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BLOOD LIPIDS AND PEAK OXYGEN CONSUMPTION IN YOUNG DISTANCE RUNNERS

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BLOOD LIPIDS AND PEAK OXYGEN CONSUMPTION IN YOUNG DISTANCE RUNNERS

By

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ABSTRACT

BLOOD LIPIDS AND PEAK OXYGEN CONSUMPTION IN YOUNG DISTANCE RUNNERS

By

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This dissertation includes a series of papers on blood lipids and peak Vo_2 in young male and female distance runners, 9 to 19 yrs of age. Two independent samples - a mixed-longitudinal cohort of 27 males and 27 females (Young Runners Study I [YRS I]), and a cross-sectional cohort of 48 males and 22 females (Young Runners Study II [YRS II]) - were used in the analysis.

The development of blood lipids in young distance runners appears to be similar to the general population - total cholesterol (TC) and low-density lipoprotein (LDL) remain stable, high-density lipoprotein (HDL) declines during adolescence (especially in males), and triglycerides (TG) increases with age. The lack of the attenuation in HDL may lend to the robustness of normal growth and maturation, including genes, hormones, and fat distribution, on the development of HDL in males regardless of exercise training. A superior blood lipid profile was not observed in young distance runners compared to age- and sex-specific reference values for United States youth, except for higher HDL prior to age14 yrs. In contrast to mean values, there was considerable variability in blood lipids including dyslipidemic values.

Heterogeneity in blood lipids among young distance runners was also considered. Determinants included training volume (TV, km per wk), peak oxygen consumption (peak Vo_2, $ml \cdot kg^{-1} min^{-1}$), and body fatness (sum of six skinfolds, SSF; trunk-to-extremity

ratio, TER). Increased weekly running distance was not related to blood lipids in young distance runners. However, TV may be indirectly related with HDL through its relationship with peak Vo_2 in males. A unique finding was the differential relationships between TV and HDL when the entire sample was grouped according to modified clinical cut-points. Partial correlations indicate that the association between peak Vo_2 and HDL remained significant after controlling for the concomitant variation in SSF and explained 9% of the variance in HDL. The association between SSF and HDL did not remain significant after controlling for the concomitant variation in peak Vo_2. The role of genes, peak Vo_2, and body fatness in the modulation of elevated blood lipid levels has also been indicated.

As expected, an age-related increase in absolute peak Vo_2 occurred in both sexes with sex differences emerging during adolescence. When expressed per unit body mass, peak Vo_2 ($ml \cdot kg^{-1} min^{-1}$) remains stable until age 15 when it increases in boys, and decreases in girls. In contrast, relative peak Vo_2 ($ml \cdot kg^{-0.75} min^{-1}$) increases throughout the age range in boys and increases in girls until age15 yrs, and peak Vo_2 adjusted for body mass ($ml \cdot min^{-1}$) increases with age in boys and girls. Allometric scaling factors varied by analytical methods. The overall mean cross-sectional scaling factor was 1.01 ± 0.03 (SE) in boys and 0.85 ± 0.05 (SE) in girls. Mean ontogenetic allometric scaling factors were 0.81 and 0.61 in males and females, respectively. Thus, it was concluded that the interpretation of growth-related changes in peak Vo_2 of young distance runners was dependent upon the manner of expressing peak Vo_2 relative to body size and/or the statistical technique employed.

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CHAPTER 1

INTRODUCTION

It is a basic assumption that physical activity has an essential influence on biological growth and maturation (Malina, 1969; Rarick, 1960), although the specific amount of physical activity that is needed has not been established. Physical activity occurs across a broad spectrum, from very light activities to intensive training for sport. Both extremes of the spectrum have received attention due to the potential influences of physical activity on biological and psychological processes, and the health of the human organism. Possible negative consequences of intensive training during childhood and adolescence are often a concern among physicians, coaches, and parents. The potential physiological benefits of intensive training during growth and maturation have received corresponding attention by the scientific community.

This dissertation considers the influence of biological growth, maturation, and intensive endurance exercise training on blood lipids and peak oxygen consumption (peak Vo_2) and contributes to the disciplines of human growth, cardiovascular disease epidemiology, and pediatric exercise physiology. The timing of this work is relevant to the progress of pediatric exercise science given current emphasis on the health outcomes of exercise in children related to the prevention of chronic disease, and the expression of physiological variables relative to variation in body size of growing children and adolescents.

This dissertation is divided into two parts, each consisting of a literature review and a series of papers that adds to our understanding of the child and adolescent athlete. Each paper is in manuscript form (i.e., abstract, introduction, methods, results, and discussion). Some aspects of each paper, particularly the methods sections, are repetitive,

but lend to the readability of the paper. The final chapter provides a summary and recommendations for future research.

Part I focuses on blood lipids of competitive young distance runners and encompasses Chapters 2 through 5. Chapter 2 introduces the reader to the importance of the study of physical activity and blood lipids during childhood and adolescence, and reviews several aspects of the topic including: blood lipids and coronary heart disease, evidence for the early origins of atherosclerosis, the development of blood lipids in the general pediatric population and in young athletes, and the relationship between physical activity and blood lipids in youth. Chapters 3 and 4 describe age-associated variation and distribution of blood lipids in young distance runners compared to the general population. Chapter 5 examines the heterogeneity of blood lipid phenotypes in young distance runners by considering the influence of training volume, peak Vo_2, and body fatness.

Part II focuses on growth-related changes in peak Vo_2 of competitive young distance runners and encompasses Chapters 6 and 7. Chapter 6 provides an introduction to the problem of interpreting growth-related changes in peak Vo_2 and reviews age-, sex-, and maturity-associated variation in peak Vo_2 in the general population of youth and in youth athletes, and the concept of allometric scaling. Chapter 7 compares the use of traditional and allometric scaling techniques in the interpretation of growth-related changes in peak Vo_2 of young distance runners.

Two independent samples of young distance runners from the mid-Michigan area are included in the analysis. An earlier mixed-longitudinal study of 27 male and 27 female distance runners (Young Runners Study, YRS I) aged 8-18 years was used to examine the age-related changes in blood lipids and peak Vo_2 across the adolescent age

range. The study was conducted by the Institute for the Study of Youth Sports at Michigan State University as part of an interdisciplinary investigation of the influence of intensive endurance training and competition on biological and psychological outcomes from 1982 and 1986 (Seefeldt, 1986). During the 1999-2000 academic year, a cross-sectional study was conducted to examine the dose-response relationship between training volume (i.e., running mileage) and blood lipids in young distance runners (Young Runners Study II, YRS II). Body size and peak Vo_2 were also measured in this study.

REFERENCES

Malina RM (1969) Exercise as an influence upon growth. Clin Pediar 8:16-26.

Rarick GL (1960) Exercise and growth. In WR Johnson (ed.): Science and Medicine of Exercise and Sport. New York: Harper and Brothers, pp. 440-465.

Seefeldt VD (1986) Elite young runners: an interdisciplinary perspective. In M Weiss and D Gould (eds.): Sport for Children and Youths. Champaign, IL: Human Kinetics, pp. 213-284.

CHAPTER 2

REVIEW OF LITERATURE

PART I

INTRODUCTION

There is a considerable current interest in the physical activity and health-related physical fitness of youth (Malina, 1997), particularly related to risk factors for coronary heart disease (CHD) (Casperson et al., 1998; Despres et al., 1990a). Although the clinical manifestations of atherosclerosis are not evident until adulthood, childhood precursors of the disease are clearly evident (Berenson et al., 1998; Mahoney et al., 1996). As a result, preventive strategies for CHD during childhood and adolescence have been recommended.

A unique approach to understanding the association between a causal factor (i.e., physical activity) and a health outcome (i.e., blood lipids) is the study of a special exposure cohort (Rothman and Greenland, 1998). Although this approach is limited due to selection bias, special exposure cohorts permit the study of a range of exposures and outcomes that may not be common in the general population, thus providing a comprehensive model of the health effects of a given exposure.

Since regular physical activity, a relatively high aerobic fitness level, and a low amount of adiposity have beneficial effects on CHD risk factors, morbidity, and mortality in adults (Blair et al., 1989; Paffenbarger and Lee, 1996), many investigators have been interested in the blood lipid profile of well-trained endurance athletes (Haskell, 1984). In general, adult endurance-trained athletes have superior blood lipid profiles compared to the general population (Haskell, 1984). However, limited information is available on the blood lipid profile of young athletes.

The purpose of this review is to examine the early origins of atherosclerosis, the development of plasma triglycerides and lipoproteins, and the associations between physical activity, aerobic fitness, body fatness and blood lipids with special reference to the child and adolescent athlete.

BLOOD LIPIDS AND CORONARY HEART DISEASE

Atherosclerosis is generally described as a slowly progressing disease in which there are focal lesions in the large arteries that rarely produces symptoms until middle age and that often go undiagnosed until the time of the first myocardial infarction (Woolf, 1999). Several risk factors or biomarkers have been identified for CHD (Hopkins and Williams, 1981). Since Part I of this dissertation focuses on the blood lipids of young distance runners, lipoprotein metabolism, the etiology of blood lipids in atherosclerosis, and the causal relationship between blood lipids and CHD will be briefly considered here. For a complete discussion of lipoproteins in health and disease, the reader is referred elsewhere (Betteridge et al., 1999).

Lipoprotein metabolism is a dynamic and complex system designed to transport lipids between the intestine, liver, and peripheral tissues via the plasma and interstitial fluid. In the blood circulation, blood lipids and lipoproteins undergo a complex series of modifications that alter their structure, composition, and function. After binding to a receptor, lipoproteins are internalized by cells and used for energy production or storage, membrane biogenesis, or sex steroid synthesis. Given the dynamic nature of this system, a single cholesterol or triglyceride measurement is at best a snap shot of a moving picture.

Cholesterol is carried in the bloodstream by protein-lipid combinations known as lipoproteins. Four basic classes of lipoproteins have been categorized according to their gravitational density: chylomicrons, very-low density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Other lipoprotein subfractions include intermediate-density lipoprotein (IDL) and lipoprotein (a) [Lp (a)]. Most (60-75%) of the cholesterol in humans is carried by LDL. The cholesterol-rich LDL particles infiltrate the arterial intima and form a major part of the buildup in the artery wall to form atherosclerotic plaque. In contrast, HDL carries cholesterol away from the arterial wall to the liver for catabolism and excretion, thus providing a protective effect against atherosclerosis. Any disruption of the delivery of cholesterol to peripheral tissues (referred to as the LDL receptor pathway or the lipolytic cascade) and/or the return of cholesterol to the liver (referred to as reverse cholesterol transport or the HDL cascade) can cause changes in the plasma lipoprotein profile and result in CHD.

In 1984, the National Heart, Lung, and Blood Institute (NHLBI) and the National Institutes of Health Office of Medical Applications of Research conducted a Consensus Development Conference on Lowering Blood Cholesterol to Prevent Heart Disease to address the causal relationship between blood cholesterol levels and CHD (NIH Consensus Statement, 1985). Based on the genetic, experimental, and epidemiological data, the panel of experts concluded as follows:

"Elevation of blood cholesterol levels is a major cause of coronary artery disease. It has been established beyond a reasonable doubt that lowering definitely elevated blood cholesterol levels (specifically, blood levels of low-density lipoprotein cholesterol) will reduce the risk of heart attacks caused by coronary heart disease (p. 2080)."

In a more recent consensus, the importance of HDL and triglycerides (TG) in the pathogenesis of atherosclerosis was explored (NIH Consensus Development Panel on

Triglyceride, 1993). The panel confirmed findings of four major studies that a 1 mg/dl increase in HDL results in a 2 to 3% decrease in CHD risk after adjustment for other risk factors. However, the independent contribution of TG on CHD risk remains inconclusive.

EARLY ORIGINS OF ATHEROSCLEROSIS

Even though the clinical manifestations of CHD occur in adulthood, various studies have shown that atherosclerosis has its origins early in life (Berenson et al., 1998; Enos et al., 1955; Mahoney et al., 1996; McNamara et al., 1971; Strong et al., 1997). This rationale stems from autopsy reports of coronary atherosclerotic lesions in youth, the prevalence of CHD risk factors in youth, the tracking of CHD risk factors from childhood to adolescence to young adulthood, and the predictability of adult heart disease from childhood and adolescent CHD risk factors.

Early autopsy studies of soldiers. Fatty streak and plaque formation of the coronary arteries and aorta has been documented by autopsy studies of American soldiers from the Korean and Vietnam Wars. The first report indicated that 232 of 300 (77.3%) young (mean age, 22.1 yrs) American soldiers of the Korean War demonstrated some gross evidence of CHD (Enos et al., 1955). In a study of U.S. soldiers (mean age, 22.1 yrs, range 18-37 yrs) of the Vietnam War, 79 of 105 (75.2%) cases demonstrated some gross evidence of CHD (McNamara et al., 1971). In a more detailed analysis, 47 (44.8%) exhibited some degree of atherosclerosis, 27 (25.7%) had involvement of two or more vessels, and 5 (4.8%) had severe evidence of atherosclerosis.

The Bogolusa and Muscatine Studies. In the 1970s, two major epidemiological studies, the Bogolusa Heart Study and the Muscatine Study, began to investigate the development of CHD risk factors in children and adolescents. The Bogolusa Heart Study initially began during the 1973-74 school year in Washington Parish, Louisiana, a political ward consisting of a bi-racial population of approximately 22,000 (63% White, 37% Black). The center was designated as a Specialized Center of Research for Atherosclerosis by the National Heart, Lung, and Blood Institute. Since the initial cross-sectional survey, several follow-up surveys have been conducted (1976-77, 1978-79, 1981-82, 1984-85, 1987-1988, 1993-94).

The Muscatine Study began during the 1971-72 and 1972-73 academic years and thereafter included biennial surveys in school-aged children and adolescents and a follow-up survey between the ages of 20 and 34 yrs (Muscatine Young Adult Follow-Up Survey). The initial study population included school children of Muscatine, Iowa. Like the Bogolusa site, Muscatine was chosen due to the relative stability of the population and its proximity to the medical examining team (University of Iowa, Iowa City). In contrast to the Bogolusa Heart Study, the sample in the Muscatine Study consisted of a majority of Caucasians (about 96%).

The first published reports from both studies consisted of the descriptive epidemiology of CHD risk factors in preschool children, school-aged children and adolescents (Berenson et al., 1978; Frerichs et al., 1976; Lauer et al., 1975; Srinivasan et al., 1976). The age-, sex-, and race-associated variation for lipids will not be described here but rather as part of the section of the review on the development of blood lipids (see below). During subsequent follow-up studies, the tracking of CHD risk factors has been

determined over various time periods (i.e., 3-8 yr intervals) (Bao et al., 1994; Bao et al., 1995b; Clarke et al., 1978; Shear et al., 1986). Along with the critical issue of the persistence of CHD risk factors and the predictability of adult CHD, another major component in establishing evidence in the early origins of atherosclerosis has been to determine the inter-relationships of CHD risk factors, environmental factors, and family history. An important finding from such analyses has been that CHD risk factors cluster in obese children and adolescents (Smoak et al., 1987). Furthermore, 61% of those subjects in the upper quartile of multiple risk factors during childhood remained in the upper quartile as young adulthood (Bao et al., 1994).

Familial studies have indicated that adverse CHD risk factors are more common in offspring of parents and relatives with hypertension, diabetes, obesity, hyperlipidemia, and history of myocardial infarction (Bao et al., 1997; Bao et al., 1995a; Muhonen et al., 1994). Besides the associations between familial history of CHD and CHD risk factors in offspring, genetic studies have also been conducted to determine candidate genes for CHD risk factors in these two studies (Amos et al., 1989; Anderson et al., 1989; Bucher et al., 1982; Srinivasan et al., 1996).

Recent autopsy reports from the Bogolusa Heart Study have furthered understanding of the relationship between antemortem childhood CHD risk factors and the extent of fatty streaks and fibrous plaques in the aorta and coronary arteries (Berenson et al., 1998). In 204 autopsy cases, 2-39 yrs of age, 93 cases had data on antemortem risk factors. Results indicate that the body mass index (BMI), blood pressure (BP), TC, TG, LDL, and HDL, as a group, are strongly associated with the extent of lesions (canonical correlation, r=0.70). The effect of multiple risk factors, or clustering, on the percent of

intimal surface covered with fatty streaks indicate that risk factors during childhood or adolescence are strongly related to the extent of lesions in the aorta and coronary arteries of young adults, and that as the number of risk factors increases so does the severity of asymptomatic coronary and aortic atherosclerosis in young people.

Using a noninvasive method known as computerized beam tomography to detect the presence of atherosclerotic plaque in asymptomatic subjects with CHD, The Muscatine Study has also shown the relationship between childhood CHD risk factors and coronary calcification in young adulthood (29 to 37 yrs, mean age = 33 yrs) (Mahoney et al., 1996). Results indicate that 31% of men and 10% of women have coronary artery calcification. Although CHD risk factors measured during the previous and most recent visits showed the strongest associations with coronary artery calcification, childhood (8-18 yrs, mean age=15 yrs) body weight was a significant predictor of adult coronary artery calcification [Odds ratio (OR) = 3.0]. SBP, DBP, TC, and TG measured during childhood were not significantly different ($p>0.05$) between young adults showing the presence and absence of coronary artery calcification. Body weight, the BMI and triceps skinfold thickness were larger ($p<0.01$) in males, but not females, during childhood among those who displayed coronary calcification. Unfortunately, HDL, LDL, and apolipoprotein levels were not screened during childhood in this sample.

The Bogolusa Heart Study and the Muscatine Study have provided valuable information regarding the development and persistence of CHD risk factors from childhood through adolescence into young adulthood. As these studies continue, they

will provide additional information on the long-term persistence of CHD risk factors into mid- and late-adulthood.

Pathobiological Determinants of Atherosclerosis in Youth (PDAY). In 1984, a multi-institutional (9 centers) study was organized to document the pathobiology of lesion development and its association with postmortem CHD risk factors in 15 to 34 yr olds who died from external causes (i.e., homicide, accident, or suicide) (Strong et al., 1998). Between June 1, 1987, and August 31, 1994, arteries and other tissues from about 3000 autopsy cases were examined for lesions and surrogates or markers for preexisting risk factors. Post-mortem risk factors included serum lipoprotein cholesterol, serum thiocyanate (smoking), wall thickness of the small renal arteries (BP), glycohemoglobin (impaired glucose tolerance and diabetes), the BMI, panniculus thickness (adiposity), adipose tissue fatty acids (diet), and apolipoprotein polymorphisms. The degree of atherosclerosis was measured as follows: collagen and cholesterol content in lesion-prone and lesion-resistant areas of the aorta; macrophage, smooth muscle cell, T-lymphocytes, and mast cell counts in various lesion types; and apolipoprotein B, Lp (a) and oxidized LDL in the arterial wall measured chemically and morphometrically by pathologists and by computer image analysis. Results indicate that fatty streaks covering 15-25% of the intimal surface are well established by age 15-19 yrs and progress until 30-34 yrs of age. Among the postmortem risk factors, VLDL, LDL, glycohemoglobin, and thiocyanate are positively, and HDL negatively related to fatty streak involvement. The prevalence of raised lesions (5% or greater of intimal surface) 2-fold greater in hypertensive (classified by renal index) men 15-24 yrs of age. The BMI was associated with more extensive fatty streaks and raised lesions in right coronary artery but not in the aortas of men. No

association between the BMI and lesions were found in women. Thickness of panniculus adiposus was associated with more extensive lesions in the right coronary artery in both men and women.

Summary. Historically, insight into the early origins of atherosclerosis were gained from autopsy studies of children and American soldiers. Since the early autopsy studies, three studies - Bogolusa, Muscatine, and PDAY - have provided greater insights into the development of CHD risk factors, the natural history of CHD, and the association of risk factors with the development of CHD. The findings indicate that atherosclerosis is a progressive disease that has its origins in childhood and adolescence, and highlight the importance of the prevention of adult CHD during childhood and adolescence.

DEVELOPMENT OF BLOOD LIPIDS IN THE GENERAL PEDIATRIC POPULATION

With the realization of the early origins of atherosclerosis, pediatricians and other health professionals recognized the need to begin examining the CHD risk factors of children and adolescents as a means of establishing primary prevention. Besides the Bogolusa Heart Study and the Muscatine Study, the major population study of blood lipid distributions in U.S. children and adolescents is the Lipid Research Clinics Prevalence Study (The Lipid Research Clinics, 1980). This study was initiated in 1971 and included 13, 665 children and adolescents 6 to 18 yrs old. Data from this large population study has been used to establish reference values for clinical medicine and the descriptive epidemiology of blood lipid distributions in children and adolescents. The Third National Health and Nutrition Examination Survey (NHANES III) conducted between

1988 and 1994 provides current data on the blood lipid distributions of U.S. children and adolescents (Hickman et al., 1998). Age-, sex-, maturity-, race-, and time-associated variation in blood lipid distributions in children and adolescents are subsequently described.

Age-associated variation. Age-associated variation in TC, HDL, LDL, and TG during childhood and adolescence are shown in Figures 2.1 and 2.2. Following the first year of life, median values for TC, HDL, and LDL are somewhat stable throughout the first two decades of life, whereas TG increase throughout this period. The pattern of development for TC and LDL shows relatively stable levels until adolescence (about 160-165 mg/dl and 90 mg/dl, respectively), a decline during adolescence, and an increase in TC and LDL during late adolescence. The pattern of development for HDL shows relatively stable levels until adolescence (about 50 mg/dl) and a decline during adolescence (especially in males, see below), which remain at relatively stable levels into young adulthood. The decrease in TC is mainly due to the decrease in HDL as the decrease in LDL is modest. During late adolescence, the increase in TC is a result of the increase in LDL. Depending upon how the data are reported, the age-related trend for TG is quite variable. Some reports show a relatively stable level prior to adolescence with an increase during and following adolescence (Cresanta et al., 1984), whereas others indicate an increase from 6 to 19 yrs of age (Tamir et al., 1981). The discrepancy between studies appears to be due to the age groups of the subjects (i.e., 1 year vs. multiple year grouping).

Sex-associated variation. Sex differences in TC, HDL, LDL, and TG during childhood and adolescence are also shown in Figures 2.1 and 2.2. Results from

NHANES III indicate that females have slightly greater mean levels of TC (167 v. 163 mg/dl) and LDL (99 vs. 91 mg/dl) compared to males (Hickman et al., 1998). This observation is consistent across age and ethnic groups. Prior to adolescence, HDL is slightly greater in boys, but the sharp decline during puberty results in higher levels of HDL in girls that persists into adulthood. TG increases during this period with a marked sex difference. Boys exhibit an increase from about 50 mg/dl at age 6 to 90 mg/dl at age 18, while the increase in girls during this same age span is from 65 to 80 mg/dl (Tamir et al., 1981).

