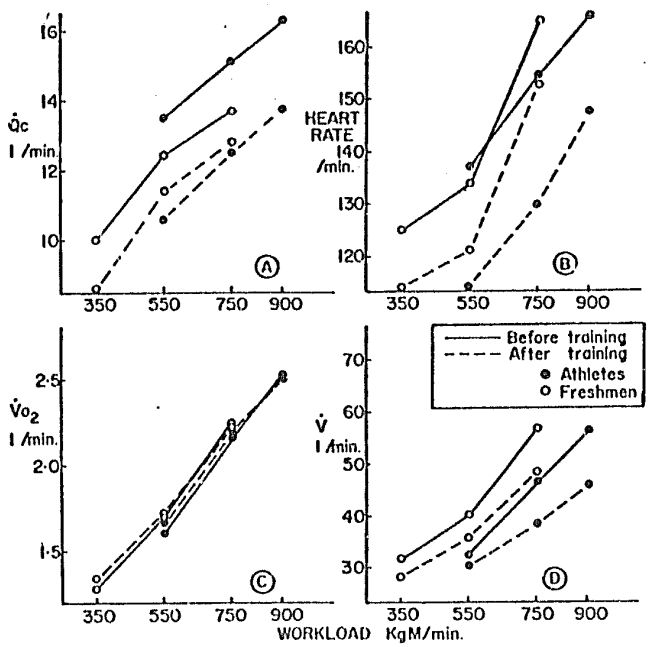


FIG. 2. Mean values for *A*: $\dot{Q}c$; *B:* heart rate; *C:* $\dot{V}O_2$; and *D:* $\dot{V}$, in athletes (filled circles) and nonathletes (open circles), plotted against external exercise load as the independent variable on the *x* axis.

did not affect O_2 uptake, it seems more likely that the fall in cardiac output occurs in areas such as skin, in which blood flow is regulated by factors other than O_2 requirements. Indeed, a reduction in skin blood flow might enable body-core temperature to rise more quickly on exercise, thereby increasing the diffusion rates of gases and metabolites in body tissues (10). If this were so, the athlete could reach more quickly the metabolic level required by the exercise, an advantage for such games as ice hockey though perhaps not for endurance sports.

Differences between the athlete and the nonathlete. As pointed out previously, this study was designed to examine the cardiorespiratory effects of athletic training rather than

TABLE 3. *Mean rise in* $F_{A_{N_2O}}$* *and mean fall in* $F_{E_{N_2}}$† *during measurement of* $\dot{Q}c$,‡ *before and after training*

	Athletes				Nonathletes			
	Rise in $F_{A_{N_2O}}$, mm		Fall in $F_{E_{N_2}}$, mm		Rise in $F_{A_{N_2O}}$, mm		Fall in $F_{E_{N_2}}$, mm	
	Before	After	Before	After	Before	After	Before	After
Mean	1.71	1.33	0.79	0.38	1.32	0.82	0.59	0.55
±SD	1.1	1.3	0.7	0.4	1.1	1.7	0.2	0.1

No value differed significantly from any other value in this table. *$F_{A_{N_2O}}$—reflecting recirculation. †$F_{E_{N_2}}$—reflecting lung-gas replacement. ‡1 mm on N_2O meter equivalent to 0.08% N_2O; 1 mm on N_2 meter equivalent to 1% N_2.

the differences between athletes and nonathletes in respect to exercise adaptation. Nevertheless, it is of interest to compare the two groups we studied both in the untrained and in the trained state. Definite differences in the untrained state in respect to ventilation, respiratory frequency, and stroke volume were noted and were still apparent after training. By contrast, the lower values for $\dot{Q}c$ and heart rate characterizing the athletes became apparent only after training. This suggests that the athlete may be better endowed in terms of his ventilatory ability but that rigorous training is necessary to develop circulatory advantages. Alternatively, if ventilatory training persists longer than circulatory training, differences in the untrained state might be attributable to the athlete's previous training, despite the lapse of some time.

Finally, it is of interest to note that, had the present experimental design been a comparison of group mean values (untrained nonathletes with trained athletes), the only significant difference between groups would have been in respect to heart rate at equivalent work loads. This emphasizes the fact that the effects of training can be studied only by consecutive measurement, each subject acting as his own control.