Maturity-associated variation. Biological maturation refers to the timing and tempo of progress toward a mature (adult) state (Malina and Bouchard, 1991). Biological maturation is associated with dynamic changes in body size and composition, sex hormones, and various physiological parameters. Therefore, it is important to consider biological maturation in pediatric studies, particularly during adolescence, as a distinct measure from chronological age.

Biological maturation can be assessed by skeletal, sexual, or somatic maturity characteristics. Typically, sexual maturation has been used in studies examining blood lipids during adolescence (Armstrong et al., 1992; Berenson et al., 1981; Morrison et al., 1979; Tell, 1985). The assessment of sexual maturation is based on the development of the secondary sex characteristics - breasts, gentitals, and pubic hair - in both sexes as described by Tanner (1962). When reviewing studies, it is important to consider the presentation of sexual maturity status. A specific stage should be characterized for each indicator (i.e., pubic hair stage 2), rather than an "average" stage or simply "Tanner stage 2".

As with many other biological variables, there are dynamic changes in blood lipids during pubescence before adult patterns are established. In general, the pattern of development of blood lipids during pubescence follows that for age-related changes - TC, HDL, and LDL decline and TG increases (Armstrong et al., 1992; Berenson et al., 1981; Morrison et al., 1979; Tell, 1985). However, blood lipids are more closely related to sexual maturity status than to chronological age (Tell, 1985), and greater changes are observed when plotted by maturity status than chronological age (Siervogel et al., 1989; Tell, 1985). Additionally, early maturers have lower HDL compared to late maturers when assessed by sexual maturity (Tell et al., 1985), but not by skeletal or somatic maturity (Siervogel et al., 1989).

Maturity-associated changes in blood lipids have led to investigations of the inter-relationship of pubertal changes in sex hormones, body size, and blood lipids. In the Princeton Maturation Study, estradiol, testesterone, the Quetelet index (BMI), and their interactions explained 47%, 76%, 87%, and 56% of the variance in HDL, LDL, LDL:HDL, and TG, respectively in 30 adolescent boys (Laskarzewski et al., 1983). Complex interactions between blood lipids and testosterone at varying levels of estradiol and the Quetelet index were also demonstrated. This study highlights the significant contributions and complex interactions of sex hormones and body size on blood lipids during adolescence in boys.

Race-associated variation. Given the bi-racial sample of the Bogolusa Heart Study, the first reports of racial differences in blood lipids were demonstrated in early publications from this study. In general, Black children have higher mean levels of TC and HDL, and lower TG than White children (Frerichs et al., 1976). Recent data from

NHANES III confirm these findings and also allow comparison to Mexican-American children (Hickman et al., 1998). Non-Hispanic Blacks had the highest mean TC and HDL, whereas values were similar between non-Hispanic Whites and Mexican Americans for TC. LDL in 12 to 19 yr olds indicated similar values between White and Black females and greater values in Black males. Similar values for TG were also observed between Mexican American and White adolescents of both sexes.

International comparisons of a given variable indicate the biological variability among diverse populations. Geographic variation is present among the available data representing world populations. Labarthe et al. (1994) concluded that there is no unique population, but rather a continuous distribution of values and no distinct outliers. Among world populations, African youth have the lowest TC values (about 130 mg/dl) and Finnish youth have the highest (about 195 mg/dl).

Secular trends in lipid distributions of children and adolescents. Based on the data from three national representative samples (NHES III, NHANES I, and NHANES III), there appears to be a downward trend in mean TC among sex- and race-groups 12 to 17 yrs (Hickman et al., 1998). Mean declines in TC among White males and females and Black males and females are 8, 7, 5, and 4 mg/dl, respectively. The mean decline in TC is 7 mg/dl when the total sample is considered. Secular changes in lipoprotein subfractions and TG were not considered. Compared to the LRC data, it appears that TG has increased and HDL has decreased in White males and females, while LDL has declined in White males and increased in White females. Cautioned is urged in the comparisons as age-group classifications vary between surveys.

Prevalence of hypercholesterolemia. The National Cholesterol Education Program (NCEP), Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents recommends that an acceptable TC value for youth 2-19 yr of age be <170mg/dl (4.4mmol/l), which corresponds with the 75th percentile of the US population and abnormally elevated levels be determined by a TC >200mg/dl (5.17mmol/l) which corresponds to the 95th percentile of the U.S. population (National Cholesterol Education Program, 1992). Recommended clinical cut-points for other lipoproteins are found in Table 2.1.

Despite a detailed account of the developmental pattern of blood lipid levels in youth, the prevalence of hypercholesterolemia in the pediatric population is often not reported. Results from 6500 White middle-class children (mean age, 6.4 yrs) seen at private pediatrician offices for well-child visits indicate that 19% had a TC exceeding 185 mg/dl and 8.5% had a TC exceeding 200 mg/dl (Garcia and Moodie, 1989). The estimation of the prevalence of hypercholesterolemia in this study may be questioned due to the representiveness of clinical samples.

BLOOD LIPIDS IN CHILD AND ADOLESCENT ATHLETES

Cross-sectional comparisons of individuals engaged in endurance training and the general population have been used to demonstrate differences between trained and untrained individuals and by inference the influence of physical activity or exercise training on the blood lipid profile. As previously mentioned, comparisons of athletes and controls introduce selection bias. However, establishing an understanding of the influence of intensive training on the blood lipid profile requires the recruitment of

individuals engaged in endurance training since the general population does not regularly engage in such energy expenditure or vigorous physical activity. Despite the possible genetic pre-disposition of the athletes, some of the variation in a biological variable can be explained by environmental factors and the genotype-environmental interaction in an athlete.

Compared to adult athletes, little attention has been given to the study of the blood lipid profile in child and adolescent athletes. The child and adolescent athlete is often ill-defined, so that the evaluation and comparability of studies can be difficult. Table 2.2 provides a summary of serum lipoproteins in seven studies of child and adolescent athletes. Based on these reports, Rowland (1993) concluded that prepubertal athletes possess a favorable lipoprotein profile. The appropriateness of this conclusion can be questioned given that the comparisons were made to control subjects. The blood lipid levels of the control subjects should have also been compared to reference values since the control subjects were a convenient sample rather than a random sample in most, if not all, instances. If the control values were different than the reference medians (i.e., TG lower, etc.) the interpretation of results from the individual studies and the general conclusions may be questioned.

Aside from selection bias, other limitations also exist in studies of blood lipids in young athletes. Sample sizes are generally small and even smaller when considered by specific age groups (i.e., 7.0-7.99). It is thus difficult to establish age-associated variation for blood lipids of young athletes across the pediatric age range. The normal pattern of development of blood lipids in this group remains to be established by a longitudinal study. Some studies also combine sexes, thus not allowing for the

consideration of sex-associated variation. Limited and inconsistent information on training history is generally provided. When training information beyond frequency (days per week, months per year, etc.) is provided, it is often reported as hours per week. Many activities may occur during exercise training such as warm-up, flexibility exercises, etc., which actually do not increase energy expenditure at levels near those obtained during vigorous exercise training. By observing activity patterns during practice and competition, it has been determined that about 40% of the total time spent during sport activities (basketball, soccer) was occupied by sitting and standing (Katzmarzyk and Malina, 1997). More than likely, the percentage of time spent in inactivity for distance running or swimming is minimal given the nature of the sports. Finally, as with cross-sectional studies in the general population, studies of young athletes have failed to consider other biological factors that influence blood lipids (i.e., biological maturity, fatness, diet, family history, etc.).

Since it is generally assumed that child and adolescent athletes have a superior lipid profile given their levels of habitual physical activity and intensive training, little information is available on the prevalence of hyperlipidemia in young athletes. Recent attention has been given to pre-participation screening examinations, including blood pressure and cholesterol, of young athletes due to sudden cardiac death among some young athletes (Gutgessel et al., 1997). In a 1988 survey of 777 student athletes (454 males, 323 females) 11 to 15 yrs, 15.4% and 13.6% of boys and girls, respectively, had TC levels above 185 mg/dl (>90th percentile of LRC) (Kyle et al., 1991). Mean TC in boys and girls were 155 and 158 mg/dl, respectively, and the range for the entire sample was 65 to 274 mg/dl. Of the 114 student athletes with an initial TC >185 mg/dl, 74

(response rate = 65%) were returned for a second cholesterol test. Total cholesterol remained above normal in 38 (51%) of those re-tested. Unfortunately, the sample was not stratified by sport and information on the training experience or other confounding variables (family history, sexual maturity status, etc.) were not considered. Thus, despite participation in youth sports, young athletes may display hypercholesterolemia. Future research should provide descriptive information and establish prevalence rates of dyslipidemia among youth athletic groups (i.e., endurance, strength/power) and in specific sports (cross-country, basketball, football, etc.).

PHYSICAL ACTIVITY AND BLOOD LIPIDS IN CHILDREN AND ADOLESCENTS

Current interest in the prevention of CHD and influence of exercise intervention on blood lipids in childhood and adolescence has gained attention among researchers in clinical pediatric cardiology, cardiovascular disease epidemiology and pediatric exercise science. The relationship between physical activity and blood lipids in children and adolescence has been reviewed extensively (Armstrong and Simons-, 1994; Casperson et al., 1998; Despres et al., 1990a; Tolfrey et al., 2000). Complete summary tables of cross-sectional, prospective cohort, and experimental studies conducted within various samples of children and adolescents are provided in these reviews. Only major large-population cross-sectional studies are reviewed here, along with a limited number of prospective and retrospective cohort and experimental studies available. No case-control studies have been apparently been reported in the literature.

Cross-sectional studies.

Young Hearts Study. The Young Hearts Study began in 1990 and is an ongoing study of CHD risk factors in youth from Northern Ireland (Boreham et al., 1997). The study population consisted of 1015 schoolchildren (251 12 yr old boys, 258 12 yr old girls, 252 15 yr old boys, 254 15 yr old girls) randomly selected from 16 schools. Physical activity was assessed by an interviewer-administered questionnaire and a physical activity score was computed. Sports participation was based on the number of sports or other physical activity sessions reported aside from school-related physical activity. Blood lipids were assayed according to World Health Organization (WHO) standards. Results of stepwise multiple linear regression controlling for dietary intake, cigarette smoking, social class, school type, sexual maturity, and body size indicated that physical activity was associated with TC:HDL in 15 yr old boys. In boys, a 20% difference in physical activity was associated with a 1.54 -fold increase in the probablilty of being in the high risk group for TC:HDL (>4.0). No significant relationships between physical activity, sports participation, and TC:HDL were found in girls.

Oslo Heart Study: In a sample of 431 boys and 397 girls 10-15 yrs from six Oslo schools, self-reported physical activity was related to TG in girls (r= -0.13) but not boys. When grouped by activity status, TG was found to be similar in boys participating in little to moderately frequent physical activity and significantly lower in girls reporting engaging in physical activity at least 2-3 times per week compared to infrequently (54.8 mg/dl v. 65.3 mg/dl) (Tell and Vellar, 1988). TC, HDL and TC:HDL were not significantly associated with physical activity. Physical activity frequency and intensity

was based on the response to how often the subject exercised (for at least half an hour) so that they were out of breath and sweating.

Maximal aerobic power was positively associated with HDL and HDL:TC and negatively associated with TC and TG in both boys and girls. However, correlations were low ($0.05>r<0.25$). When subjects were grouped into quartiles of peak Vo_2, there was a significant linear trend for HDL and TG in girls. TC was lower in more aerobically fit boys and girls, but there was no significant trend. These data suggest a dose-response relationship between aerobic fitness and blood lipids in youth.

Singapore Youth Coronary Risk and Physical Activity Study. This sample included 1579 schoolchildren 6-18 yr of age from 12 schools in six geographic regions of Singapore (Schmidt et al., 1998). Physical activity was assessed by self-report. In boys, physical activity was significantly correlated with TC ($r = -0.13$) and TG ($r = -0.18$), while no significant relationships were found in girls. When boys and girls were grouped by an arbitrary cut-point of physical activity status (inactive to vigorous physical activity), the only significant difference was between those with relatively no activity and those with vigorous physical activity (TC, 159.7 v. 136.7 mg/dl, respectively). The other three groups possessed a mean TC of 147 mg/dl.

Cardiovascular Risk in Young Finns Study. The Young Finns Study is a multicenter study of atherosclerotic precursors in Finnish children and young adults (Raitakari et al., 1997). The initial cohort in 1980 included 3596 children and young adults aged 3, 6, 9, 12, 15, and 18 yrs of age. Two follow-up studies were conducted in 1983 and 1986. Physical activity was assessed by questionnaire including frequency and intensity. An index of physical activity was calculated from the product of frequency,

intensity, and duration. Subjects were then grouped into high, moderate, and low levels of physical activity based on arbitrary cut-points of the activity index. Blood lipid measurements included TC, HDL, HDL2, HDL3, LDL, Apolipoprotein B (Apo B), and serum lecithin:cholesterol acyltransferase (LCAT).

Although not significant, TC and LDL were lower in boys in the high physical activity group. A linear trend for an increase in HDL and HDL_2 and a decrease in Apo B with increasing physical activity level was found in boys, whereas a decrease in TG was associated with increasing physical activity in both sexes. No significant association was found between physical activity and LCAT.

Summary: In general, correlations between physical activity and blood lipids are low and often non-significant. When grouped by physical activity or aerobic fitness level, youth in the upper extreme display a better blood lipid profile. This difference is apparent moreso in boys than girls. However, the data are inconsistent. Methodological shortcomings limit previous cross-sectional studies in this area (Armstrong and Simons-, 1994; Casperson et al., 1998). Specifically, the measurement of habitual physical activity and the lack of control of confounding variables may distort the findings from cross-sectional studies.

Prospective and retrospective cohort studies. A limited number of prospective and retrospective cohort studies have been conducted to examine the influence of physical activity on blood lipids in children and adolescents. Results from two prospective cohort studies suggest that baseline physical activity level is inversely related with TG levels in 3-4 yr olds in a1 yr follow-up (DuRant et al., 1993), and 12, 15, and 18-yr old youth in the Young Finns Study in a 3 yr follow-up (Porkka et al., 1994)

In cohort studies, sports participation or physical education interventions have been used as a proxy for habitual physical activity in youth. Using this approach to determine high school activity status in middle-aged men, a retrospective cohort study was conducted by researchers from the Institute for Aerobics Research. The results indicated that TG and TC did not differ between former high school or college athletes and non-athletes (Brill et al., 1989). In a prospective study of the long-term effects of increased physical education on adult health outcomes, the blood lipid profile did not differ between experimental and control men or women (Trudeau et al., 2000). Thus, prior athleticism or physical education, which are assumed to be associated with higher energy expenditure, have little apparent impact on adult health outcomes, including blood lipids.

Experimental studies. Few well-designed experimental studies have examined the influence of increased physical activity or exercise training on blood lipids. In general, exercise training studies have failed to have a significant impact upon the lipoprotein profile of children and adolescents (Casperson et al., 1998). Tolfrey et al. (1998b) noted that several deficiencies in the available exercise training studies and attempted to overcome such limitations. Twenty-eight (14 boys, 14 girls) "prepubertal" children (mean age 10.7 + 0.7 years) completed a 12 week exercise training program consisting of stationary cycling 3 times per week at 80% of maximum heart rate for 30 minutes. To control for possible confounding, alterations in the pre- and post-intervention values for peak Vo_2, habitual physical activity, and percentage body fat were included in the analyses in an effort to identify the independent effects of the exercise training program. Age- and sexual maturity-matched controls were used. Sexual maturity status was

assessed pre- and post-intervention and although not reported in this paper, a companion paper (Tolfrey et al., 1998a) examining the training effect on peak Vo2 indicated that sexual maturity status did not change. However, a few comments regarding the sexual maturity classification and status reported by the authors should be considered. First, the authors described the inclusion of subjects by a "sexual maturity status no more than two according to the criteria of Tanner for breast, pubic hair, and genital development in girls and boys, respectively". According to the criteria, Tanner stage 1 is the prepubertal state; so the authors misidentify the subjects as prepubertal in this study. Second, even though subjects did not advance in sexual maturity stage as indicated by the criteria of Tanner, it is important to note that the processes of biological maturation vary in timing and tempo and "prepubertal" subjects vary in skeletal maturation (Malina and Bouchard, 1991). Nonetheless, the exercise training group demonstrated a significant increase in HDL-C (9.3%, 1.08 to 1.18 mmol/L), decrease in LDL-C (10.2%, 2.94 to 2.64 mmol/L), decrease in TC/HDL-C (11.6%, 4.13 to 3.65), and decrease in LDL-C/HDL-C (17.2%, 2.85 to 2.36 mmol/L). Although not significant, TC also declined (4.2%, 4.33 to 4.15 mmol/L). All significant differences involved an interaction for group and time except for HDL-C that showed only a significant main effect.

Summary. In general, TC is not associated with physical activity in children and adolescents. Some studies suggest that HDL-C and TG are higher and lower, respectively, in more active than inactive youth, and LDL-C may also be lower in more active youth. Armstrong and Simons- (1994) conclude that the evidence for these conclusions are not as compelling as that for adults. It has also been noted that the results are confounded in part by methodological difficulties in estimating habitual physical

activity in children and adolescents (i.e., misclassification), body fatness, variation in maturity status and progress, and the interaction among these variables and blood lipids.

Why do some cross-sectional studies show no association between physical activity and blood lipids, and some exercise training studies fail to show an improvement in the blood lipid profile? First, the subjects in these studies probably display a normal metabolic profile (Despres et al., 1990a). In the case where blood lipids did change following exercise training, it is important to consider baseline values of the blood lipids as increased physical activity often improves a hyperlipidemic profile (Tolfrey et al., 1998b) . Second, confounding variables such as body composition, chronological age, biological maturity status, diet, and/or aerobic fitness are not considered. Third, the appropriate exercise training protocol including training frequency, intensity, and duration for altering blood lipids in adolescents has not yet been established. Armstrong and Simons-Morton (1994) suggest that blood lipids may not vary greatly in children and adolescents since there is relatively less variance in both physical activity and blood lipid levels in children and adolescents compared to adults.

DOSE-RESPONSE ISSUES

A major question in the physical activity epidemiology literature is the optimal amount of physical activity required to alter health outcomes, risk factors, morbidity, and mortality (Blair and Connelly, 1996; Lee and Paffenbarger, 1996; Morris, 1996). Haskell (1994) points out that minimal and adequate amounts are also important to determine. To establish recommendations for an appropriate exercise prescription, or a general statement regarding physical activity and health, requires empirical data to support some

minimal, adequate, or optimal level of physical activity that has a favorable effect on a selected biological outcome. Currently, there is no clear answer to how long (duration) or how intense physical activity needs to be to produce favorable results. Despite some uncertainty about appropriate levels of physical activity, the Centers for Disease Control (CDC) and American College of Sports Medicine (ACSM) have recommended that individuals accumulate 30 minutes or more of moderate physical activity most days of the week (Pate et al., 1995). It is quite probable that the minimal, adequate, and optimal amount of physical activity varies by individual, especially in the context of emerging knowledge on genotype-environmental interactions.

Recommendations for appropriate levels of physical activity in youth are currently based upon the adult model and expert opinion. In their review, Armstrong and Simons-Morton (1994) concluded that the empirical dose-response data relating the effect of physical activity to blood lipids in adolescents are nonexistent. However, more recent studies provide some evidence to support a dose-response relationship. Among quintiles of physical activity groups, the most active group (highest quintile) showed a lower TC in Singapore youth (Schmidt et al., 1998). In the males participating in the Young Finns Study, TC ($p < 0.15$), LDL ($p < 0.19$), and TG ($p < 0.0003$) tended to be lower and HDL ($p < 0.04$) and HDL:TC ($p < 0.02$) tended to be higher in the active group (Raitakari et al., 1997). Further study is warranted to establish the dose-response relationship in the general population of youth.

TRAINING VOLUME AND BLOOD LIPIDS IN DISTANCE RUNNERS

Related to the issue of dose-response is the idea that health benefits accrue at levels greater than the current recommendations. It has been shown that blood lipids are superior in endurance trained adults, but whether the benefits are related to training volume (i.e., distance run per week) has received limited attention. Observation of a special exposure group allows for a unique opportunity to examine a comprehensive model of the relationship between an exposure and outcome.

In an early report of 90 middle-aged male runners, distance run per week was positively correlated with HDL (r=0.50) and remained significant after adjustment for percentage body fat (r=0.40) (Rotkis et al., 1982). When runners were grouped by mileage (low mileage, 10 to 19 miles per week; intermediate mileage, 20 to 39 miles per week; and high mileage, 40 or more miles per week), HDL increased across groups (47 mg/dl, 53 mg/dl, and 60 mg/dl, respectively), whereas TC (217 mg/dl, 211 mg/dl, 203 mg/dl, respectively), non-HDL cholesterol (170 mg/dl, 158 mg/dl, 143 mg/dl, respectively), and TC:HDL (4.52, 3.99, and 3.31, respectively) decreased. However, values across training groups were not adjusted for differences in age or body fatness. In contrast, there was no relationship between TV and HDL (r=0.05) in a smaller sample of 33 middle-aged men (Williams, 1990). In both reports, training volume was estimated by averaging self-reported weekly training mileage of the preceding six months.

Recently, Williams (1996, 1997) demonstrated that the benefits of exercise accrue in a dose-response manner at levels of physical activity exceeding the current minimal guidelines. Subjects included 8,283 male and 1,837 female adult recreational distance runners participating in the National Runners' Health Study. Data were compiled from a

questionaire distributed at races and to subscribers of *Runner' World* and clinical records. Training volume was calculated as the average distance run per week based on the preceding 5 years. Significant linear trends were reported for HDL and TC:HDL in both sexes and TG in men. No significant trend was evident for LDL.

Based on the aforementioned studies, it has been suggested that an exercise level equivalent to jogging 10-15 miles/wk is necessary to significantly alter blood lipids (Superko, 1991; Williams, 1994). Armstrong and Simons-Morton (1994) extrapolated this recommendation to establish physical activity guidelines for youth, The authors suggested that an adolescent would need to jog at a speed of 8 km/hr for approximately 2 hours per week, which from their own experiences was equivalent to about 80% of maximal heart rate with young adolescents and about 75% of maximal heart rate for young adults. They, therefore, recommended that four 30 minute exercise sessions per week at 75-80% of maximum heart rate may be an appropriate prescription. Recall that Tolfrey et al. (1998b) showed changes in the blood lipid profile of prepubertal subjects following an 8 week training program consisting of three (rather than four) 30 minute exercise sessions per week at 80% of maximal heart rate. However, it still remains to be shown whether a dose-response or threshold effect of physical activity on blood lipids exists in children and adolescents at or greater than the recommended exercise volume. The study of adolescent distance runners provides a unique opportunity to evaluate the current recommendations.