REFERENCES

1. ASMUSSEN, E., AND M. NIELSEN. Cardiac output during muscular work and its regulation. *Physiol. Rev.* 35: 778–800, 1955.
2. ASMUSSEN, E., AND M. NIELSEN. Physiological dead space and alveolar gas pressures at rest and during muscular exercise. *Acta Physiol. Scand.* 38: 1–21, 1956.
3. ÅSTRAND, P. O. Human physical fitness with special reference to sex and age. *Physiol. Rev.* 36: 307–335, 1956.
4. BECKLAKE, M. R., H. FRANK, G. R. DAGENAIS, G. L. OSTIGUY, AND C. A. GUZMAN. Influence of age and sex on exercise cardiac output. *J. Appl. Physiol.* 20: 938–947, 1965.
5. BECKLAKE, M. R., C. J. VARVIS, L. D. PENGELLY, S. KENNING, M. MCGREGOR, AND D. V. BATES. Measurement of pulmonary blood flow during exercise using nitrous oxide. *J. Appl. Physiol.* 17: 579–586, 1962.
6. BEVEGÅRD, S., A. HOLMGREN, AND B. JONSSON. The effect of body position on the circulation at rest and during exercise, with special reference to the influence on the stroke volume. *Acta Physiol. Scand.* 49: 279–298, 1960.
7. BEVEGÅRD, S., A. HOLMGREN, AND B. JONSSON. Circulatory studies in well-trained athletes at rest and during heavy exercise, with special reference to stroke volume and the influence of body position. *Acta Physiol. Scand.* 57: 26–50, 1963.
8. BOCK, A. V., C. VANCAULAERT, D. B. DILL, A. FÖLLING, AND L. M. HURXTHAL. Studies in muscular activity. III. Dynamical changes occurring in man at work. *J. Physiol., London* 66: 136–161, 1928.
9. BROUHA, L. Training. In: *Science and Medicine of Exercise and Sports*, edited by W. R. Johnson. New York: Harper, 1960, Chapt. 21, pp. 403–416.
10. BUSKIRK, E. R., AND D. E. BASS. Climate and exercise. In: *Science and Medicine of Exercise and Sports*, edited by W. R. Johnson. New York: Harper, 1960, Chapt. 17, pp. 311–338.
11. COTES, J. E., AND F. MEADE. Physical training in relation to the energy expenditure of walking and to factors controlling respiration during exercise. *Ergonomics* 2: 195–206, 1959.
12. ELSNER, R. W., AND L. D. CARLSON. Postexercise hyperemia in trained and untrained subjects. *J. Appl. Physiol.* 17: 436–440, 1962.
13. FREEDMAN, M. E., G. L. SNIDER, P. BROSTOFF, S. KIMELBLOT, AND L. N. KATZ. Effects of training on response of cardiac output to muscular exercise in athletes. *J. Appl. Physiol.* 8: 37–47, 1955.
14. HOLMGREN, A., F. MOSSFELDT, T. SJÖSTRAND, AND G. STROM. Effect of training on work capacity, total hemoglobin, blood

volume, heart volume and pulse rate in recumbent and up, right positions. *Acta Physiol. Scand.* 50: 72–83, 1960.
15. KNEHR, C. A., D. B. DILL, AND W. NEUFELD. Training and its effects on man at rest and at work. *Am. J. Physiol.* 136: 148–156, 1942.
16. LINDHARD, J. Über das Minutenvolum des Herzens bei Ruhe und bei Muskelarbeit. *Arch. Ges. Physiol.* 161: 233–383, 1915.
17. MCGREGOR, M., W. ADAM, AND P. SEKELJ. Influence of posture on cardiac output and minute ventilation during exercise. *Circulation Res.* 9: 1089–1092, 1961.
18. MILIC-EMILI, G., J. M. PETIT, AND R. DEROANNE. Mechanical work of breathing during exercise in trained and untrained subjects. *J. Appl. Physiol.* 17: 43–46, 1962.
19. MOSTYN, E. M., S. HELLE, J. B. L. GEE, L. BENTIVOGLIO, AND D. V. BATES. Pulmonary diffusing capacity of athletes. *J. Appl. Physiol.* 18: 687–695, 1963.
20. MUSSHOFF, K., H. REINDELL, AND H. KLEPZIG. Stroke volume-arterio-venous difference, cardiac output and physical working capacity, and their relationship to heart volume. *Acta Cardiol.* 14: 427–452, 1959.
21. NEWMAN, F., B. F. SMALLEY, AND M. L. THOMSON. Effect of exercise, body and lung size on CO diffusion in athletes and nonathletes. *J. Appl. Physiol.* 17: 649–655, 1962.
22. PENGELLY, L. D. Cardiac dye injector synchronizer. *IRE Trans. Bio-Med. Electron.* 8: 113–116, 1961.
23. ROBINSON, S., AND P. M. HARMON. The effects of training and of gelatin upon certain factors which limit muscular work. *Am. J. Physiol.* 133: 161–169, 1941.
24. SCHNEIDER, E. C., AND C. B. CRAMPTON. A comparison of some respiratory and circulatory reactions of athletes and non-athletes. *Am. J. Physiol.* 129: 165–170, 1940.
25. SLOAN, A. W. Effect of training on physical fitness of women students. *J. Appl. Physiol.* 16: 167–169, 1961.
26. TABAKIN, B. S., J. S. HANSON, AND A. M. LEVY. Effects of physical training on the cardiovascular and respiratory response to graded upright exercise in distance runners. *Brit. Heart J.* 27: 205–210, 1965.
27. WADE, O. L., AND J. M. BISHOP. *Cardiac Output and Regional Bloodflow.* Oxford, England: Blackwell, 1962, p. 107.
28. WEST, J. B. Diffusing capacity of the lung for carbon monoxide at high altitude. *J. Appl. Physiol.* 17: 421–426, 1962.