AEROBIC FITNESS AND BLOOD LIPIDS

A low level of aerobic fitness is an independent predictor of an increased risk for cardiovascular disease in adults (Blair et al., 1989). In youth, more aerobically fit youth generally have higher HDL and lower TG, although not all studies show such results (Armstrong and Simons-, 1994; Despres et al., 1990a; Tolfrey et al., 2000). However, this may be related to body composition as highly fit individuals are generally leaner than unfit individuals. Chronological age may also influence the relationship, as HDL declines during adolescence in males. Therefore, it is important to control for body composition, age, and biological maturity when examining the relationship between aerobic fitness and blood lipids. In studies that have controlled for some index of body size and/or composition, the relationship between peak Vo_2 and blood lipids no longer remains significant (Al-Hazzaa et al., 1994; Armstrong et al., 1991; Hager et al., 1995; Sallis et al., 1988). For example, Sallis et al (1988) reported significant correlations between predicted peak Vo_2 and HDL of 0.18 and 0.29 in 5th and 6th grade males and females, respectively. Partial correlations, controlling for the BMI, reduced the coefficients to 0.01 and 0.04 in males and females, respectively.

Few studies have examined the relationship between peak vo_2 and blood lipids in athletic populations. In a previous mixed-sample (males and females) of 8 to 15 yr old mid-Michigan distance runners, peak Vo_2 was related to HDL (r=0.39) (Smith et al., 1986). Atomi et al. (1986) and Macek et al. (1989) both reported a significant relationship between peak Vo_2 and TG and HDL in mixed-samples that included youth athletes. Valimaki et al. (1980) also reported a significant relationships between total work per unit body weight and HDL in 20 boys (r=0.53) and TG in 11 girls (r= -0.83).

Unfortunately, these studies did not conduct separate analyses for athletes. In a study of national level adult athletes, peak Vo_2 explained 25% of the variance in HDL (Berg and Keul, 1985), and was significantly related to HDL (r=0.26) in Olympic athletes (Tsopanakis et al., 1986).

Genetic factors may also play a role in the modulating the relationship between aerobic fitness and blood lipids. In a study of healthy, untrained adult men and women, associations between peak Vo2 and blood lipids varied according to apolipoprotein (apo) E phenotype (St.-Amand et al., 1999). There were significant relationships in men and women between peak Vo_2 and TG in carriers of the apo E2 isoform and apoE3 homozygotes. Peak Vo_2 was significantly related to HDL in male Apo E3 homozygotes, and to all blood lipids (TC, HDL, LDL, TG) in female Apo E3 homozygotes. There were no significant relationships among male apo E4 carriers, and only HDL was related to peak Vo_2 in female apo E4 carriers. When fat mass and glucose tolerance were controlled, only HDL_2 remained significantly correlated with peak Vo_2 in men and women. It appears that a high level of aerobic fitness is associated with a favorable blood lipid profile in individuals homogenoues for the apo E3 isoform and with reduced TG in individuals who are apo E2 carriers. However, these associations were largely attributed to the covariance of body fatness and glucose tolerance.

BODY FATNESS AND BLOOD LIPIDS

Various measures of body fatness and fat distribution (e.g., BMI, waist circumference, waist-to-hip ratio, skinfold thickness, estimated percent body fatness) are positively associated with atherogenic blood lipids and negatively associated with HDL

across the lifespan (Guo et al., 1994). Children and adolescents with excess adiposity generally have a poorer blood lipid profile compared to leaner youth (Fripp et al., 1985; Johnston, 1985; Smoak et al., 1987; Williams et al., 1992).

Few studies have examined the relationship between adiposity and blood lipids in athletes. Athletes are generally characterized by relative leanness. However, some variability does exist in measures of adiposity within this group. In a study of national level athletes from a broad spectrum of sports (i.e., sprinters, cyclists, hammer throwers, etc.), relative body weight (kg/(cm-100)) explained about 7% of the variance in TC and TG and 20% of the variance in LDL (Berg and Keul, 1985). Unfortunately, discipline-specific relationships were not explored. In Olympic athletes, relative body weight was significantly related to HDL (r= -0.22), LDL (r= 0.18), and VLDL (r= 0.17) (Tsopanakis et al., 1986). In middle-age distance runners, percentage body fat and HDL (r= -0.36), TC (r=0.38) and non-HDL cholesterol (r=0.48) were significantly related (Rotkis et al., 1982). In contrast, correlations between various measures of body size (e.g., BMI, relative weight, percentage body fat) and HDL were low in another sample of middle-aged distance runners (r =0.05- 0.08) (Williams, 1990). The reason for the discrepancy in the relationship of percentage body fat and HDL between the two studies of middle-aged distance runners is not known.

Only two studies have examined the relationship between adiposity and blood lipids in young athletes. Atomi et al. (1986) reported a significant relationship between percentage body fat and TC and HDL in a mixed-sample of 10-12 yr old Japanese boys and girls that included soccer players. Unfortunately, the correlation coefficients were not reported. In a study of young (mean age = 12 yrs) female athletes (22 gymnasts, 20

swimmers), relationships between the sum of four skinfolds and estimated fat mass and blood lipids were low to moderate ($r < 0.45$) (Valimaki et al., 1980). Surprisingly, the relationship between adiposity and HDL was positive (i.e., increased fatness associated with higher HDL).

Besides total body fatness, relative fat distribution, and specifically a truncal and/or visceral fat patterning, has been strongly linked to an adverse blood lipid profile in youth and adults (Baumgartner et al., 1989; Despres et al., 1990b; Freedman et al., 1989). During adolescence, an increase in subcutaneous abdominal adipose tissue and redistribution of fatness to the trunk results in an increase in the trunk-to-extremity skinfold ratio in boys (Malina et al., 1999). The redistribution of adipose tissue during male adolescence is associated with a decrease in HDL (Baumgartner et al., 1989; van Lenthe et al., 1998). This relationship may also be augmented by hormonal changes during male puberty (Laskarzewski et al., 1983; Roemmich and Rogol, 1999; Srinivasan et al., 1985).

Only one study has apparently examined the contribution of relative fat distribution to blood lipids in athletes. Williams (1990) reported a low correlation ($r = -0.13$) between the ratio of abdominal girth and bi-iliac diameter and HDL in middle-aged male distance runners. No study has apparently examined the relationship between fat distribution and blood lipids in young athletes.

The role of genes and body fatness in the modulation of elevated blood lipid levels has also been indicated (Katzmarzyk et al., 1999). Maximal heritability estimates of abdominal visceral fatness measured by computerized tomography approximate 50-55% with a major gene associated with total fat mass either directly or indirectly

affecting abdominal fatness. Polymorhpisms in lipoprotein genes (ApoA-II MspI, HindIII, and apoB-100 EcoRI) may also influence the relationship between abdominal visceral fatness and blood lipid levels.

PHYSICAL ACTIVITY AND BLOOD LIPIDS: MECHANISMS

It is clear from the literature in adults that regular aerobic physical activity attenuates the natural progression of atherosclerosis by favorably altering the blood lipid profile (Haskell, 1984). What mechanisms are responsible for the alteration of lipoproteins by increased physical activity? Several studies have found that increased clearance of TG, increased lipoprotein lipase (LPL) activity, decreased hepatic lipase activity, and increased lecithin:cholesterol acyltransferase (LCAT) activity may be considered as possible mechanisms for the observed changes in blood lipids in humans (Haskell, 1984; Stefanik and Wood, 1994).

The relationships between physical activity, peak Vo_2, body fatness and blood lipids have been discussed previously. What remains to be distinguished is whether the blood lipid profile is influenced primarily by increased physical activity, increased aerobic fitness, changes in body composition, or a combination of these variables (Krauss, 1989; Thompson, 1990; Williams, 1993). Some authors suggest that weight loss is critical to an exercise effect on blood lipids, particularly HDL, while others have shown that changes in blood lipids may occur without weight loss (Thompson, 1990). However, weight gain is expected during childhood and adolesence, thus the applicability of the adult model has limitations. On the other hand, peak Vo_2 is thought to be related to HDL (Tikkanen et al., 1991) through its association with the percentage of slow-twitch

muscle fibers and oxidative capacity of skeletal muscle (Bergh et al., 1978). The possibility that leaner and more aerobically fit individuals are more likely to engage in higher training levels also cannot be dismissed (Williams et al., 1982).

SUMMARY

Several areas related to physical activity, aerobic fitness, body fatness, and blood lipids in children and adolescents have been reviewed. The evidence of early atherosclerosis in youth is suggestive of the need to begin preventive measures during childhood and adolescence. However, definitive data showing the association of physical activity and aerobic fitness on the blood lipid profile of children and adolescents is lacking, and thus the role of physical activity and aerobic fitness during childhood on the etiology of atherosclerosis remains to be established. The association of body fatness and blood lipids during childhood and adolescence is clear, particularly among obese children and adolescents. Changes in truncal fatness and sex hormones during adolescence also contribute to the decline in HDL during male adolescence.

Several methodological issues, particularly the quantification of physical activity, need to be addressed in cross-sectional and prospective studies examining the association between physical activity and blood lipids (and other health-related outcomes) in youth. Perhaps the simple observation that a relatively small variance in both physical activity and blood lipids in children and adolescents compared to adults may explain the lack of, or low associations reported in cross-sectional studies. Likewise, the lack of a training effect in experimental studies has been explained by the eulipidemic profile, failure to account for confounding variables (pre- and post-test), and/or an inadequate exercise

training volume. The recent study of Tolfrey et al. (1998b) was a well-designed experimental trial that showed changes in the blood lipid profile of prepubertal subjects and may serve as a model for future exercise training studies in youth. Genetic factors such as the apo E4 phenotype may also explain the variability in blood lipids and their response to physical activity and should be considered in future studies.

Clearly, the blood lipid profile of young athletes has not been fully described. The available cross-sectional data suggest that young athletes possess a superior blood lipid profile compared to the general population. However, hypercholesterolemia does exist in young athletes (Kyle et al., 1991) and requires further exploration. Likewise, the heterogeneity of blood lipids in young athletes remains to be investigated. The study of young athletes, as a special exposure group, would also allow the opportunity to examine the influence of physical activity levels equal to and greater than the current recommendations (4 days/wk, 30 min/session, 75-80% maxHR) on the blood lipid profile. It remains to be established whether a dose-response relationship, or a threshold effect, exists between physical activity and blood lipids in the pediatric population. Longitudinal study of physically active pubertal boys would allow study of the potential attenuation of the decline in HDL during puberty by regular endurance exercise.

The determinants of blood lipids during adolescence are multi-factorial and involve a complex interaction of genetic and environmental factors. It is the aim of Part I of this dissertation to examine the contribution of age, sexual maturity, physical activity, aerobic fitness, and body fatness to the blood lipid profile of young distance runners.

REFERENCES

Al-Hazzaa HM, Sulaiman MA, Al-Matar AJ, Al-Mobaireek KF (1994) Cardiorespiratory fitness, physical activity patterns and coronary risk factors in preadolescent boys. Int J Sports Med 15:267-272.

Amos CI, Cohen JC, Srinivasan SR, Freedman DS, Elston RC, Berenson GS (1989) Polymorphism in the 5' -flanking region of the insulin gene and its potential relation to cardiovascular disease risk: observations in a biracial community. The Bogolusa Heart Study. Atherosclerosis 79:51-57.

Anderson RA, Burns TL, Lee J, Swenson D, Bristow JL (1989) Restriction fragment length polymorphisms associated with abnormal lipid levels in an adolescent population. Atherosclerosis 77:227-237.

Armstrong N, Balding J, Gentle P, Kirby B (1992) Serum lipids and blood pressure in relation to age and sexual maturity. Ann Hum Biol 19:477-487.

Armstrong N, Simons- B (1994) Physical activity and blood lipids in adolescents. Pediatr Exerc Sci 6:381-405.

Armstrong N, Williams J, Balding J, Gentle P, Kirby B (1991) Cardiorespiratory fitness, physical activity patterns, and selected coronary artery risk factor variables in 11- to 16-year-olds. Pediatr Exerc Sci 3:219-228.

Atomi Y, Kuroda Y, Asami T, Kawahara T (1986) HDL-cholesterol of children (10 to 12 years of age) related to Vo2max, body fat, and sex. In J Rutenfranz, R Mocellin and F Klimt (eds.): Children and Exercise XII. Champaign, IL: Human Kinetics, pp. 167-172.

Bao W, Srinivasan S, Wattigney W, Berenson G (1994) Persistence of multiple cardiovascular risk clustering related to syndrome X from childhood to young adulthood. Arch Intern Med 154:1842-1847.

Bao W, Srinivasan SR, Valdez R, Greenlund KJ, Wattigney WA, Berenson GS (1997) Longitudinal changes in cardiovascular risk from childhood to young adulthood in offspring of parents with coronary artery disease: the Bogolusa Heart Study. JAMA 278:1749-1754.

Bao W, Srinivasan SR, Wattigney WA, Berenson GS (1995a) The relation of parental cardiovascular disease to risk factors in children and young adults: the Bogolusa Heart Study. Circulation 91:365-371.

Bao W, Threefoot SA, Srinivasan SR, Berenson GS (1995b) Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: the Bogolusa Heart Study. Am J Hypertens 8:657-665.

Baumgartner RN, Siervogel RM, Chumlea WC, Roche AF (1989) Associations between plasma lipoprotein cholesterols, adiposity and adipose tissue distribution during adolescence. Int J Obes 13:31-41.

Berenson GS, Foster TA, Frank GC, Frerichs RR, Srinivasan SR, Voors AW, Webber LS (1978) Cardiovascular disease risk factor variables at the preschool age: The Bogolusa Heart Study. Circulation 57:603-612.

Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE, Wattigney WA (1998) Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. N Engl J Med 338:1650-1656.

Berenson GS, Srinivasan SR, Cresanta JL, Foster TA, Webber LS (1981) Dynamic changes of serum lipoproteins in children during adolescence and sexual maturation. Am J Epidemiol 113:157-170.

Berg A, Keul J (1985) Influence of maximum aerobic capacity and relative body weight on the lipoprotein profile in athletes. Atherosclerosis 55:225-231.

Bergh U, Thorstensson A, Sjodin B, Hulten B, Piehl K, Karlsson J (1978) Maximal oxygen uptake and muscle fiber types in trained and untrained humans. Med Sci Sports 10:151-154.

Betteridge DJ, Illingworth DR, Shepherd J, eds. (1999) Lipoproteins in Health and Disease. London: Arnold.

Blair SN, Connelly JC (1996) How much physical activity should we do?: the case for moderate amounts and intensities of physical activity. Res Q Exerc Sport 67:193-205.

Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW (1989) Physical fitness and all-cause mortality: a prospective study of healthy men and women. JAMA 17:2395-2401.

Boreham CA, Twisk J, Savage MJ, Cran GW, Strain JJ (1997) Physical activity, sports participation, and risk factors in adolescents. Med Sci Sport Exerc 29:788-793.

Brill PA, Burkhalter HE, Kohl HW, Goodyear NN, Blair SN (1989) The impact of previous athleticism on exercise habits, physical fitness, and coronary heart disease risk factors in middle-aged men. Res Q Exerc Sport 60:209-215.

Bucher KD, Schrott HG, Clarke WR, Lauer RM (1982) The Muscatine Cholesterol Study: distribution of cholesterol levels within families of probands with high, low, and middle cholesterol levels. J Chron Dis 35:385-400.

Casperson CJ, Nixon PA, DuRant RH (1998) Physical activity epidemiology applied to children and adolescents. Exerc Sci Sports Rev 26:341-403.

Clarke WR, Schrott HG, Leaverton PE, Connor WE, Lauer RM (1978) Tracking of blood lipids and blood pressure in school age children: the Muscatine Study. Circulation 58:626-634.

Cresanta JL, Srinivasan SR, Webber LS, Bereneson GS (1984) Serum lipid and lipoprotein cholesterol grids for cardiovascular risk screening of children. Am J Dis Child 138:379-387.

Despres J-P, Bouchard C, Malina RM (1990a) Physical activity and coronary heart disease risk factors during childhood and adolescents. Exerc Sport Sci Rev 18:243-261.

Despres J-P, Moorjani S, Lupien P, Tramblay A, nadeau A, Bouchard C (1990b) Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Atherosclerosis 10:497-511.

DuRant R, Baranowski T, Rhodes T, Gutin B, Thompson W, Carroll R, Puhl J, Greaves K (1993) Association among serum lipid and lipoprotein concentrations and physical activity, physical fitness, and body composition in young children. J Pediatr 123:185-192.

Enos WF, Beyer JC, Holmes RH (1955) Pathogenesis of coronary disease in American soldiers killed in Korea. JAMA 158:912-914.

Freedman DS, Srinivasan SR, Harsha DW, Webber LS, Berenson GS (1989) Relation of body fat patterning to lipid and lipoprotein concentrations in children and adolescents: the Bogolusa Heart Study. Am J Clin Nutr 50:930-939.

Frerichs RR, Srinivasan SR, Webber LS, Berenson GS (1976) Serum cholesterol and triglyceride levels in 3,446 children from a biracial community: The Bogolusa Heart Study. Circulation 54:302-308.

Fripp R, Hodgson J, Kwiterovich P, Werner J, Schuler H, Whitman V (1985) Aerobic capacity, obesity, and atherosclerotic risk factors in male adolescents. Pediatr 75:813-818.

Garcia R, Moodie D (1989) Routine cholesterol surveillance in childhood. Pediatr 84:751-755.

Guo S, Salisbury S, Roche AF, Chumlea WC, Siervogel RM (1994) Cardiovascular disease risk factors and body composition: a review. Nutr Rev 14:1721-1777.

Gutgessel HP, Atkins DL, Day RW (1997) Common cardiovascular problems in the young: Part II. Hypertension, hypercholesterolemia and preparticipation screening of athletes. Am Fam Physician 56:1993-1998.

Hager RL, Tucker LA, Seljaas GT (1995) Aerobic fitness, blood lipids and body fat in children. Am J Public Health 85:1702-1706.

Haskell WL (1984) The influence of exercise on the concentrations of triglyceride and cholesterol in human plasma. Exerc Sport Sci Rev 12:205-244.

Haskell WL (1994) Health consequences of physical activity: understanding and challenges regarding dose-response. Med. Sci. Sports Exerc. 26:649-660.

Hickman TB, Briefel RR, Carroll MD, Rifkind BM, Cleeman JI, Maurer KR, Johnson CL (1998) Distributions and trends of serum lipid levels among United States children and adolescents ages 4-19 years: data from the Third National Health and Nutrition Examination Survey. Prev Med 27:879-890.

Hopkins PN, Williams RR (1981) A survey of 246 suggested coronary risk factors. Atherosclerosis 40:1-52.

Johnston F (1985) Health implications of childhood obesity. Ann Intern Med 103:1068-1072.

Katzmarzyk PT, Malina RM (1997) The contribution of participation in organized youth sports to daily energy expenditure in children and youth. East Lansing, MI: Institute for the Study of Youth Sports.

Katzmarzyk PT, Pérusse L, Bouchard C (1999) Genetics of abdominal visceral fat levels. Am J Hum Biol 11:225-235.

Krauss RM (1989) Exercise, lipoproteins, and coronary artery disease. Circulation 79:1143-1145.

Kyle JM, Walker RB, Riales RR, Petty GJ, Thomas JA, Roberts MD (1991) Student athletes cholesterol screening during routine precompetition examination. J Fam Pract 33:172-176.

Laskarzewski P, Morrison J, Gutai J, Orchard T, Khoury P, Glueck C (1983) High and low density lipoprotein cholesterols in adolescent boys: relationships with endogenous testosterone, estradiol, and quetelet index. Metabolism 32:262-271.

Lauer R, Connor W, Leaverton P, Reiter M, Clarke W (1975) Coronary heart disease risk factors in school children: The Muscatine Study. J Pediatr 86:697-706.

Lee I-M, Paffenbarger RS (1996) How much physical activity is optimal for health?: methodological considerations. Res Q Exerc Sport 67:206-208.

Macek M, Bell D, Rutenfranz J, Vavra J, Masopust J, Neidhart B, Schmidt K-H (1989) A comparison of coronary risk factors in groups of trained and untrained adolescents. Eur J Appl Physiol 58:577-582.

Mahoney LT, Burns TL, Stanford W, Thompson BH, Witt JD, Rost CA, Lauer RM (1996) Coronary risk factors measured in childhood and young adult life are associated with coronary artery calcification in young adults: the Muscatine Study. J Am Coll Cardiol 27:277-284.

Malina RM (1997) Activity and fitness of youth: are they related? do they track? In K Froberg, O Lammert, H St. Hanson and CJR Blimkie (eds.): Exercise and Fitness-Benefits and Risks: Children & Exercise XVIII: Odense University Press, pp. 161-171.

Malina RM, Bouchard C (1991) Growth, Maturation, and Physical Activity.Champaign, IL: Human Kinetics.

Malina RM, Koziel S, Bielicki T (1999) Variation in subcutaneous adipose tissue distribution associated with age, sex, and maturation. Am J Hum Biol 11:189-200.

McNamara JJ, Molot MA, Stremple JF, Cutting RT (1971) Coronary artery disease in combat casualties in Vietnam. JAMA 216:1185-1187.

Morris JN (1996) Exercise versus heart attack: questioning the consensus? Res Q Exerc Sport 67:216-220.

Morrison JA, Laskarzewski PM, Rauh JL, Brookman R, Mellies M, Frazer M, Khoury P, deGroot I, Kelly K, Glueck CJ (1979) Lipids, lipoproteins, and sexual maturation during adolescence: the Princeton Maturation Study. Metabolism 28:641-649.

Muhonen LE, Burns TL, Nelson RP, Lauer RM (1994) Coronary risk factors in adolescents related to their knowledge of familial coronary heart disease and hypercholesterolemia: the Muscatine Study. Pediatr 93:444-451.

National Cholesterol Education Program (1992) Report of the expert panel on blood cholesterol levels in children and adolescents. Pediatr 89 (Suppl 3): Part 2:525-584.

NIH Consensus Development Panel on Triglyceride HDL, and Coronary Heart Disease, (1993) Triglyceride, high density lipoprotein, and coronary heart disease. JAMA 269:505-510.

NIH Consensus Statement (1985) Lowering blood cholesterol to prevent heart disease. JAMA 253:2080-2086.

Paffenbarger RS, Lee I-M (1996) Physical activity and fitness for health and longevity. Res Q Exerc Sport 67 (Suppl. 3):11-28.

Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, Buchner D, Ettinger W, Heath GW, King AC, Kriska A, Leon AS, Marcus BH, Morris J, Paffenbarger RS, Patrick K, Pollock ML, Rippe JM, Sallis J, Wilmore JH (1995) Physical activity and

health: A recommendation from the Centers of Disease Control and Prevention and the American College of Sports Medicine. JAMA 273:402-407.

Porkka KVK, Viikari JSA, Taimela S, Dahl M, Akerblom HK (1994) Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: a 1-yr follow-up. Am J Epidemiol 140:196-1110.

Raitakari O, Taimela S, Porkka K, Telama R, Valimaki I, Akerblom H, Viikari J (1997) Associations between physical activity and risk factors for coronary artery disease: The Cardiovascular Risk in Young Finns Study. Med Sci Sports Exerc 29:1055-1061.

Roemmich J, Rogol A (1999) Hormonal changes during puberty and their relationship to fat distribution. Am J Hum Biol 11:209-224.

Rothman KJ, Greenland S (1998) Modern Epidemiology. 2nd, Philadelphia: Lippincott-Raven.

Rotkis TC, Cote R, Coyle E, Wilmore JH (1982) Relationship between high density lipoprotein cholesterol and weekly running mileage. J Cardiac Rehab 2:109-112.

Rowland TW (1993) The physiological impact of intensive training on the prepubertal athlete. In BR Cahill and AJ Pearl (eds.): Intensive Participation in Children's Sports. Champaign, IL: Human Kinetics, pp. 167-193.

Sallis JF, Patterson TL, Buono MJ, Nader PR (1988) Relation of cardiovascular fitness and physical activity to cardiovascular disease risk factors in children and adults. Am J Epidemiol 127:933-941.

Schmidt G, Walkuski J, Stensel D (1998) The Singapore Youth Coronary Risk and Physical Activity Study. Med Sci Sports Exerc 30:105-113.

Shear CL, Burke GL, Freedman DS, Berenson GS (1986) Value of childhood blood pressure measurements and family history in predicting future blood pressure status: results from 8 years of follow-up in the Bogolusa Heart Study. Pediatr 77:862-869.

Siervogel RM, Baumgartner RN, Roche AF, Chumlea WC, Glueck CJ (1989) Maturity and its relationship to plasma lipid and lipoprotein levels in adolescents: the Fels Longitudinal Study. Am J Hum Biol 1:217-226.

Smith BW, Metheny WP, Sparrow AW (1986) Serum lipid and lipoprotein profiles in age-group runners. In MR Weiss and D Gould (eds.): Sport for Children and Youths. Champaign, IL: Human Kinetics, pp. 269-273.

Smoak CG, Burke GL, Webber LS, Harsha DW, Srinivasan S, Berenson GS (1987) Relation of obesity to clustering of cardiovascular disease risk factors in chidren and young adults. Am J Epidemiol 125:364-372.

Srinivasan SR, Ehnholm C, Wattigney WA, Bao W, Berenson GS (1996) The relation of apolipoprotein E polymorphism to multiple cardiovascular risk in children: the Bogolusa Heart Study. Atherosclerosis 123:33-42.

Srinivasan SR, Frerichs RR, Webber LS, Berenson GS (1976) Serum lipoprotein profile in children from a biracial community: The Bogolusa Heart Study. Circulation 54:309-318.

Srinivasan SR, Sundaram GS, Williamson GD, Webber LS, Berenson GS (1985) Serum lipoproteins and endogenous sex hormones in early life: observations in children with different lipoprotein profiles. Metabolism 34:861-867.

St.-Amand J, Prud'homme D, Moorjani S, Nadeau A, Tremblay A, Bouchard C, Lupien PJ, Després J-P (1999) Apolipoprotein E polymorphism and the relationships of physical fitness to plasma lipoprotein-lipid levels in men and women. Med Sci Sports Exerc 31:692-697.

Stefanik ML, Wood PD (1994) Physical activity, lipid and lipoprotein metabolism, and lipid transport. In C Bouchard, S R.J. and T Stephens (eds.): Physical Activity, Fitness, and Health. Champaign, IL: Human Kinetics, pp. 417-431.

Strong JP, Malcom GT, McMahon CA, Tracy RE, Newman III WP, Herderick EE, Corhill JF (1998) Prevalence and extent of atherosclerosis in adolescents and young adults. JAMA 281:727-735.

Strong JP, Malcom GT, Oalmann MC, Wissler RW (1997) The PDAY Study: natural history, risk factors, and pathobiology. Ann NY Acad Sci 811:226-235.

Superko HR (1991) Exercise training, serum lipids, and lipoprotein particle: is there a change threshold? Med Sci Sports Exerc 23:677-685.

Tamir I, Heiss G, Glueck CJ, Christensen B, Kwiterovich P, Rifkind BM (1981) Lipid and lipoprotein distributions in White children ages 6-19 yr: the Lipid Research Clinics Program Prevalence Study. J Chron Dis 34:27-39.

Tanner JM (1962) Growth at Adolescence. 2nd Edition, Oxford: Blackwell.

Tell GS (1985) Cardiovascular disease risk factors related to sexual maturation: the Oslo Youth Study. J Chron Dis 38:633-642.

Tell GS, Mittelmark MB, Vellar OD (1985) Cholesterol, high density lipoprotein cholesterol and triglycerides during puberty: the Oslo Youth Study. Am J Epidemiol 122:750-761.

Tell GS, Vellar OD (1988) Physical fitness, physical activity, and cardiovascular disease risk factors in adolescents: The Oslo Youth Study. Prev Med 17:12-24.

The Lipid Research Clinics (1980) Population Studies Data Book: Aggregrate distributions of lipids, lipoproteins and selected variables in 11 North American populations. Washington, DC: U.S. Department of Health and Human Services.

Thompson PD (1990) What do muscles have to do with lipoproteins? Circulation 81:1428-1430.

Tikkanen HO, Harkonen M, Naveri H, Hamalainen E, Elovainio R, Sarna S, Heikki Frick M (1991) Relationship of skeletal muscle fiber type to serum high density lipoprotein cholesterol and apolipoprotein A-I levels. Atherosclerosis 90:49-57.

Tolfrey K, Campbell IG, Batterham AM (1998a) Aerobic trainability of prepubertal boys and girls. Pediatr Exerc Sci 10:248-263.

Tolfrey K, Campbell IG, Batterham AM (1998b) Exercise training induced alterations in prepubertal children's lipid-lipoprotein profile. Med Sci Sports Exerc 30:1684-1692.

Tolfrey K, Jones AM, Campbell IG (2000) The effects of aerobic exercise training on the lipid-lipoprotein profile of children and adolescents. Sports Med 29:99-112.

Trudeau F, Espindola R, laurencelle L, Dulac F, Rajic M, Shephard RJ (2000) Follow-up of participants in the Trois-Riviéres Growth and Development Study: examing their health-related fitness and risk factors as adults. Am J Hum Biol 12:207-213.

Tsopanakis C, Kotsarellis D, Tsopanakis AD (1986) Lipoprotein and lipid profiles of elite athletes in Olympic sports. Int J Sports Med 7:316-321.

Valimaki I, Hursti M-L, Pihlakoski L, Viikari J (1980) Exercise performance and serum lipids in relation to physical activity in schoolchildren. Int J Sports Med 1:132-136.

van Lenthe FJ, van Mechelen W, Kemper HCG, Twisk JWR (1998) Association of a central pattern of body fat with blood pressure and lipoproteins from adolescence into adulthood. Am J Epidemiol 147:686-693.

Williams DP, Going SB, Lohman TG, Harsha DW, Srinivasan S, Webber LS, Berenson GS (1992) Body fatness and risk for elevated blood pressure, total cholesterol, and serum lipoproteins ratios in children and adolescents. Am. J. Public Health 82:358-363.

Williams PT (1990) Weight set-point theory predicts HDL-cholesterol levels in previously obese long-distance runners. Int J Obes 14:421-427.

Williams PT (1993) High-density lipoproteins and lipase activity in runners. Atherosclerosis 98:251-254.

Williams PT (1994) Lipoproteins and adiposity show improvement at substantially higher exercise levels than those currently recommended. Circulation 90:I-471 (Abstract).

Williams PT (1996) High-density lipoprotein cholesterol and other risk factors for coronary heart disease in female runners. N Engl J Med 334:1298-1303.

Williams PT (1997) Relationship of distance run per week to coronary heart disease risk factors in 8283 male runners. Arch Intern Med 157:191-198.

Williams PT, Wood PD, Haskell WL, Vranizan K (1982) The effects of running mileage and duration on plasma lipoprotein levels. JAMA 247:2674-2679.

Woolf N (1999) Pathology of atherosclerosis. In DJ Betteridge, DR Illingworth and J Shepherd (eds.): Lipoproteins in Health and Disease. London: Arnold, pp. 533-540.

Table 2.1. Guidelines for interpreting blood lipid values in children and adolescents.

Category	Level (mg/dl)	
TC		
High	≥200	
Borderline high	170-199	
Desirable	≤170	
LDL		
High	≥130	
Borderline high	110-129	
Desirable	≤110	
HDL	2-9 yrs of age	10-19 yrs of age
Low	≤40	≤35
Borderline low	40-45	35-45
Desirable	≥45	≥45
TG		
High	≥100	≥130
Borderline high	75-99	90-129
Desirable	≤75	≤90

TC, total cholesterol; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; TG, triglycerides.

Adapted from Kwiterovich (1989).

Table 2.2. Summary of blood lipid studies in child and adolescent athletes.

Study	Location	Sport	Training	N	Sex	Age (yrs)	TC	HDL	LDL	TG
Valimaki et al. (1980)	Finland	T&F	regular participants; systematic training for at least 1 yr prior to study	9	M	11-13	185 (25)	65 (10)		59 (18)
				7	F		173 (24)	62 (6)		55 (9)
Nizankowska -Blaz and Abrahamson (1983)	Poland	Sport school	ten 45 min periods per week of basketball or light athletics (short distance running, long jump, high jump, etc.)	38 (20 M, 18 F)	M, F	x=14.5	160 (26)	52 (9)	93 (22)	68 (23)
Smith et al., (1983)	Michigan	Distance running	Not provided	28 (15 M, 13F)	M, F	10-15 x=12.6	182 (6)*	71 (3)	98 (5)	68 (6)
Smith et al. (1985)	Michigan	Swimming	at least 8 mo/yr	18 (9 M, 9 F)	M, F	9-12	173 (7)*	65 (3)	93 (6)	71 (6)
Atomi et al., (1986)	Tokyo	Soccer	participating in soccer club for >3 yrs; 3 hrs/d, 6d/wk throughout the yr	21	M	10-12	177 (5)*	75 (3)		70 (4)
Macek et al., (1989)	Czechoslovakia	Swimming and various athletics	5 hrs/d plus weekend competition	29	M	16-18	161 (17)	53 (9)	71 (8)	54 (22)
				20	F		162 (21)	59 (12)	77 (11)	59 (19)
Kyle et al., (1991)	West Virginia	?	?	454	M	11-15	155			
				323	F		158			

Mean (SD) unless otherwise noted (* Standard error).
Blood lipids values are expressed in mg/dl.

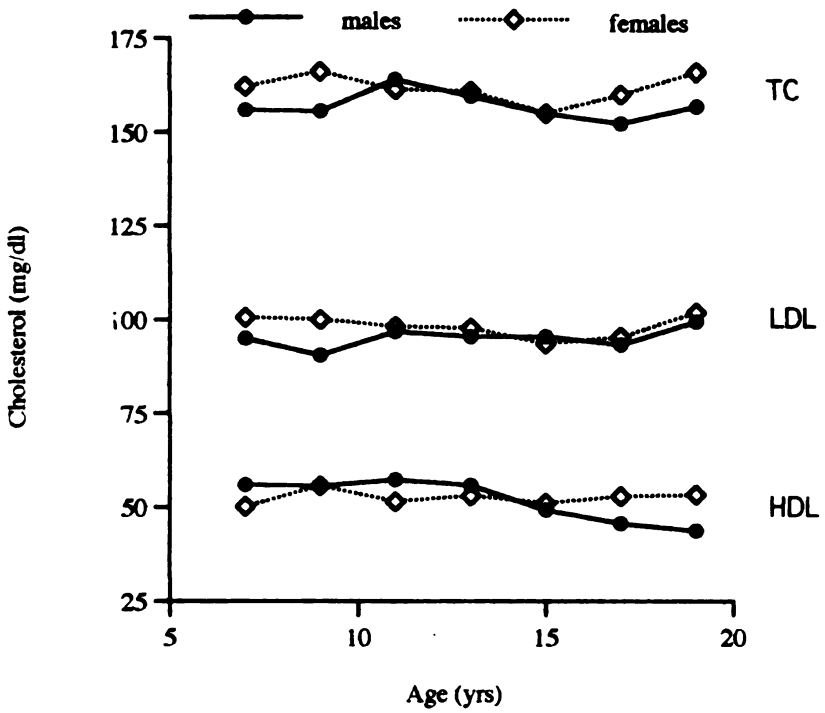

Figure 2.1. Mean values by age and sex for cholesterol. Data from Lipids Research Clinics Prevalence Study (1980).

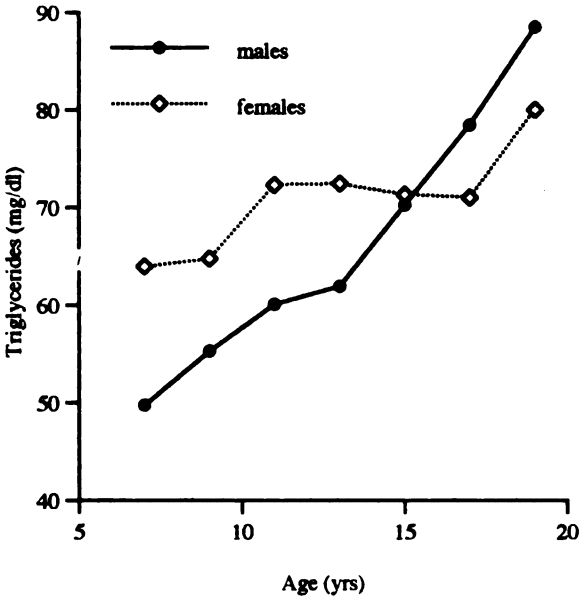

Figure 2.2. Mean triglyceride values by age and sex. Data from Lipids Research Clinics Prevalence Study (1980).

CHAPTER 3

MIXED-LONGITUDINAL ANALYSIS OF BLOOD LIPIDS IN YOUNG DISTANCE RUNNERS

ABSTRACT

Limited information is available on age-and sex-associated variation in blood lipids among young athletes. A mixed-longitudinal design was used to examine the development of blood lipids of competitive young distance runners followed from 1982 to 1985. Total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG) were determined by standard procedures. Serial data included 99 annual measurements for 27 males and 84 annual measurements for 27 females aged 9 to 18 yrs. In general, TC and LDL remained stable, and HDL declined with age, especially in males. TG increased with age. Age-related trends were statistically significant for HDL and TG in boys only ($p<0.05$). TC and LDL were slightly greater in boys at all ages except 11, 15, and 17 yrs ($p>0.05$). HDL was similar between the sexes until 13 yrs when values became greater in girls (3.2 to 13.8 mg/dl) ($p<0.05$ in 17+ yrs). No clear pattern of sex differences emerged for TG. Compared to the general population, blood lipids of young distance runners showed the following trends: 1) TC was above reference medians, 2) LDL tended to approximate or to be slightly above reference medians, 3) TG fluctuated about the reference medians, and 4) HDL was higher in distance runners compared to the reference medians prior to age 14 yrs, but in the older age groups, especially males, HDL either approximated or fell slightly below the reference medians. There was considerable variability in blood lipid levels among the runners. In 21 males and 18 females with serial data for 3 to 5 yrs, HDL declined 22.4 and 18.3 mg/dl ($p<0.05$) whereas TG increased 18.0 and 14.0 mg/dl ($p<0.05$ in females only) in males and females, respectively. Tracking coefficients over intervals of 3 to 5 yrs were moderate to high (0.48-0.90), except for TG in males (0.08).

INTRODUCTION

Although clinical manifestations of coronary heart disease (CHD) are not evident until adulthood, the origins of CHD are well established in childhood and adolescence (Berenson et al., 1998; Enos et al., 1955; Mahoney et al., 1996; Strong et al., 1997). Given evidence on the pediatric origins of atherosclerosis, it has been suggested that preventive strategies, including increased physical activity, begin during childhood and adolescence. Epidemiological studies in adults indicate that regular physical activity and relatively high aerobic fitness have beneficial effects on CHD risk factors, morbidity, and mortality (Blair et al., 1989; Paffenbarger and Lee, 1996). However, the roles of physical activity and aerobic fitness during childhood and adolescence on the etiology of atherosclerosis are complex and remain to be established.

Age- and sex-associated variation of blood lipids in children and adolescents are well described in the general population (Hetzel and Berenson, 1987). In contrast, little information is available on age- and sex-associated variation of blood lipids in young athletes, a subgroup of the population that is generally exposed to high levels of physical activity on a regular basis and possesses high levels of aerobic fitness. Studies of the blood lipid profiles of young athletes are limited (Atomi et al., 1986; Kyle et al., 1991; Macek et al., 1989; Nizankowska-Blaz and Abramowicz, 1983; Smith et al., 1985; Valimaki et al., 1980; Zonderland et al., 1984). Many of these cross-sectional studies have methodological shortcomings including small sample sizes, narrow age ranges, mixed samples (i.e., sexes combined), inconsistent and/or lack of information on training history, and failure to consider confounding variables such as maturity status, dietary intake, adiposity, smoking, and family history of vascular disease.

Cross-sectional comparisons of endurance-trained individuals and control subjects have been used to demonstrate the influence of physical activity or exercise training on various biological variables. Comparisons of athletes and control subjects have a selection bias that limits generalizations. However, to establish an understanding of the influence of intensive training on the blood lipid profile requires the recruitment of individuals regularly engaged in endurance training since the general population does not participate in high levels of vigorous physical activity. Although there may be genetic pre-disposition among athletes, part of the variation in a biological variable in elite athletes may also be explained by environmental factors and genotype-environmental interactions. Thus, the phenotypic expression of a biological variable in athletes also expresses the influence of an environmental factor such as regular physical activity.

Unlike cross-sectional approaches, longitudinal study of young distance runners provides an opportunity to examine the potential intervention of regular endurance training on the modification of the blood lipid profile during the early years of life when the atherosclerotic process begins. Although such a study has been proposed (Macek et al., 1989), apparently it has not been conducted. As a result, the pattern of development of blood lipids in young athletes is incomplete. This paper describes age- and sex-associated variation of blood lipids in a mixed-longitudinal sample of male and female distance runners, 9 to 18 yrs of age. Specific questions include the following: (1) How does the blood lipid profile of young distance runners compare to the general pediatric population?, and (2) Is the decline in high-density lipoprotein during male adolescence attenuated by regular endurance exercise training? It was hypothesized that the blood lipid profile of young distance runners will be superior to that in the general population as

observed in well-trained adult endurance athletes (Haskell, 1984), and the decline in high-density lipoprotein in males during adolescence would be attenuated in young distance runners.

METHODS

Subjects. Runners between the ages of 8 and 15 yrs who consistently placed within the top five finishers of road races 10 km or more by age and sex were identified and contacted for the study. Race results were obtained from a statewide running publication, *Michigan Runner*, between May and August 1981. Of the runners contacted (response rate unknown), 27 male and 27 female distance runners participated in the study. Subjects entered the study between 8.0 to 15.7 yrs of age. Of the total sample, 21 males and 18 females were followed at approximately annual intervals for 3 to 5 yrs. The remainder of the subjects (6 boys and 9 girls) participated in 1 or 2 annual visits. Overall, 99 and 84 annual observations were available for males and females, respectively. In a sub-sample of subjects (16 boys, 19 girls), mean ($\pm$SD) reported weekly training volumes were 1503$\pm$920 and 1865$\pm$790 km per year in males and females, respectively. Parental consent and child assent was obtained prior to the study. The study was approved by the Michigan State University Committee on Research Involving Human Subjects.

Blood lipids. A venous blood sample was drawn from an antecubital vein after a 12 hour fast. Lipid analysis was performed according to the procedures described by the Lipid Research Clinics (Lipid Research Clinics Manual of Laboratory Operations, 1974). The ratios TC:HDL and LDL:HDL were derived from the respective concentrations.

Statistical analysis. Subjects were divided into whole year age groups (i.e., 11.0 to 11.99), except for the youngest age group that consisted of subjects 9.0 to 10.99 yrs. Each age and sex group included only one observation per subject, and subjects were regarded as independent in each age group. Descriptive statistics were calculated for each sex within each age group. A one-sample t-test was conducted to examine the age- and sex-specific means between the runners and United States reference values (Christenson et al., 1980). This approach was taken instead of comparison to a control group since control groups are often convenient samples and are not a random representative sample. Linear regression was used to determine age-related trends for each blood lipid. Age-specific sex differences were determined by a series of independent t-tests. Paired t-tests were used to examine changes in blood lipids between baseline and last visit in the 21 males and 18 females with serial data for 3 to 5 yrs . Tracking coefficients were determined by Pearson correlations controlling for age at baseline. An alpha level of 0.05 was used for significance and adjusted according to the Bonferroni procedure for multiple comparisons.

RESULTS

Age- and sex-specific values for blood lipids are shown in Tables 3.1 and 3.2 and Figures 3.1a-d and 3.2a-d. The variability in blood lipids among individuals should be noted.

Males. In boys, mean TC remains between 170-180 mg/dl from 9 to14 yrs, decreases to 164 mg/dl at 15 and 16 yrs, and increases to 180 mg/dl in the oldest age group. The

pattern for HDL shows an age-related decline in boys. Mean HDL is stable at 60 mg/dl in 9 to 12 year olds and progressively declines to 40.9 mg/dl in the oldest age group. Mean LDL remains fairly constant across age groups between 96.2 and 108.1 mg/dl. Mean TG fluctuates irregularly between 56.3 and 79.3 mg/dl from 9 and 15 yrs and increases in the oldest age groups. The mean TC:HDL ratio remains relatively stable between 2.98 and 3.17 until 13 yrs and increases consistently thereafter reaching a high value of 4.64 in the oldest age group. The same pattern emerges for the mean LDL:HDL ratio with values between 1.73 and 1.92 until 13 yrs and a peak value of 2.82 in the oldest age group. Only HDL and TG show significant ($p<0.05$) age-related trends in males.

Females. In girls, mean values of TC varies between 165 and 180 mg/dl with the exception of a value of 194 mg/dl at 11 yrs and a low value of 159 mg/dl at 16 yrs. Mean HDL is highest in the youngest age group and remains stable at about 60 mg/dl from 11 to 15 yrs before declining in the oldest age groups. There is no clear age-related pattern for LDL with values fluctuating between 92 and 119 mg/dl. Mean TG levels are lower between 9 and 13 yrs (51.5 to 65.8 mg/dl) than between 14 and 18 yrs (69.5 to 82.8 mg/dl). Both the mean TC:HDL and LDL:HDL ratios are lowest in the youngest and highest in oldest age groups. After a modest increase, both the TC:HDL and LDL:HDL ratios progressively decline from age 11 to 14 yrs. No significant age-related trends are evident in females.

Sex differences. TC and LDL are greater in male runners at all ages except 11, 15 and 17 yrs. HDL is similar between sexes until age 13 yrs, after which values remain greater in girls (3.2 to 13.8 mg/dl) ($p<0.05$ in 17+ yrs). No clear pattern of sex differences emerges

for TG, although TG values are significantly greater in the oldest age group of boys ($p<0.05$).

Comparison to reference values. Compared to reference medians for United States youth (Figures 3.1a-d and 3.2a-d), TC is above reference medians in both sexes across the age range studied. TC is 7.1-25.1 mg/dl greater in males ($p<0.05$ at 10 and 14 yrs) and 3.0-30.9mg/dl greater in females ($p<0.05$ at 11 and 14 yrs). In boys, HDL is slightly above (1.5-7.5 mg/dl; $p<0.05$,14 yrs) the reference medians until 15 yrs when values decline to the median. In girls, HDL is above (2.7-15.1 mg/dl; $p<0.05$, at 10 and 14 yrs) reference medians at all ages except 16 yrs when values are equal to reference medians. LDL is slightly greater (1.2-13.5 mg/dl; $p<0.05$, at 14 yrs) than reference medians in males and fluctuates (-2 to 24.5 mg/dl; $p<0.05$, at 11 yrs) about reference medians in females. TG fluctuates (1.3 to 24.3 mg/dl; $p<0.05$, at 13 yrs) about reference medians in males with the exception of a large increase in the oldest age group. In females, TG is less than the reference medians from 9 to 13 yrs but increases with age so that by 15 yrs values were above the reference.

Longitudinal analyses. Means and standard deviations for blood lipids at baseline and the last visit are shown in Table 3.3. The mean duration of follow-up is 3.29 ± 0.57 and 3.21 ± 0.78 yrs in males and females, respectively. TC and HDL decreases significantly ($p<0.05$) in both sexes and TG increases in both sexes ($p<0.05$ in females only). Correlations are significant between baseline and follow-up values for all blood lipids (0.48-0.90), except TG in males (0.07).

DISCUSSION

This study provides information on the development of blood lipids in a mixed-longitudinal sample of young distance runners. A major strength of this study is the mixed-longitudinal design which permits analysis of serial observations during adolescence in young athletes.

The results indicate that the development of blood lipids in young distance runners is similar to youth in the general population - TC and LDL remain stable, HDL declines during adolescence (especially in males), and TG increases with age. In contrast to observations in adult endurance athletes, the young distance runners do not possess a superior blood lipid profile except for HDL in the younger age groups. Compared to age- and sex-specific reference values for United States youth (Christenson et al., 1980), TC remains above the medians, LDL tends to approximate or to be slightly above the medians, and TG fluctuates about the medians. HDL values are higher in male and female runners prior to age 14 yrs. In the older age groups, especially in males, HDL either approximates or falls below the reference medians. Sex differences in young distance runners are similar to those observed in the general population except for the development of LDL, which is higher in males (Christenson et al., 1980).

Few studies have examined blood lipids in young endurance athletes. In a review, Rowland (1993) concluded that prepubertal athletes possess a superior lipoprotein profile compared to the general pediatric population. The appropriateness of this conclusion can be questioned given that comparisons were made with controls and not representative reference values. If the control and reference values differ (i.e., TG lower than 50th percentile, etc.), the interpretation of results may be questioned. Reference values from

the Lipids Research Clinics Prevalence Study were used as the comparison in the present study since they were based on a large, random representative sample from the United States during approximately the same time period as the study of young distance runners.

The variability of blood lipids among runners in this sample is of interest. The results are apparently not related to dietary composition. Compared to a small control sample at the time of the first visit, the young runners did not significantly differ in dietary intake of energy, protein, or fats among the runners (Schemmel et al., 1986). No subjects indicated frequent smoking.

Some runners displayed blood lipid levels that would be considered borderline or dyslipidemic based on clinical guidelines. On the other hand, most of the runners have blood lipid levels that are within desirable clinical guidelines, particularly HDL and TG. Nevertheless, despite regular participation in an endurance sport, some young athletes may display undesirable levels of cholesterol. Kyle et al. (1991) reported the variability in TC (65 to 274 mg/dl) in young athletes, but did not address it in the discussion. On the other hand, the prevalence of hypercholesterolemia in the young athletes was 15.4% and 13.6% in boys and girls, respectively [TC levels above 185 mg/dl (>90th percentile of reference values)]. Future research should recognize dylipidemias in young athletes and establish prevalence rates of dyslipidemia among youth athletic groups in general (i.e., endurance, strength/power, speed) and in specific sports (cross-country, basketball, football, etc.).

The rationale for the hypotheses of this study was based on the exposure of young distance runners to high levels of vigorous physical activity. Age-specific means indicated that HDL in runners less than 14 yrs was the only blood lipid that appeared to

be enhanced compared to the general population. The absence of lower LDL levels in young distance runners may be masked by the effect of exercise training on the biologically important LDL subfractions. Trained adult runners show lower levels of small, dense LDL particles compared to non-runners (Williams et al., 1986). The inability to demonstrate a superior blood lipid profile in adolescent distance runners may be due to the presence of desirable values in both runners and the general population of youth. Compared to the blood lipid profile of the adult endurance athlete, young distance runners have lower levels of TC, LDL, and TG (Table 3.4). This comparison would suggest that compared to adult endurance athletes, young endurance athletes, and youth in general, possess a more favorable blood lipid profile. Thus, the prevention of atherosclerosis may have the greatest impact during the transition from adolescence into adulthood.

In contrast to the finding of greater HDL in runners prior to 14 yrs, the age-related decline in HDL during adolescence in boys was not attenuated, suggesting that regular endurance training during adolescence does not attenuate the decline in HDL in boys. Longitudinal analysis also indicated a decline in HDL in female runners. The age-related decline in HDL during adolescence in boys has been explained by corresponding changes in androgens and body fat distribution (Baumgartner et al., 1989; Laskarzewski et al., 1983). Previous studies indicate that HDL remains stable in girls during adolescence (Baumgartner et al., 1989; Christenson et al., 1980). The initial values are significantly higher than the general population, and although values decrease with age, they remain slightly above those observed in the general population.

The representativeness of the sample of young runners limits generalizations of the results of this study. Subjects were not chosen randomly and the response rate was unknown. A representative sample of 'elite' young athletes from various sports would provide greater insights into the development of blood lipids among active youth.

In conclusion, the results of this study do not support the hypothesis that young distance runners possess a superior blood lipid profile compared to the general population during adolescence, except for HDL in the younger age groups. Likewise, the attenuation of the decline in HDL during male adolescence was not observed in young distance runners. During adolescence, it appears that blood lipids show a similar pattern of development in well-trained endurance athletes and the general population. In contrast to the comparison of mean values with reference values, most young distance runners possess a favorable blood lipid profile when compared to clinical values. However, dyslipidemic values are present. Further longitudinal study of the influence of regular exercise on the blood lipid profile during adolescence is warranted.

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REFERENCES

Atomi Y, Kuroda Y, Asami T, Kawahara T (1986) HDL-cholesterol of children (10 to 12 years of age) related to Vo_2max, body fat, and sex. In J Rutenfranz, R Mocellin and F Klimt (eds.): Children and Exercise XII. Champaign, IL: Human Kinetics, pp. 167-172.

Baumgartner RN, Siervogel RM, Chumlea WC, Roche AF (1989) Associations between plasma lipoprotein cholesterols, adiposity and adipose tissue distribution during adolescence. Int J Obes 13:31-41.

Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE, Wattigney WA (1998) Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. N Engl J Med 338:1650-1656.

Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW (1989) Physical fitness and all-cause mortality: a prospective study of healthy men and women. JAMA 17:2395-2401.

Christenson B, Glueck C, Kwiterovich P, Degroot I, Chase G, Heiss G, Mowery R, Tamir I, Rifkind B (1980) Plasma cholesterol and triglyceride distributions in 13,665 children and adolescents: the Prevalence Study of the Lipid Research Clinics Program. Pediatr Res 14:194-202.

Enos WF, Beyer JC, Holmes RH (1955) Pathogenesis of coronary disease in American soldiers killed in Korea. JAMA 158:912-914.

Haskell WL (1984) The influence of exercise on the concentrations of triglyceride and cholesterol in human plasma. Exerc Sport Sci Rev 12:205-244.

Hetzel BS, Berenson GS, eds. (1987) Cardiovascular Risk Factors in Childhood: Epidemiology and Prevention. Amsterdam: Elsevier.

Hickman TB, Briefel RR, Carroll MD, Rifkind BM, Cleeman JI, Maurer KR, Johnson CL (1998) Distributions and trends of serum lipid levels among United States children and adolescents ages 4-19 years: data from the Third National Health and Nutrition Examination Survey. Prev Med 27:879-890.

Kyle JM, Walker RB, Riales RR, Petty GJ, Thomas JA, Roberts MD (1991) Student athletes cholesterol screening during routine precompetition examination. J Fam Pract 33:172-176.

Labarthe DR, O'Brien B, Dunn K (1991) International comparisons of plasma cholesterol and lipoproteins. Ann NY Acad Sci 301:108-119.

Laskarzewski P, Morrison J, Gutai J, Orchard T, Khoury P, Glueck C (1983) High and low density lipoprotein cholesterols in adolescent boys: relationships with endogenous testosterone, estradiol, and quetelet index. Metabolism 32:262-271.

Lipid Research Clinics Manual of Laboratory Operations (1974) Lipid and Lipoprotein Analysis. Washington, DC: United States Department of Health, Education, and Welfare.

Macek M, Bell D, Rutenfranz J, Vavra J, Masopust J, Neidhart B, Schmidt K-H (1989) A comparison of coronary risk factors in groups of trained and untrained adolescents. Eur J Appl Physiol 58:577-582.

Mahoney LT, Burns TL, Stanford W, Thompson BH, Witt JD, Rost CA, Lauer RM (1996) Coronary risk factors measured in childhood and young adult life are associated with coronary artery calcification in young adults: the Muscatine Study. J Am Coll Cardiol 27:277-284.

Nizankowska-Blaz T, Abramowicz T (1983) Effects of intensive physical training on serum lipids and lipoproteins. Acta Paediatr Scand 72:357-359.

Paffenbarger RS, Lee I-M (1996) Physical activity and fitness for health and longevity. Res Q Exerc Sport 67 (Suppl. 3):11-28.

Rowland TW (1993) The physiological impact of intensive training on the prepubertal athlete. In BR Cahill and AJ Pearl (eds.): Intensive Participation in Children's Sports. Champaign, IL: Human Kinetics, pp. 167-193.

Schemmel RA, Stone M, Conn C (1986) Comparison of dietary habits and nutrient intake of competitive runners with age- and gender-matched controls. In MR Weiss and D Gould (eds.): Sport for Children and Youths. Champaign, IL: Human Kinetics, pp. 230-236.

Smith BW, Metheny WP, Van Huss WD, Seefeldt VD, Sparrow AW (1983) Serum lipids and lipoprotein profiles in elite age-group endurance runners. Circulation :III-191 (Abstract).

Smith BW, Sparrow AW, Heusner WW, Van Huss WD, Conn C (1985) Serum lipid profiles of pre-teenage swimmers. Med Sci Sports Exerc 17:220 (Abstract).

Strong JP, Malcom GT, Oalmann MC, Wissler RW (1997) The PDAY Study: natural history, risk factors, and pathobiology. Ann NY Acad Sci 811:226-235.

Valimaki I, Hursti M-L, Pihlakoski L, Viikari J (1980) Exercise performance and serum lipids inrelation to physical activity in schoolchildren. Int J Sports Med 1:132-136.

Williams PT, Krauss RM, Wood PD, Lindgren FT, Giotas C, Vranizan KM (1986) Lipoprotein subfractions of runners and sedentary men. Metabolism 35:45-52.

Zonderland ML, Erich WBM, Peltenburg AL, Havekes L, Bernink MJE, Huisveld IA (1984) Apolipoprotein and lipid profiles in young female athletes. Int J Sports Med 5:78-82.

Table 3.1. Age-associated variation in blood lipids of young male distance runners.

	n	TC	HDL	LDL	TG	TC:HDL	LDL:HDL
9-10	12	180.9 (25.9)	60.5 (15.2)	105.0 (24.4)	76.8 (38.1)	3.17 (0.88)	1.88 (0.74)
		132-218	37-81	48-137	27-162	1.87-4.36	0.65-2.84
11	13	170.1 (24.8)	61.8 (15.8)	96.2 (26.5)	60.5 (39.0)	2.98 (1.08)	1.73 (0.81)
		136-205	28-83	52-128	25-173	1.69-5.82	0.62-3.57
12	12	178.6 (35.0)	61.1 (19.2)	106.3 (34.8)	56.3 (18.7)	3.12 (0.95)	1.92 (0.90)
		130-232	39-108	58-155	21-82	1.64-5.20	0.54-3.97
13	17	170.6 (23.1)	56.5 (13.6)	98.2 (21.5)	79.3 (34.6)	3.13 (0.65)	1.84 (0.62)
		126-208	41-87	68-139	45-179	2.12-4.37	0.93-3.10
14	17	177.1 (21.4)	55.5 (13.5)	107.5 (19.5)	70.2 (33.3)	3.35 (0.82)	2.08 (0.76)
		135-204	36-78	76-135	33-168	2.48-4.86	1.27-3.56
15	13	164.8 (26.8)	48.8 (10.9)	102.8 (17.9)	65.5 (22.9)	3.47 (0.66)	2.18 (0.54)
		117-228	27-67	71-141	30-104	2.68-5.33	1.42-3.56
16	8	164.2 (35.6)	46.0 (9.1)	100.7 (26.0)	87.1 (52.2)	3.65 (0.79)	2.27 (0.66)
		127-247	33-63	69-154	58-213	2.38-4.94	1.09-3.08
17+	7	180.0 (43.5)	40.9 (9.9)	108.1 (34.2)	120.7 (65.1)	4.64 (1.47)	2.82 (1.12)
		133-251	25-54	70-169	70-227	2.68-6.37	1.30-4.03

See text for abbrevations.
All values are expressed in mg/dl.
Values are Mean (SD) and range.

Table 3.2. Age-associated variation in blood lipids of young female distance runners.

	n	TC	HDL	LDL	TG	TC:HDL	LDL:HDL
9-10	8	173.9 (23.9)	65.1 (8.9)	98.6 (19.6)	51.5 (14.0)	2.69 (0.37)	1.54 (035)
		142-223	47-77	65-134	22-66	2.22-3.36	1.02-2.15
11	11	193.9 (33.9)	61.2 (20.2)	119.5 (35.8)	65.8 (21.8)	3.44 (1.19)	2.19 (1.06)
		127-249	37-111	61-158	39-105	1.72-5.70	0.65-4.16
12	13	173.8 (30.9)	59.8 (19.0)	102.2 (29.6)	58.8 (19.3)	3.10 (0.82)	1.88 (0.77)
		117-232	35-102	63-147	36-86	1.76-4.40	0.68-3.08
13	15	165.5 (27.4)	59.7 (20.0)	93.0 (25.1)	63.9 (36.6)	2.99 (0.92)	1.74 (0.83)
		132-228	31-109	61-149	27-179	1.84-5.29	0.75-3.81
14	12	175.5 (34.4)	61.9 (15.6)	98.0 (28.5)	79.0 (39.0)	2.94 (0.68)	1.66 (0.56)
		126-243	40-93	76-154	40-156	1.99-4.19	0.90-2.65
15	12	179.6 (48.2)	59.1 (18.5)	101.9 (37.9)	82.8 (57.4)	3.23 (1.05)	1.86 (0.76)
		127-274	27-99	66-177	39-240	2.18-5.70	0.79-3.09
16	5	159.0 (10.6)	52.0 (5.3)	92.4 (13.0)	73.6 (33.6)	3.09 (0.44)	1.80 (0.34)
		146-174	44-58	77-111	52-133	2.52-3.57	1.33-2.22
17+	8	186.6 (52.6)	54.7 (15.1)	118.9 (46.9)	69.5 (34.1)	3.57 (1.07)	2.30 (0.96)
		119-271	33-78	65-191	29-118	2.14-4.84	1.04-3.41

See text for abbreviations.
All values are expressed in mg/dl.
Values are Mean (SD) and range.

Table 3.3. Means and standard deviations for blood lipids at baseline and at last visit in longitudinal cohorts of male and female distance runners.

Variable	Males (n=21)	Females (n=18)
TC (mg/dl)		
Baseline	177.6 (23.0)	180.2 (36.1)
Last visit	163.1 (29.6)*	170.0 (34.3)*
HDL (mg/dl)		
Baseline	66.7 (9.2)	71.2 (16.8)
Last visit	44.3 (9.2)*	52.9 (13.0)*
LDL (mg/dl)		
Baseline	97.1 (24.3)	97.8 (31.7)
Last visit	101.5 (26.3)	103.3 (31.9)
TG (mg/dl)		
Baseline	68.5 (39.1)	54.4 (26.9)
Last visit	86.5 (45.5)	68.4 (29.9)*

* significantly different from baseline ($p<0.05$).

Table 3.4. Comparison of blood lipid profiles of adolescent and adult distance runners and non-athletes. Data from present study, Christenson et al., (1980), and Haskell (1984).

	13 yr old runner	13 yr old reference	16 yr old runner	16 yr old reference	Adult runner	Sedentary adult
Males						
TC	171	160	164	152	200	212
HDL	56	56	46	46	64	43
LDL	98	95	101	93	125	139
TG	79	62	87	68	70	146
Females						
TC	165	162	159	160	193	209
HDL	60	53	52	53	75	56
LDL	93	93	92	95	113	124
TG	64	72	74	68	56	123

See text for abbreviations.
All values are expressed in mg/dl.

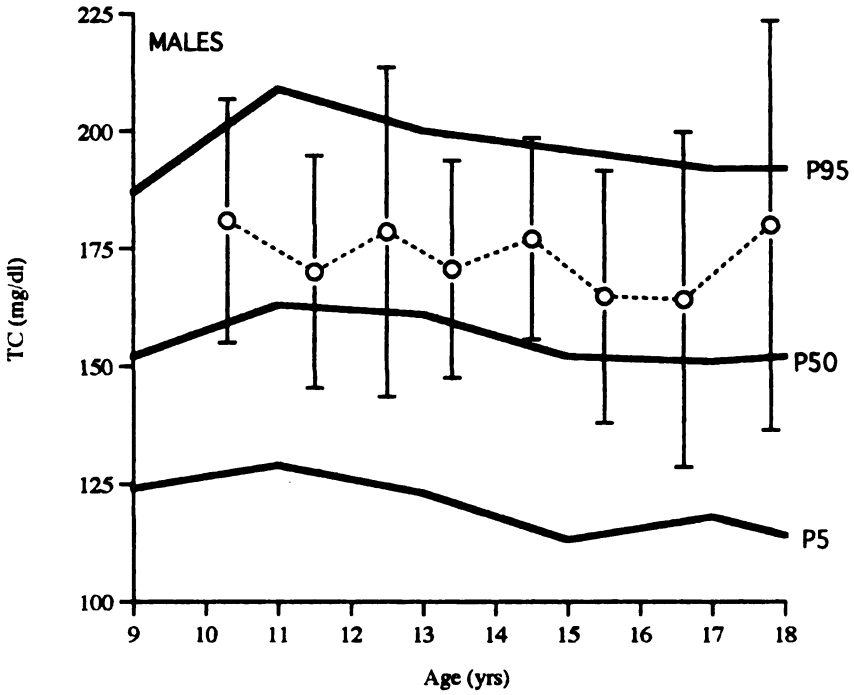

Figure 3.1a. Total cholesterol in male distance runners compared to age-specific reference values (Christenson et al., 1980).

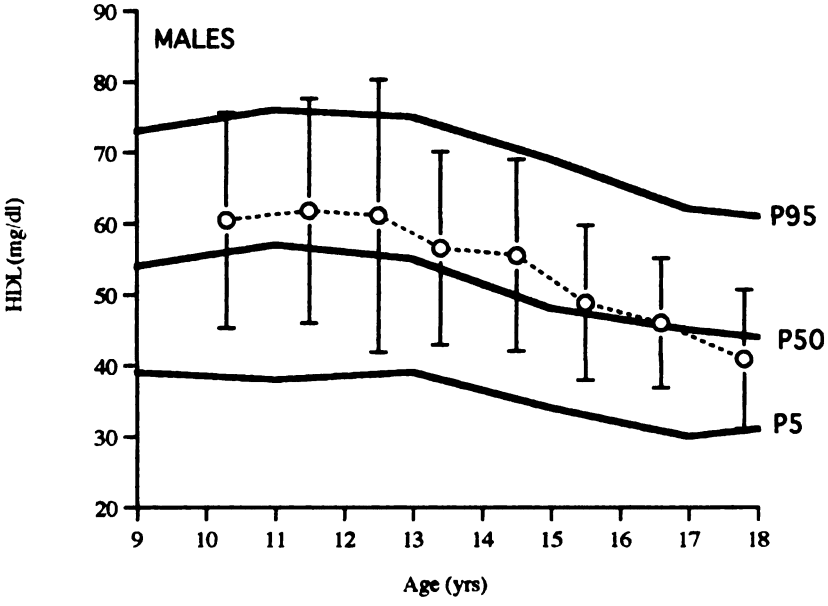

Figure 3.1b. High-density lipoprotein (HDL) cholesterol in male distance runners compared to age-specific reference values (Christenson et al., 1980).

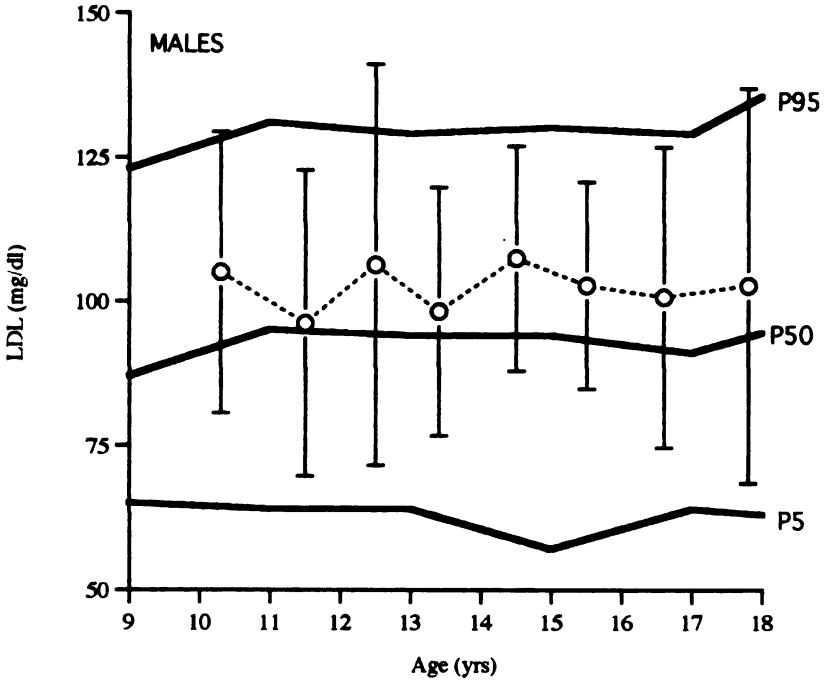

Figure 3.1c. Low-density lipoprotein (LDL) cholesterol in male distance runners compared to age-specific reference values (Christenson et al., 1980).

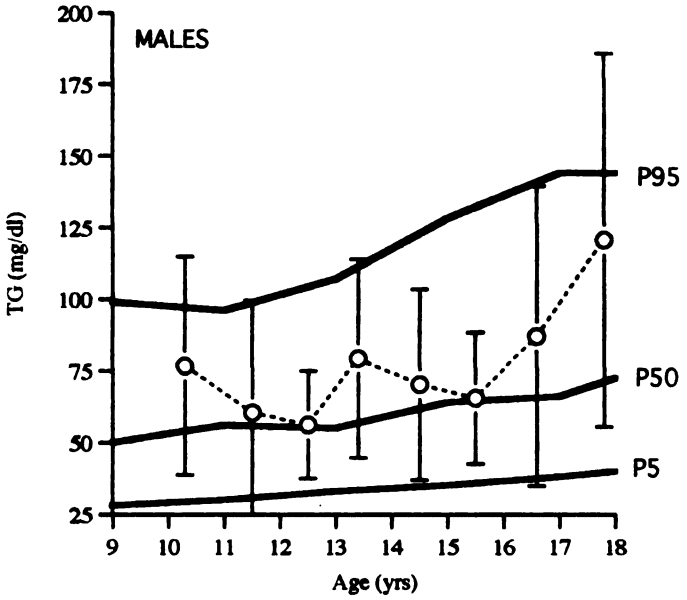

Figure 3.1d. Triglycerides (TG) in male distance runners compared to age-specific reference values (Christenson et al., 1980).

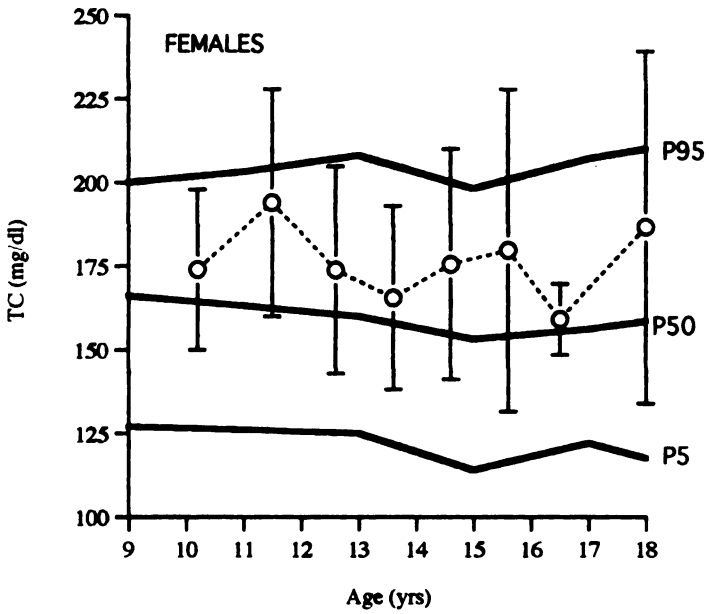

Figure 3.2a. Total cholesterol in female distance runners compared to age-specific reference values (Christenson et al., 1980).

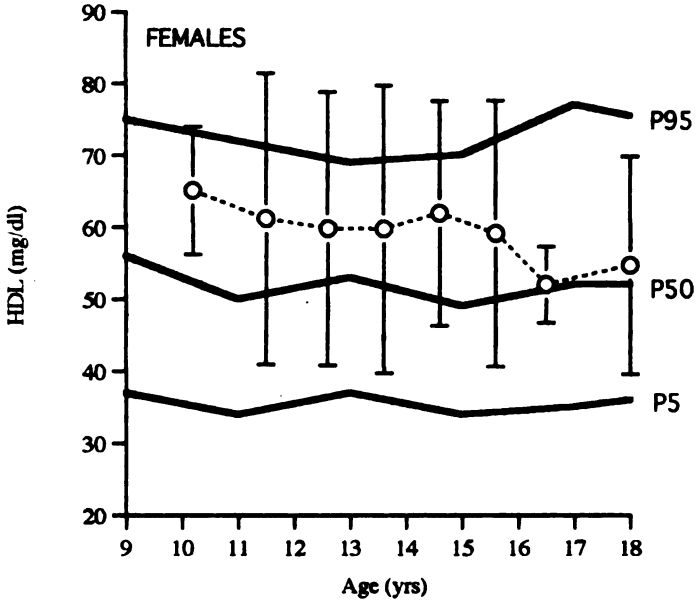

Figure 3.2b. High-density lipoprotein (HDL) cholesterol in female distance runners compared to age-specific reference values (Christenson et al., 1980).

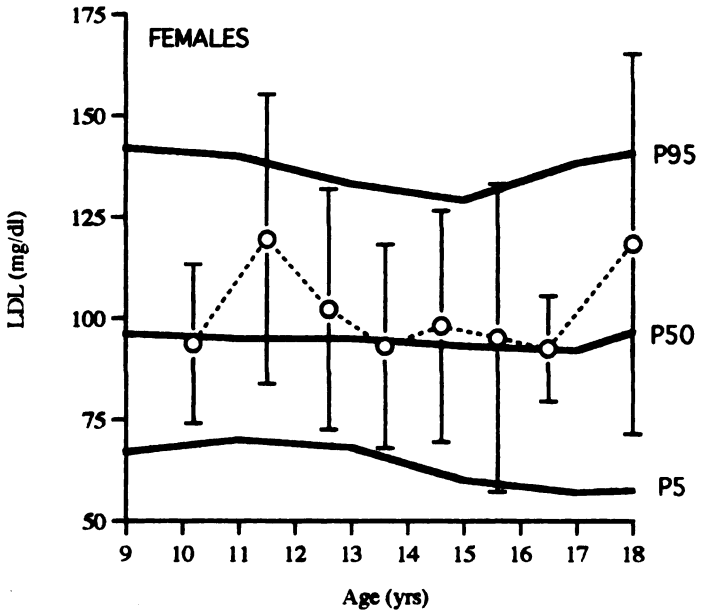

Figure 3.2c. Low-density lipoprotein (LDL) cholesterol in female distance runners compared to age-specific reference values (Christenson et al., 1980).

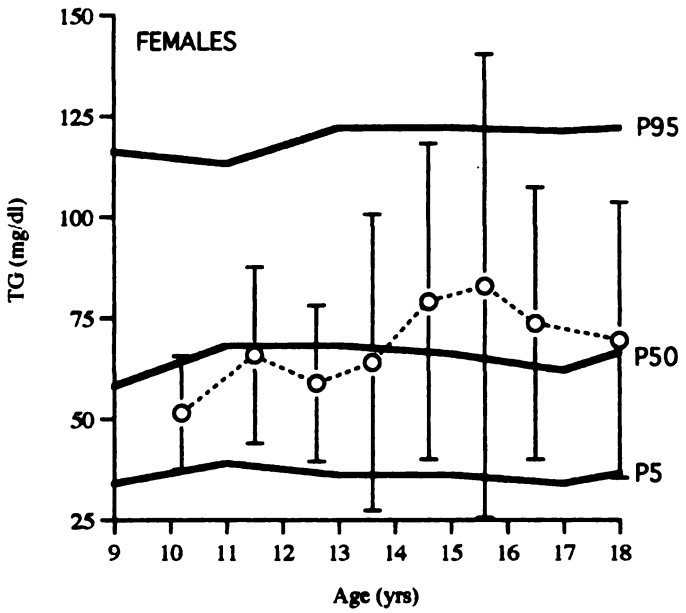

Figure 3.2d. Triglycerides (TG) in female distance runners compared to age-specific reference values (Christenson et al., 1980).

CHAPTER 4

BLOOD LIPIDS OF YOUNG DISTANCE RUNNERS: DISTRIBUTION AND COMPARISON TO REFERENCE VALUES AND CLINICAL CUT-POINTS

ABSTRACT

This report describes the distribution of blood lipids in a sample of 48 male and 22 female young distance runners,10-19 yrs of age. A fasting blood sample was obtained by fingerprick. Total cholesterol (TC), high-density lipoprotein (HDL), and triglycerides (TG) were analyzed by a portable cholesterol analyzer (Cholestech LDX). Low-density lipoprotein (LDL) was estimated by the Friedewald equation. Comparisons were made between sexes, and to a current reference sample (NHANES III, 1988-1994) and clinical cut-points. LDL was significantly greater in male compared to female runners. Males also had a greater likelihood of having "undesirable" levels of blood lipids (i.e., above desirable levels based on clinical cut-points) than females. Compared to current reference medians, mean values of TC ($p=0.07$) and LDL ($p<0.005$) were higher, while HDL ($p=0.24$) was slightly higher in male distance runners. Blood lipids in female distance runners were comparable to reference medians. Compared to reference means, TC, LDL, and TG in female runners are significantly lower ($p<0.05$). Although some subjects had dyslipidemic values, most possessed desirable levels of blood lipids. Thus, blood lipids of young male distance runners from the mid-Michigan area are not, on average, superior to the general population of U.S. youth. In females, results depend on the reference of comparison (i.e., means or medians). Young distance runners show considerable heterogeneity in blood lipid phenotypes, including dyslipidemic values.

INTRODUCTION

Adult long-distance runners generally display a superior blood lipid profile (i.e., elevated high-density lipoprotein, lower low-density lipoprotein and triglycerides) compared to the general population (Haskell, 1984). Relatively few studies have examined the blood lipid profile of young athletes (Atomi et al., 1986; Kyle et al., 1991; Macek et al., 1989; Nizankowska-Blaz and Abramowicz, 1983; Smith et al., 1985; Valimaki et al., 1980; Zonderland et al., 1984). Results of these studies suggest that young athletes also have a superior blood lipid profile compared to non-athletic control samples. The studies are limited, however, by subject selection, sample size, mixed samples (either by sex or sport), and inappropriate control groups. Further, the inter-individual variability of blood lipids among young athletes is not ordinarily considered.

This brief report provides descriptive data on the distribution of blood lipids in a current sample of young distance runners. Comparisons are made to a current reference sample, clinical cut-points, and previous studies of young athletes.

METHODS

Subjects. Males and females 10 to19 years of age participating on mid-Michigan junior or senior high school cross-country and track teams during Fall 1999 and Spring 2000 were invited to participate in the current study. Subjects were also recruited by advertisements in the local newspaper and at local road races. Exclusion criteria included current smokers, excessive alcohol intake, current use of blood cholesterol lowering and anti-hypertensive medication, anabolic steroid use, hepatic, renal, and thyroid disease, or training less than 30-40 weeks per year or the past three consecutive months. The total

number of eligible subjects in the mid-Michigan area during recruitment is difficult to determine given the exclusion criteria. Forty-eight males and 22 females volunteered to participate in the study. Parental consent and subject assent were obtained prior to testing. The study was approved by the Michigan State University Committee on Research Involving Human Subjects.

Blood lipids. Data collection occurred between the hours of 7:00 a.m.-12:00 p.m. A fasting blood sample was obtained by fingerprick after the subject had been seated for 10 minutes. Blood was collected in a 35 micro-liter capillary tube. Upon collection, samples were analyzed for total cholesterol (TC), high-density lipoprotein (HDL), and triglycerides (TG) within 5 minutes by a portable cholesterol analyzer according to the protocol of the manufacturer (Cholestech LDX System, Hayward, CA). The lower limit of analytic capacity of the Cholestech LDX for TG is 45 mg/dl. In the present study, eight individual values were recorded at the lower limit (e.g., <45 mg/dl). Low-density lipoprotein (LDL) cholesterol was estimated by the Friedewald equation (Friedewald et al., 1972).

The total error of measurement of the Cholestech LDX analyzer has been determined as 12.7%, 18.8%, and 19.7% for TC, HDL, and TG, respectively. The reference laboratory measurement error is 8.1%,12.9%, and 5.1% for TC, HDL, and TG, respectively (Bard et al., 1997). The total error for HDL met the standard set forth by National Cholesterol Education Program (<22%), but TC and TG were slightly higher than the respective standards (8.9 and 15%).

Within-day reliability was determined prior to the onset of the study by five consecutive measurements with Cholestech Level 1 and 2 liquid control reagents. Day-to-day reliability was determined by daily calibration prior to each testing session throughout the study. Within-subject reliability was determined by duplicate measures of 1 of every 5 male and female subjects. Coefficients of variation were used to express the precision of the within-day and day-to-day trials and compared to national standards. The coefficients of variation (CV) for within-day and day-to-day trials were less than 2% and 4%, respectively, for standard controls of TC, HDL, and TG. Within-subject precision of blood lipid measurements was high (0.996, TC; 0.943, HDL; 0.970, TG).

Anthropometry. Stature and body mass were measured according to the procedures of the International Biology Program (Weiner and Lourie, 1969). Stature was measured with the subject standing erect, without shoes, and with weight distributed evenly between both feet, heels together, arms relaxed at the sides, and the head in the Frankfort horizontal plane with a fixed stadiometer. Body mass was measured on a beam scale with the subject attired in running shorts and T-shirt without shoes. The stadiometer and scale were calibrated throughout the study.

Sexual maturity status. Given the difficulty in direct assessment of sexual maturity status in a non-medical environment, a self- assessment of sexual maturity status was used in the current study. Self-assessment was conducted in a separate, private station following an explanation of the purpose of the assessment. Subjects rated their stage of sexual development relative to sex-appropriate sets of drawings/photos and verbal descriptions

(Van Wieringen et al., 1971) based on the criteria of Tanner (1962). In a study of 174 female and 178 male Brazilian youth age 6-26 years (Matsudo and Matsudo, 1994), the concordance between self and physician assessments of secondary sex characteristics was reasonably high (60-71.3%). Test-retest concordance (i.e., reproducibility) was also similar between self- and physician-assessments.

Statistical analysis. Descriptive statistics were calculated for anthropometric and blood lipid values. Sex differences were examined by a non-parametric Mann-Whitney U test. A one-sample independent t-test was used to examine differences between group means for distance runners and the general population. Reference values (means and medians) for blood lipids from the Third National Health and Nutrition Examination Survey (NHANES III) were used for comparison (Hickman et al., 1998). The sample was also grouped by age (12-15 yrs and 16-19 yrs) for comparative purposes. Individual values for each blood lipid were plotted by age relative to lines of identity for clinical cut-points (see Table 4.4). An alpha level of $p<0.05$ was used for statistical significance.

RESULTS

Subject characteristics are given in Table 4.1. Some of the inter-individual variability in body size can be accounted for by chronological age and sexual maturity status. Only 2 subjects are younger than 12.0 yrs of age. Both subjects are pre-pubescent, whereas the remainder are late- or post- pubescent (genital/breast stages 4 or 5) (Table 4.2). Due to the lack of variation in pubertal status, maturity-associated variation of blood lipids was not examined in this sample.

One subject was identified as an outlier and therefore eliminated from the analysis (TC=309). The subject was referred to a physician for further diagnosis. Blood lipids of young male and female distance runners and available reference medians are shown in Table 4.3. LDL is significantly greater in male compared to female runners ($p<0.05$). Mean values of TC ($p=0.07$) and LDL ($p<0.005$) are higher in male runners compared to reference medians. HDL is also slightly higher in male distance runners ($p=0.24$). Mean values in female distance runners are comparable to reference medians, but compared to reference means, TC, LDL, and TG in female runners are significantly lower ($p<0.05$).

Scatterplots of individual values in relation to clinical cut-points are shown in Figures 1a-d. Although some subjects have dyslipidemic values, most possess desirable blood lipid levels (Table 4.4). When borderline and high (or low for HDL) values are grouped together to represent "undesirable" levels, chi-square analysis indicates that males have a greater likelihood of being classified as undesirable for LDL and TG compared to females ($p<0.05$). There is a trend for a greater likelihood of males being classified as undesirable for TC ($p=0.20$) and HDL ($p=0.12$).

DISCUSSION

This is perhaps the largest sample of young male and female athletes which fasting blood lipids (TC, HDL, LDL, TG) are reported . A previous report of 777 (454 males and 323 females) athletes in West Virginia included only TC (Kyle et al., 1991). The findings from this brief report indicate that mean values for blood lipids of young male distance runners from the mid-Michigan area are not superior to the general population of U.S. youth. TC, LDL, and TG are lower in young female distance runners

compared to the general population. There is considerable inter-individual variability in blood lipids, including dyslipidemic values, among adolescent distance runners. Nevertheless, most subjects displayed desirable levels compared to clinical cut-points (Table 4.4).

Previous studies comparing the blood lipids of young athletes and controls have reported similar levels of TC, lower levels of TG and LDL, and higher levels of HDL (Atomi et al., 1986; Kyle et al., 1991; Macek et al., 1989; Nizankowska-Blaz and Abramowicz, 1983; Smith et al., 1985; Valimaki et al., 1980; Zonderland et al., 1984). Mean differences among samples for TC are generally within $\pm$10 mg/dl while mean differences for LDL and TG range from 5-25 mg/dl and 20-35 mg/dl, respectively. Two studies reported no appreciable differences in TG (Atomi et al., 1986; Smith et al., 1985). Mean differences among previous studies for HDL range from 4-17 mg/dl higher in adolescent athletes. This study is apparently the first to report higher levels of LDL in adolescent athletes. The findings in the present sample generally contrast previous studies that have shown that child and adult male endurance athletes possess a superior blood lipid profile compared to the general population. The reasons for this observation are considered subsequently.

Previous cross-sectional studies have several methodological limitations that need to be addressed. First, the main purpose of cross-sectional studies of athletes is to provide information on the status of a sample. To truly provide an accurate description of a group (i.e., adolescent distance runners), a random representative sample should be selected. An additional question is, "Who is the adolescent distance runner?" Athletes may compete at several levels (i.e., international, national, regional, state, local,

recreational), and often compete in more than one sport. In most studies, inadequate information is provided on the sample and subject selection process. No study has included a random representative sample of young distance runners or athletes. Likewise, no study has included a random sample of young athletes at different competitive levels.

Response rate is another measure of subject recruitment that has been neglected. It is also important to consider the selection of control subjects. Only one study has used randomly selected controls (Macek et al., 1989). Others are based on convenient samples. Therefore, blood lipids in control subjects may not be representative of the general population. Since most of these studies were conducted outside of the U.S., the availability of national reference data is unknown. To avoid such complications, reference medians from NHANES III (1988-1994) were used in the current study. Additional methodological issues include the analytic and biological variability that influence blood lipids.

Compared to previous studies of young athletes, mean values of TC and LDL are comparable. In contrast, levels of HDL and TG are lower and higher, respectively. The range of previously reported values of HDL and TG are 52-75 mg/dl and 54-71 mg/dl, respectively. However, comparison of the results to international samples warrants caution due to known population differences in blood lipids (Labarthe et al., 1991). Subjects in previous studies were also generally younger than in the present study. The age-related decrease in HDL and increase in TG is well documented, particularly in males (Tamir et al., 1981), and may contribute to differences between samples of young athletes and in the comparison with reference values.

A finding of potential interest in the present study is the heterogeneity in blood lipid phenotypes among young distance runners. Few studies examine variability in the phenotypic expression of a given biological variable of athletic subgroups (Eisenmann and Malina, in press). Valimiki et al. (1980) showed variability of HDL plotted against physical work capacity in a small sample of boys. Extrapolation from the figure shows values ranging from 55 to 85 mg/dl in 9 trained boys. The range of HDL (and other blood lipids) is much greater in the present sample of boys (28 to 88 mg/dl) and includes dyslipidemic values (Table 4.4). Only one study has specifically examined the prevalence of dyslipidemia in young athletes (Kyle et al., 1991). In the sample of 777 West Virginia junior high school athletes, 114 (15%) were classified as having elevated TC (>185 mg/dl). Sex-specific prevalence rates were 15.4% and 13.6% for boys and girls, respectively. Of these individuals, 8% (n=60) had values greater than 200 mg/dl. In comparison, 6 of the 69 (9%) runners in the original sample had values greater than 200 mg/dl. Overall, TC ranged from 65-274 mg/dl in the sample of Kyle et al. (1991) compared to 100-241 in the present study. Unfortunately, athletic subgroups were not identified in the West Virginia sample. In adult male runners, the prevalence of clinically diagnosed low HDL (<35 mg/dl) and high LDL (>160 mg/dl) was associated with distance run per week (Williams, 1997). These findings along with those of the present study show that even distance runners involved in high levels of training may possess dyslipidemic values. The results also provide implications for the pre-season screening of youth athletes for dyslipidemia, particularly if a family history of cardiovascular disease is present (American Academy of Pediatrics, 1992).

Variability in blood lipids may also result from analytical or biological factors. As shown by Kyle et al. (1991), a single measurement warrants consideration of daily variation and regression to the mean. Upon follow-up testing, 38 of 74 (51%) of the West Virginia athletes had values that remained above 185 mg/dl. Due to feasibility issues, repeat measurements were not taken on subjects who displayed initial dyslipidemic values in the present study. However, the day-to-day variation suggests that multiple measures may provide a better indication of individual values. Based on the single measurement obtained in this study, the coefficients of variation was low (2-4%) and similar to other reports using the same portable analyzer. Rogers et al. (1993) reported within-day and day-to-day precision between 1.5-1.8% and 2.8-3.4%, respectively for TC. These results provide evidence of the reliability and reproducibility of blood measurements in this study. Information on the precision of blood lipid measurements is not provided in previous studies of young athletes.

Biological factors that need to be considered include chronological age, seasonal variation, dietary and alcohol intake, acute and chronic exercise, family history, genotype, psychological stress, biological maturity, and body fatness. Other factors (secondary dyslipoproteinemias, medication, trauma and acute infections, pregnancy, blood collection conditions (e.g., fasted vs. non-fasted state, position, storage, etc.) (Naito and Kwak, 1992) were considered in the design of this study. Each of these analytical and biological factors should be considered when comparing blood lipid studies.

In conclusion, the results of the study suggest that young male distance runners from the mid-Michigan area do not possess a superior blood lipid profile compared to reference values for United States youth and contrast previous studies of young athletes.

Results for females depend on the reference comparison (i.e., means or medians). However, several methodological limitations need to be recognized, specifically subject selection, biological confounders, analytical errors, and comparison methods. The considerable heterogeneity in blood lipid phenotypes and dyslipidemia of young athletes warrants exploration. The contribution of training volume, peak oxygen consumption, body fatness, and family history of vascular diseases on the blood lipid profile in this sample is considered in a separate analysis.

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REFERENCES

American Academy of Pediatrics (1992) National Cholesterol Education Program Report of the expert panel on blood cholesterol levels in children and adolescence. Pediatr 89:525-577.

Atomi Y, Kuroda Y, Asami T, Kawahara T (1986) HDL-cholesterol of children (10 to 12 years of age) related to Vo2max, body fat, and sex. In J Rutenfranz, R Mocellin and F Klimt (eds.): Children and Exercise XII. Champaign, IL: Human Kinetics, pp. 167-172.

Bard RL, Kaminsky LA, Whaley MH, Zajakowski S (1997) Evaluation of lipid profile measurements obtained from the Cholestech LDX analyzer. J Cardiopul Rehab 17:413-418.

Eisenmann JC, Malina RM (in press) Body size and endurance performance. In RJ Shephard (ed.): Endurance in Sport. Oxford: Blackwell Science.

Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 18:499-502.

Haskell WL (1984) The influence of exercise on the concentrations of triglyceride and cholesterol in human plasma. Exerc Sport Sci Rev 12:205-244.

Hickman TB, Briefel RR, Carroll MD, Rifkind BM, Cleeman JI, Maurer KR, Johnson CL (1998) Distributions and trends of serum lipid levels among United States children and adolescents ages 4-19 years: data from the Third National Health and Nutrition Examination Survey. Prev Med 27:879-890.

Kyle JM, Walker RB, Riales RR, Petty GJ, Thomas JA, Roberts MD (1991) Student athletes cholesterol screening during routine precompetition examination. J Fam Pract 33:172-176.

Labarthe DR, O'Brien B, Dunn K (1991) International comparisons of plasma cholesterol and lipoproteins. Ann NY Acad Sci 301:108-119.

Macek M, Bell D, Rutenfranz J, Vavra J, Masopust J, Neidhart B, Schmidt K-H (1989) A comparison of coronary risk factors in groups of trained and untrained adolescents. Eur J Appl Physiol 58:577-582.

Matsudo SMM, Matsudo VKR (1994) Self-assessment and physician assessment of sexual maturation in Brazilian boys and girls: concordance and reproducibility. Am J Hum Biol 6:451-455.

Naito HK, Kwak Y-S (1992) Accurate measurement of serum total cholesterol: the need for standardization. J Am Coll Nutr 11 (Suppl.):8S-15S.

Nizankowska-Blaz T, Abramowicz T (1983) Effects of intensive physical training on serum lipids and lipoproteins. Acta Paediatr Scand 72:357-359.

Rogers EJ, Misner L, Ockene IS, Nicolosi RJ (1993) Evaluation of seven Cholestech LDX analyzers for total cholesterol determinations. Clin Chem 39:860-864.

Smith BW, Sparrow AW, Heusner WW, Van Huss WD, Conn C (1985) Serum lipid profiles of pre-teenage swimmers. Med Sci Sports Exerc 17:220 (Abstract).

Tamir I, Heiss G, Glueck CJ, Christensen B, Kwiterovich P, Rifkind BM (1981) Lipid and lipoprotein distributions in White children ages 6-19 yr: the Lipid Research Clinics Program Prevalence Study. J Chron Dis 34:27-39.

Tanner JM (1962) Growth at Adolescence. 2nd edition, Oxford: Blackwell.

Tikkanen HO, Harkonen M, Naveri H, Hamalainen E, Elovainio R, Sarna S, Heikki Frick M (1991) Relationship of skeletal muscle fiber type to serum high density lipoprotein cholesterol and apolipoprotein A-I levels. Atherosclerosis 90:49-57.

Valimaki I, Hursti M-L, Pihlakoski L, Viikari J (1980) Exercise performance and serum lipids inrelation to physical activity in schoolchildren. Int J Sports Med 1:132-136.

Van Wieringen JC, Wafelbakker F, Verbrugge HP, de Haas JH (1971) Growth Diagrams 1965 Netherlands: Second National Survey on 0-24-year-oldsGroningen: Wolters-Noorhoff Publishing.

Weiner JS, Lourie JA (1969) Human Biology: A Guide to Field Methods. Oxford: Blackwell Science.

Williams PT (1997) Relationship of distance run per week to coronary heart disease risk factors in 8283 male runners. Arch Intern Med 157:191-198.

Williams PT, Wood PD, Haskell WL, Vranizan K (1982) The effects of running mileage and duration on plasma lipoprotein levels. JAMA 247:2674-2679.

Zonderland ML, Erich WBM, Peltenburg AL, Havekes L, Bernink MJE, Huisveld IA (1984) Apolipoprotein and lipid profiles in young female athletes. Int J Sports Med 5:78-82.

Table 4.1. Characteristics of young distance runners.

	Males (n=47)	Females (n=22)
Age (yrs)	16.7 (2.0)	15.5 (2.6)
	10.4-19.3	9.9-18.4
Ht (cm)	174.0 (7.3)*	161.1 (9.8)
	149.2-185.1	132.7-178.1
Wt (kg)	62.1 (8.1)*	50.1 (10.4)
	39.9-85.9	27.0-71.1

Values are mean (SD) and range.
*$p<0.05$ between sexes.

Table 4.2. Distribution of subjects by pubertal status.

	M	F		M	F
G/B1	1	1	PH1	1	1
G/B2	2	1	PH2	1	1
G/B3	1	1	PH3	1	1
G/B4	20	9	PH4	8	3
G/B5	23	10	PH5	36	16

G, genital (males), B, breast (females); PH, pubic hair. The corresponding number represents the stage (e.g., PH1, stage 1 - pubic hair).

Table 4.3. Blood lipids of young distance runners compared to reference means and medians (Hickman et al., 1998).

	Males			Females		
	Runners	Reference Mean	Reference Median	Runners	Reference Mean	Reference Median
TC						
Total	165.8 (4.4)[c]	158 (1.2)	156	157.6 (3.8)[b]	167 (1.3)	161
12-15 yrs	148.5 (4.7)	158 (1.6)	157	150.7 (10.5)	164 (1.9)	159
16-19 yrs	170.1 (5.4)	158 (1.8)	155	161.0 (3.7)	171 (2.3)	163
HDL						
Total	48.2 (1.9)	47 (0.6)	46	51.7 (2.4)	52 (0.5)	51
12-15 yrs	51.8 (4.3)	48 (0.7)	46	45.2 (2.5)	51 (0.8)	50
16-19 yrs	46.9 (2.2)	46 (0.9)	45	53.9 (3.1)	52 (0.7)	52
LDL						
Total	101.6 (4.0)[a,b]	91 (2.1)	88	91.0 (3.6)[b]	99 (2.4)	92
12-15 yrs	79.6 (5.3)	88 (2.4)	83	89.5 (8.9)	94 (2.8)	90
16-19 yrs	107.1 (5.4)	94 (3.8)	89	92.6 (4.0)	103 (4.4)	94
TG						
Total	83.0 (5.6)	91 (4.0)	74	75.1 (21.8)[b]	96 (3.9)	77
12-15 yrs	74.1 (10.2)	87 (7.0)	72	82.2 (14.4)	96 (5.6)	81
16-19 yrs	86.3 (6.6)	94 (6.1)	79	72.4 (4.0)	96 (5.9)	76

Values are mean (SE).
Sample sizes for males are; total=47, 12-15 yrs=10, 16-19 yrs=36.
Sample sizes for females are; total=22, 12-15 yrs=6, 16-19 yrs=15.
[a] significant sex difference ($p<0.05$).
[b] significantly different from reference mean ($p<0.05$).
[c] significantly different from reference median ($p<0.05$).

Table 4.4. Distribution of subjects by clinical cut-points.

Category	Level (mg/dl)	Total	Males	Females
TC				
High	≥200	6 (8.7)	6 (12.8)	0 (0.0)
Borderline high	170-199	17 (24.6)	12 (25.5)	5 (22.7)
Desirable	≤170	46 (66.7)	29 (61.7)	17 (67.3)
LDL				
High	≥130	8 (12.3)	7 (16.3)	1 (4.5)
Borderline high	110-129	7 (10.8)	6 (13.9)	1 (4.5)
Desirable	≤110	50 (76.9)	30 (69.8)	20 (90.0)
HDL				
Low	≤35	8 (11.6)	7 (14.9)	1 (4.5)
Borderline low	35-45	20 (29.0)	15 (31.9)	5 (22.7)
Desirable	≥45	41 (59.4)	25 (53.2)	16 (72.7)
TG				
High	≥130	8 (11.6)	7 (14.9)	1 (4.5)
Borderline high	90-129	12 (17.4)	10 (21.3)	2 (9.1)
Desirable	≤90	49 (71.0)	30 (63.8)	19 (86.4)

TC, total cholesterol; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; TG, triglycerides.

Values represent number of subjects (%).

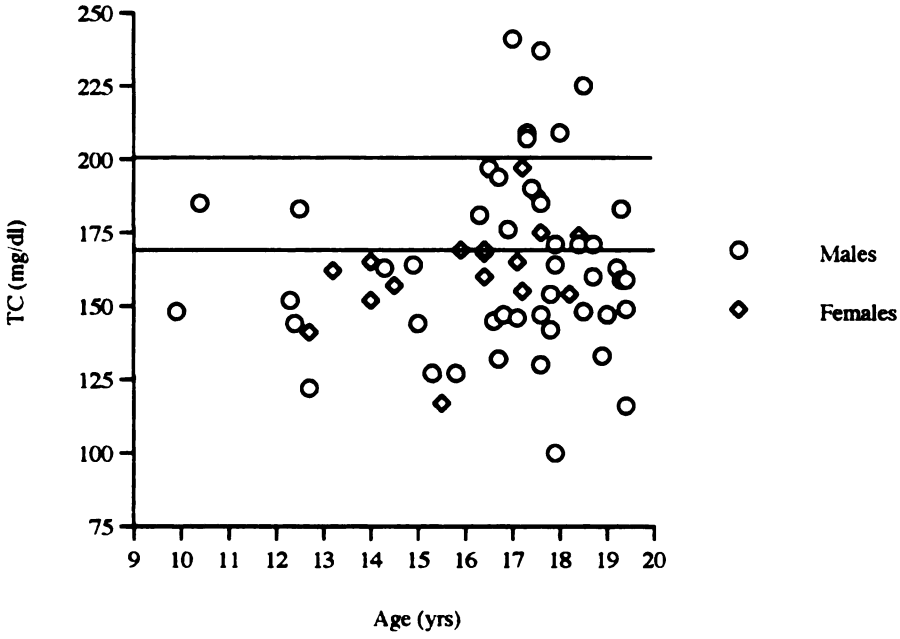

Figure 4.1a. Total cholesterol (TC) in young distance runners. Lines of identity represent clinical cut-points (see Table 4.4)

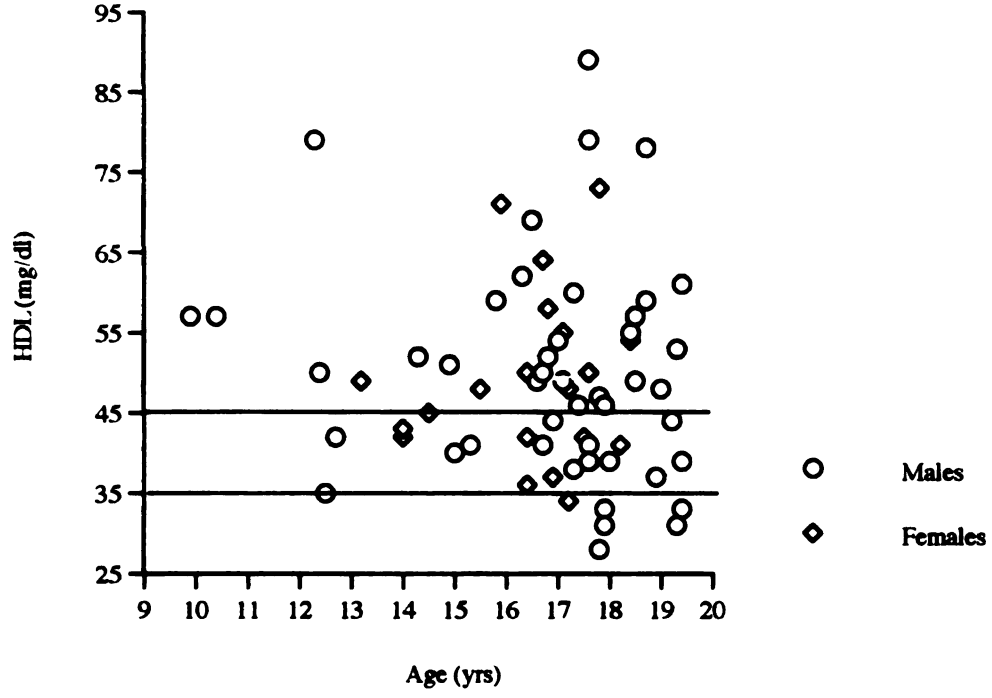

Figure 4.1b. High-density lipoprotein (HDL) in young distance runners. Lines of identity represent clinical cut-points (see Table 4.4).

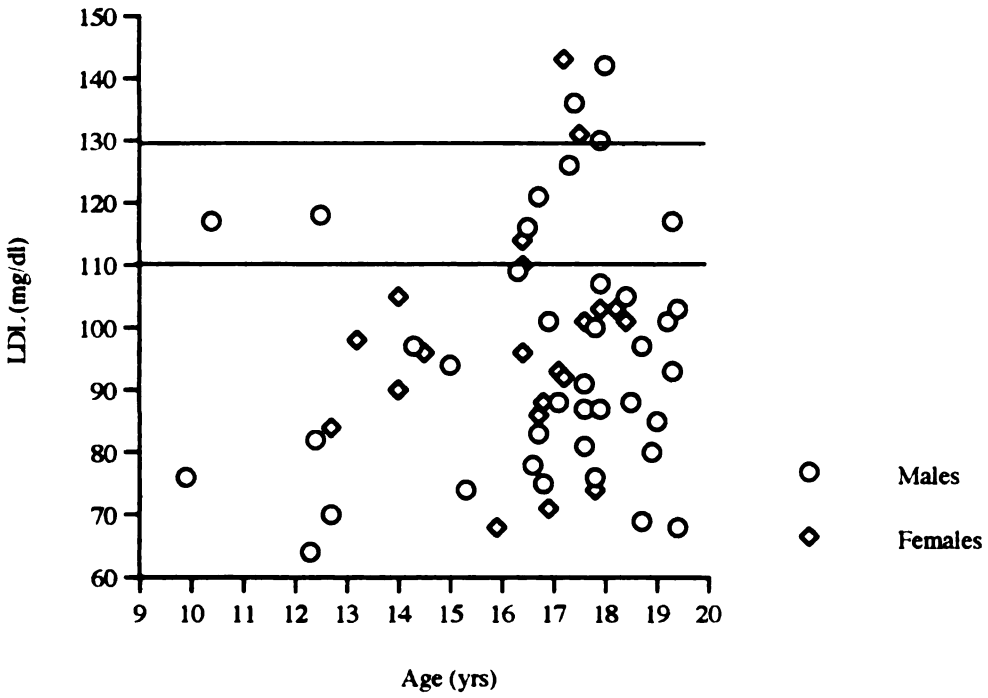

Figure 4.1c. Low-density lipoprotein (LDL) in young distance runners. Lines of identity represent clinical cut-points (see Table 4.4).

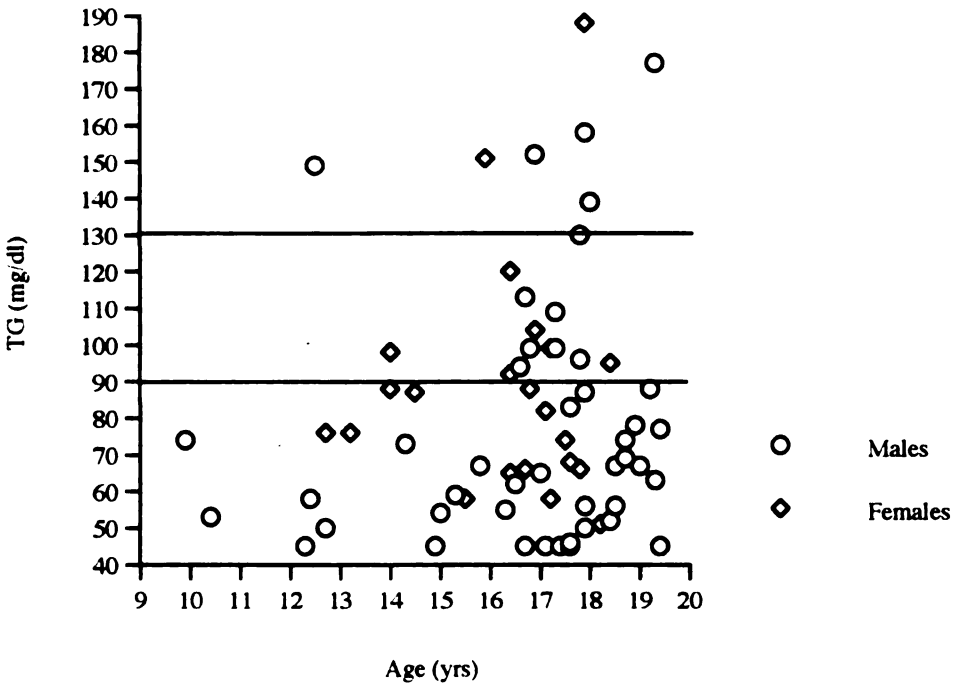

Figure 4.1d. Triglycerides (TG) in young distance runners. Lines of identity represent clinical cut-points (see Table 4.4).

CHAPTER 5

INTER-RELATIONSHIPS AMONG TRAINING VOLUME, PEAK OXYGEN CONSUMPTION, BODY FATNESS, AND BLOOD LIPIDS IN YOUNG DISTANCE RUNNERS

ABSTRACT

The inter-relationships among training volume (km per wk), peak oxygen consumption (peak Vo_2, $ml \cdot kg^{-1} min^{-1}$), body fatness, and blood lipids were examined in 45 males, 22 female young distance runners, 10 to 19 yrs of age. Training volume (TV) was estimated as the average of self-reported running habits during the past 3 months. Peak Vo_2 was measured by indirect calorimetry during an incremental treadmill test to exhaustion. Skinfold thicknesses were measured with a Lange caliper at six sites (SSF). The trunk-to-extremity ratio (TER) was calculated and used as an index of relative subcutaneous fat distribution. Blood lipids were measured in a fasted state by a portable cholesterol analyzer (Cholestech LDX). Relationships were assessed by partial correlations controlling for age and self-assessed stage of pubertal development. Overall, correlations are low to moderate. TV is weakly correlated with blood lipids, and the relationships are in the expected direction for HDL and TG in males but not in females. TV may be indirectly related with HDL through its relationship with peak Vo_2 in males ($r=0.32$). There are differential relationships between TV and HDL when the entire sample was grouped according to modified clinical cut-points. TV is significantly related to HDL in subjects with HDL<45 mg/dl ($r=0.40$, $p<0.05$). The TER is not related to blood lipids in males, with partial correlation coefficients near zero. In females, correlations between SSF, TER and blood lipids are similarly low ($r= 0.16$ to -0.27), with the exception of a moderately high correlation between TER and HDL ($r= -0.60$). The most consistent inter-relationships exist among TV, peak Vo_2, SSF, and HDL. Partial correlations range from low (0.10, TV) to moderate (0.37, SSF; 0.41, peak Vo_2). The correlation between peak Vo_2 and HDL remain significant after controlling for age and

SSF, while the partial correlation between SSF and HDL controlling for age and peak Vo_2 is reduced and not significant (r=-0.19, p=0.20). Similar relationships were found in females. When age and SSF are controlled, the correlation between peak Vo_2 and HDL is 0.32, whereas the partial correlation between SSF and HDL, controlling for age and peak Vo_2, is 0.00. The results highlight the complex inter-relationships among training volume, peak Vo_2, body fatness and HDL, and indicate the unique contribution of peak Vo_2 as an important predictor of HDL in young distance runners.

INTRODUCTION

Relationships among physical activity, physical fitness, and health are topics of considerable interest and research in pediatric exercise epidemiology (Casperson et al., 1998). In particular, the prevention of atherosclerosis by modification of the blood lipid profile with exercise has been a major focus (Despres et al., 1990; Gutin and Owens, 1996; Riopel et al., 1986). A potential outcome is the establishment of recommendations for physical activity in the adolescent population (Sallis et al., 1994). Based on currently available data, it has been recommended that four 30 minute exercise sessions per week at 75-80% of maximum heart rate may be an appropriate prescription for adolescents 12-21 years of age (Armstrong and Simons-Morton, 1994). This recommendation is derived from adult data suggesting that an exercise level equivalent to jogging 10-15 miles/wk is necessary to significantly alter or favorably maintain blood lipid levels (Superko, 1991; Williams, 1994).

A question related to the relationships between physical activity and blood lipids in children and adolescents is the following: Do health benefits accrue in youth at levels of exercise that exceed current recommendations? A possible methodological approach to this question is the use of a special exposure group (i.e., distance runners), which would allow for the examination of an exposure (i.e., high levels of physical activity) that is generally not observed in the general population. Recently, Williams (1996, 1997, 1998) has used this approach to challenge adult guidelines for physical activity (Pate et al., 1995). Results suggest that increased levels of training in adult recreational runners offers further health benefits, including an improved blood lipid profile. No study has

apparently examined the influence of training volume (distance run per week) on blood lipids in young endurance athletes.

Maximal aerobic fitness and body fatness are also correlates of blood lipids during childhood and adolescence. More aerobically fit youth generally have higher high-density lipoprotein (HDL) and lower triglycerides (TG) (Despres et al., 1990; Malina, 1990). Various measures of body fatness are positively associated with atherogenic blood lipids and negatively associated with HDL (Guo et al., 1994). Relative body fat distribution, and specifically a truncal and/or visceral fat patterning, is also strongly linked to an adverse blood lipid profile in youth and adults (Baumgartner et al., 1989; Despres, 1997; Freedman et al., 1989). The influence of whole-body aerobic fitness and fatness are thought to be mediated by skeletal muscle and adipose tissue lipoprotein lipase, and recent interest has centered on the determination of the independent contribution of aerobic fitness and adiposity to lipoprotein metabolism, particularly HDL (Krauss, 1989; Thompson, 1990; Williams, 1993). Studies of adult athletes (Berg and Keul, 1985; Tsopanakis et al., 1986) and youth (Smith et al., 1986; Valimaki et al., 1980) athletes have mainly examined the bivariate relationships among aerobic fitness, body size, and blood lipids. Few studies have examined the independent contribution of aerobic fitness and body fatness to the blood lipid profile during childhood and adolescence (Suter and Hawes, 1993; Tolfrey et al., 1999), and no study has apparently examined these factors as independent determinants of blood lipids in young endurance athletes.

This study considers the heterogeneity of blood lipids previously described in a sample of well-trained, young distance runners in the context of two specific objectives.

First, the existence of a dose-response relationship between levels of physical activity above the current recommended guidelines and blood lipids was evaluated in young distance runners. Second, the relationships among peak oxygen consumption (peak Vo_2), subcutaneous fatness and blood lipids in young distance runners with and without controlling for the concomitant variation of each predictor variable were examined in an attempt to assess independent contributions of peak Vo_2 and fatness to HDL. It was hypothesized that training volume and peak Vo_2 would be favorably associated with blood lipids, and body fatness, specifically truncal fatness, would be adversely related to blood lipids in this sample.

METHODS

Subjects. Males and females, 10 to19 years of age, participating on mid-Michigan junior or senior high school cross-country and track teams during the Fall 1999 and Spring 2000 were invited to participate in the current study. Subjects were also recruited by an advertisement in the local newspaper and at local road races. Exclusion criteria included current smokers, excessive alcohol intake, current use of blood cholesterol lowering and anti-hypertensive medication, anabolic steroid use, hepatic, renal, and thyroid disease, or training less than 30-40 weeks per year or the past three consecutive months. The total number of eligible subjects in the mid-Michigan area during recruitment is difficult to determine given the exclusion criteria. Parental consent and subject assent were obtained prior to testing. The study was approved by the Michigan State University Committee on Research Involving Human Subjects.

Blood lipids. Data collection occurred between the hours of 7 a.m.-12:00 p.m. A fasting blood sample was obtained by fingerprick after the subject had been seated for 10 minutes. Blood was collected in a 35 micro-liter capillary tube. Upon collection, samples were analyzed according to the manufacturer for TC, HDL, and TG within 5 minutes by a portable cholesterol analyzer (Cholestech LDX System, Hayward, CA). Low density lipoprotein cholesterol was estimated by the Friedewald equation (Friedewald et al., 1972).

The total error of measurement of the Cholestech LDX analyzer has been determined as 12.7%, 18.8%, and 19.7% (coefficients of variation, 1.4-4.1%, 3.5-5.6%, and 4.6-5.8%) for TC, HDL, and TG, respectively. Reference laboratory measurement errors are 8.1%,12.9%, and 5.1% for TC, HDL, and TG, respectively (Bard et al., 1997). The total error for HDL met the standard set forth by National Cholesterol Education Program (<22%), but TC and TG were slightly higher than the respective standards (8.9 and 15%).

Within-day reliability was determined prior to the onset of the study by five consecutive measurements with Cholestech Level 1 and 2 liquid control reagents. Day-to-day reliability was determined by daily calibration prior to each testing session throughout the study. Within-subject reliability was determined by duplicate measures of 1 of every 5 male and female subjects. The coefficients of variation was used to express the precision of the within-day and day-to-day trials and compared to national standards. The coefficients of variation (CV) for within-day and day-to-day trials were less than 2% and 4%, respectively for standard controls of TC, HDL, and TG. Within-subject precision of blood lipid measurements were high (0.996, TC; 0.943, HDL; 0.970, TG).

Training volume (TV). Information regarding training practices was collected using personal training records or a standard training invoice. An interview was conducted when necessary to obtain or clarify information. If the subject maintained a regular training log, they were asked for the contents for purposes of the study. Subjects who did not maintain a regular training record were asked to complete a standard training inventory (Appendix A), or in some cases, training history was obtained from coaches. Training volume was estimated by averaging the reported weekly distance over the preceding 3 months and recorded as km per week.

Peak oxygen consumption (peak Vo_2). A maximal exercise test was conducted on a motorized treadmill to exhaustion in an air-conditioned laboratory (20-22 degrees C, relative humidity 45-60%). The treadmill protocol was determined by the subject's estimated 5km race pace. Subjects walked/jogged at a speed of 3 mph and 4.5 mph for 1 min each. This initial warm-up period was followed by 4 minute stages at 6, 7.5, and 8 mph (depending on estimated %km race pace) and then an increase in grade of 2.5% every minute until exhaustion or test termination. Expired gases were collected for the measurement of oxygen consumption (Vo_2), carbon dioxide production (VCo_2), and minute ventilation. Expired gases were continually sampled and averaged every 20 seconds via the open circuit method using a metabolic cart (Gould 2900; Dayton, OH). Expired gas volumes were measured with a flow probe anemometer and expired gas concentrations were measured by electronic analyzers. Prior to testing, expired gas volumes were calibrated with a 3-L syringe and gas concentrations were calibrated with standard gases of known concentrations. Heart rate was continually monitored by pulse

telemetry (Polar Advantage). End of test criteria were established by volitional exhaustion, HR ≥90% of age-predicted maximum, respiratory exchange ratio >1.0, and a plateau in Vo_2 (defined by an increase in Vo_2 of <2.0 $ml \cdot kg^{-1} \cdot min^{-1}$ with increasing workload). Two of the latter three criteria must have been met for a subject to be included in the analysis.

Body fatness. Skinfold thicknesses were measured by standard procedures in duplicate with a Lange calipers as a double fold of skin underlying soft tissue at six anatomical sites on the right side of the body (Malina, 1995). The following skinfolds were measured to the nearest 0.5 mm: triceps, biceps, subscapular, suprailiac, abdominal, and medial calf. If the measurements varied by more than 1 mm, additional measurements were taken until the difference was less than 1 mm. Total subcutaneous skinfold thickness was expressed as the sum of the six skinfolds (SSF). The individual skinfold measurements were reproducible with intraclass correlations ≥0.96. The intra-observer technical errors of measurement ranged from 0.20 mm for the biceps to 3.0 mm for the suprailiac skinfolds. The ratio of the sum of trunk skinfolds (subscapular, suprailliac, and abdominal) to the sum of extremity skinfolds (triceps, biceps, and medial calf) (TER) was used an index of the relative subcutaneous fat distribution. The TER was then regressed on SSF, and the residuals were retained to represent an index of relative subcutaneous fat distribution independent of overall subcutaneous fatness.

Sexual maturity status. Given the difficulty in direct assessment of sexual maturity status in a non-medical environment, a self- assessment of sexual maturity status was used in

the current study. Self-assessment was conducted in a separate, private station following an explanation of the purpose of the assessment. Subjects rated their stage of sexual development relative to sex-appropriate sets of drawings/photos and verbal descriptions (Van Wieringen et al., 1971) based on the criteria of Tanner (1962). In a study of 174 female and 178 male Brazilian youth age 6-26 years (Matsudo and Matsudo, 1994), the concordance between self and physician assessments of secondary sex characteristics was reasonably high (60-71.3%). Test-retest concordance (i.e., reproducibility) was similar between self- and physician-assessment.

Statistical analysis. Exploratory data analysis was conducted to examine the distribution of data and detect any outliers. In males, two outliers (+2 SD) were identified for fatness and were not considered in the analysis. TG was not normally distributed and logarithmically transformed (logTG). Descriptive statistics (means, SD, and range) were computed for all variables. Partial correlations were calculated for each of the predictor variables and blood lipids. Chronological age and stage of genital or breast development were controlled in the analyses since both are associated with changes in blood lipids during adolescence (Morrison et al., 1979; Tell, 1985). Furthermore, it is important to control for both variables given the inter-individual differences in the timing and tempo of sexual maturation (Malina and Bouchard, 1991). Based on preliminary findings, inter-relationships between peak Vo_2, SSF, and HDL were further explored. Partial correlations were computed between HDL and (a) peak Vo_2 controlling for age and SSF, and (b) SSF, controlling for age and peak Vo2 to evaluate the independent contributions

of peak Vo2 and SSF to HDL. An alpha level of $p<.05$ was used in all analyses which were executed with the SPSS package.

RESULTS

Tables 5.1 and 5.2 provide the descriptive statistics for chronological age, body size, peak Vo_2, TV, and blood lipids. Males are taller, heavier, and have less SSF but a greater TER than females. Males also have higher values for peak Vo_2 and TV, but considerable heterogeneity exists in the sample. Some of heterogeneity in body size can be attributed to chronological age and sexual maturation. Therefore, age and stage of pubertal development (genital in boys, and breasts in girls) were controlled in correlational analyses. Compared to recent United States reference medians (Hickman et al., 1998), mean values of TC, LDL, and TG are higher in male runners. HDL is also higher in male distance runners. In females, mean values are comparable to reference medians. In contrast to mean values, most runners possess desirable blood lipid levels compared to clinical cut-points (Kwiterovich, 1989).

Table 5.3 shows the partial correlations, controlling for chronological age and stage of pubertal development, among TV, peak Vo_2, SSF, TER, and blood lipids in young distance runners. Overall, correlations are low to moderate. TV is weakly correlated with blood lipids with relationships in the expected direction for HDL and TG in males but not females. Peak Vo_2 is significantly related to HDL and LDL in males ($p<0.05$). SSF is negatively related to HDL in both sexes ($p<0.05$ in males). The correlations between SSF and LDL and TG are comparable in males and females, but the directions of the relationship differ. The TER is not related to blood lipids in males

($p>0.05$), with partial correlation coefficients near zero. Correlations between TER and blood lipids are similar to those for SSF in females, with the highest coefficient between TER and HDL ($r= -0.60$, $p<0.05$).

Figures 5.1a shows the inter-relationships among TV, peak $V0_2$, SSF, and HDL in males. Partial correlations range from 0.10 to 0.41. The only non-significant relationships are between TV and HDL ($r=0.10$, $p=0.49$) and TV and SSF ($r=-0.11$, $p=0.56$). Although TV is not directly related to HDL, it may be indirectly related through its relationship with peak Vo_2 ($r=0.32$, $p<0.05$). Given the comparable relationships among peak Vo_2, SSF, and HDL ($r=0.37$-0.41, $p<0.05$), the independent contributions of each predictor variable on HDL were further explored. When age and SSF are controlled, the correlation between peak Vo_2 and HDL remains significant ($r=0.31$, $p=0.04$), whereas the partial correlation between SSF and HDL, controlling for age and peak Vo_2, declines and is not significant ($r=-0.19$, $p=0.20$). Similar relationships occur in females. When age and SSF are controlled, the correlation between peak Vo_2 and HDL is 0.32, whereas the partial correlation between SSF and HDL, controlling for age and peak Vo_2, is 0.00. Figures 5.1b and 5.1c are provided to illustrate the inter-relationships among TV, peak Vo_2, SSF, and LDL and TG, respectively, in males.

DISCUSSION

Training volume and blood lipids. A purpose of this study was to address the role of physical activity on blood lipids in children and adolescents who have habitual physical activity levels equal to or greater than the current recommendations. It has been suggested that an exercise level equivalent to jogging 10-15 miles/wk is necessary for to

significantly alter blood lipids (Superko, 1991; Williams, 1994). Armstrong and Simons-Morton (1994) extrapolated this recommendation to the adolescent population and suggested that an adolescent would need to jog at a speed of 8 km/hr for approximately 2 hours per week, which from their own experience is equivalent to about 80% of maximal heart rate with young adolescents and about 75% of maximal heart rate for young adults. The authors, therefore, recommended that four 30 minute exercise sessions per week at 75-80% of maximum heart rate may be an appropriate prescription. Since few adolescents engage in such activity, the use of a special exposure group such as young distance runners would allow for the testing of these recommendations. Therefore, young distance runners were studied to determine if a dose-response or threshold effect of physical activity on blood lipids exists in children and adolescents with habitual physical activity levels greater than the recommended exercise volume.

It was hypothesized that training volume would be positively related to a favorable blood lipid profile among adolescent distance runners as in adult endurance athletes. Correlations between TV and HDL and TG were favorable in males, but low. However, TV may indirectly influence HDL in males through its relationship with peak Vo_2 (r=0.32) and to a lesser extent body fatness (Figure 5.1). These inter-relationships suggest the importance in considering the confounding effects on body fatness and peak Vo_2 when assessing the influence of TV on HDL. It is also possible that leaner and more aerobically fit individuals are more likely to engage in higher training levels (Williams et al., 1982).

In an early report on 90 middle-aged male runners, distance run per week was positively correlated with HDL (r=0.50) and remained significant after adjustment for

percentage body fat (r=0.40) (Rotkis et al., 1982). Recently, Williams (1996, 1997) demonstrated that the benefits of exercise continued to accrue in a dose-response manner at levels of physical activity exceeding the current minimal guideline in large samples of non-smoking, recreational male (n= 8283) and female (n=1837) adult distance runners. Significant linear trends were reported for HDL and TC:HDL in both sexes and TG in men. No significant trend was reported for LDL. In a smaller sample of 33 middle-aged men (mean age = 45 yrs), Williams (1990) reported no relationship between TV and HDL (r=0.05). The results of the current study of young distance runners may thus be due to sample size.

An alternative explanation may be that increased levels of training do not influence lipoprotein metabolism when blood lipids are already at desirable levels during childhood and adolescence. Cross-sectional studies of habitual physical activity and blood lipids generally show low associations (Armstrong and Simons-Morton, 1994; Tolfrey et al., 2000). In contrast to cross-sectional studies, prospective studies suggest that pre-training levels of blood lipids influence the response to exercise training (Tolfrey et al., 2000). Likewise, Barr et al. (1991) found that increasing TV in collegiate male swimmers from 22,000 m/wk to 44,000 m/wk over a six week period did not alter HDL or TG, and lowered LDL only slightly relative to baseline levels. It is possible that when blood lipids are already desirable in youth and/or physical activity levels are relatively high, increased levels of training do not influence their metabolism. This observation has been referred to as a 'ceiling' or 'floor' effect (Tolfrey et al., 2000). To explore this hypothesis, the sample was divided into sub-groups based on clinical cut-points. The cut-points were modified since the number of subjects with blood lipid levels greater than the

clinical cut-point of dyslipidemia was limited. Therefore, individual values classified as borderline dyslipidemic or dyslipidemic were grouped together as "undesirable" (HDL < 45 mg/dl). Results indicated that HDL was positively related to TV (r=0.40) in the undesirable group, but was unrelated and in the opposite direction as expected in the desirable group (HDL $\geq$ 45 mg/dl, r= -0.23). Perhaps, the reason that LDL or TG values were not modulated by levels according to the clinical cut-point is that the values were not excessively dyslipidemic compared to the HDL values. In other words, low levels of HDL may be more sensitive to exercise training than moderately elevated levels of TG and LDL. This preliminary finding suggests that relationship between TV and HDL may be modulated by level according to clinical cut-point. Additional cross-sectional and prospective training studies are required to further examine this suggestion.

Other factors that were not considered in the present study, but may influence the relationship between TV and blood lipids, include: the intensity of exercise training (Williams, 1998), genotype and genotype-environmental interactions (Taimela et al., 1996), dietary intake and composition (Brown and Cox, 1998; Leddy et al., 1997; Lukaski et al., 1984; Thompson et al., 1984). Additional factors that are known to influence blood lipids were controlled in the design of this study. No subject reported regular alcohol intake, smoking, anabolic steroid use, nor medication or metabolic disorders (e.g., liver, kidney, or thyroid disease), which may adversely influence lipoprotein metabolism.

The estimation of TV may also influence the results. TV was determined as the average distance run per week in the preceding 3 months. In the National Runners' Health Study, TV was estimated by averaging yearly distances for the preceding 5 years

and the reliability was 0.89 (Williams, 1997). The intensity of exercise training was not addressed in the current study and may influence the results. Future studies should establish the reliability and validity of self-reported training volume in young athletes, while the continuous measurement of heart rate during training sessions would provide valuable information with regards to the role of exercise intensity and training volume on blood lipids in endurance athletes.

Peak Vo_2 and blood lipids. The positive association between peak Vo_2 and HDL is consistent with previous studies of youth (Al-Hazzaa et al., 1994; Armstrong et al., 1991; Macek et al., 1989; Sallis et al., 1988; Suter and Hawes, 1993; Tell and Vellar, 1988; Valimaki et al., 1980). The association between peak Vo_2 and HDL (r=0.41) is similar to previous studies of well-trained athletes as well. In a previous mixed-sample (males and females) of mid-Michigan distance runners, peak Vo_2 was related to HDL (r=0.39) (Smith et al., 1986). In a study of national level adult athletes, peak Vo_2 explained 25% of the variance in HDL (Berg and Keul, 1985) and was significantly related to HDL (r=0.26) in Olympic athletes (Tsopanakis et al., 1986). The proposed mechanism for this relationship involves properties of skeletal muscle and adipose tissue that influence peak Vo_2 and lipid metabolism (Tikkanen et al., 1991). Skeletal muscle and adipose tissue lipoprotein lipase (LPL) activity is higher in trained versus untrained individuals (Nikkila et al., 1978), and the percentage of slow oxidative muscle fibers is positively correlated with HDL (Tikkanen et al., 1991). In combination, a higher proportion of slow oxidative fibers favors fatty acid metabolism and increases the likelihood that LPL activity will be increased with exercise (Stefanik and Wood, 1994).

The role of genes and aerobic fitness levels in the modulation of blood lipid levels has also been indicated (Katzmarzyk et al., 1999a; St.-Amand et al., 1999). Heritability estimates for peak Vo_2 per unit kg approximate 25-40% (Bouchard et al., 1997). Polymorphisms in lipoprotein genes (apolipoprotein E) may also influence the relationship between aerobic fitness and blood lipid levels (St.-Amand et al., 1999). It is possible that blood lipids in adolescent distance runners are moderated by the genetic contribution of aerobic fitness or the pleiotropy (shared genes) of aerobic fitness and blood lipids.

The positive relationship between peak Vo_2 and LDL is a unique finding that lacks an explanation. Although other studies of youth found a similar positive relationship, the relationship was not as strong (Suter and Hawes, 1993; Tolfrey et al., 1999).

Body fatness and blood lipids. The relationships between SSF and HDL and TG are consistent with the literature, but once again the relationship with LDL lacks an explanation. In general, indicators of body fatness are positively related to TG, TC, and LDL, and negatively to HDL throughout the lifespan (Guo et al., 1994). No previous study of young male athletes has examined the relationship of body size or adiposity with blood lipids. Relative body weight (kg/(cm-100)) explained about 7% of the variance in TC and TG, and 20% of the variance in LDL in national level adult athletes (sprinters, hammer throwers, distance runners, etc.) (Berg and Keul, 1985). In Olympic athletes, relative body weight was significantly related to HDL (r= -0.22), LDL (r=0.18), and VLDL (r=0.17) (Tsopanakis et al., 1986). Rotkis et al. (1982) found significant relationships between percentage body fat and HDL (r= -0.36), TC (r=0.38) and non-

HDL cholesterol (r=0.48) in middle-aged distance runners. In contrast, correlations between various measures of body size (e.g., BMI, relative weight, percentage body fat) and HDL were low in 33 middle-aged distance runners (r =0.05- 0.08) (Williams, 1990). The relationship between body fatness and HDL can be partly explained by adipose tissue lipoprotein lipase (LPL) activity (Nikkila et al., 1978),

The findings for TER in males are inconsistent with previous findings in youth that show that a central fat patterning, or truncal/visceral fatness, is associated with adverse blood lipids (Baumgartner et al., 1989; Freedman et al., 1989; van Lenthe et al., 1998). During adolescence, an increase in subcutaneous abdominal adipose tissue and redistribution of body fatness to the trunk results in an increase in the TER in boys (Malina et al., 1999). The relationships between TER and blood lipids were actually more pronounced in females, especially for HDL. The use of the TER as an appropriate index of relative subcutaneous fat distribution in young distance runners has not been considered. Since young distance runners possess a low level of whole-body fatness and a relatively low level of periperal (i.e., extremity) fatness, even a slightly greater sum of trunk skinfolds results in a higher TER. The relatively low amount of peripheral fatness probably reflects morphological properties necessary for success in endurance sport. The relationship could also be attributed to the independent effects of somatotype, namely ectomorphy, on blood lipids (Katzmarzyk et al., 1999b). Similarly, a low correlation (r=-0.13) between the ratio of abdominal girth and bi-iliac diameter and HDL in middle-aged male distance runners (Williams, 1990).

The role of genes and body fatness in the modulation of elevated blood lipid levels has also been indicated (Katzmarzyk et al., 1999c). Heritability estimates of

abdominal visceral fatness measured by computerized tomography approximate 50-55% with a major gene associated with total fat mass either directly or indirectly affecting abdominal fatness. Furthermore, polymorhpisms in lipoprotein genes (ApoA-II MspI, HindIII, and apoB-100 EcoRI) may influence the relationship between abdominal visceral fatness and blood lipid levels. The correlation between parental BMI and measures of fatness in adolescent distance runners were positive and ranged from 0.01 (paternal BMI and TER) to 0.36 (maternal BMI and SSF). Parental BMI was calculated from self-reported heights and weights of the parents. Correlations are stronger between maternal BMI and offspring fatness. A possible cross-trait familial resemblance for body fat and bloods lipids has also been hypothesized (Pérusse et al., 1997). This hypothesis suggests that trait 1 in a parent (e.g., body fat) is linked with trait 2 in an offspring (e.g., blood lipids) and provides an indication about the contribution of shared genes and/or environmental factors. In the present study, low correlations (r=0.12-0.23) existed between paternal BMI and offspring blood lipids. Therefore, it is possible that blood lipids in adolescent distance runners are moderated by the genetic contribution of body fatness and/or the pleiotropy (shared genes) of body fatness and blood lipids. It is also possible that shared environmental factors (i.e., dietary intake) could contribute to the relationship between parental fatness, offspring fatness and blood lipids.

This is apparently the first study to examine multiple determinants of blood lipids in adolescent distance runners. Previous reports examining the univariate relationships between relative body size, peak Vo_2 and blood lipid levels have been discussed. However, the unique contribution of peak Vo_2 and adiposity were not established in these studies. One study of male master level athletes using multivariate linear regression

showed that percentage body fat explained 29 and 41% of the variance in HDL and TG, and peak Vo_2 accounted for an increase of 6 and 2% of the variance in HDL and TG, respectively (Yataco et al., 1997). In the present study, partial correlations were computed to separate the independent contributions of peak Vo_2 and SSF on HDL. Results indicate that the association between peak Vo_2 and HDL remained significant after controlling for the concomitant variation in SSF and explained 9% of the variance in HDL. The association between SSF and HDL did not remain significant after controlling for the concomitant variation in peak Vo_2. This finding would suggest that skeletal muscle properties are an important factor in determining HDL in young well-trained distance runners, although the influence of adipose tissue cannot be dismissed.

Conclusions. In conclusion, it appears that health benefits (i.e., blood lipid levels) do not accrue in young distance runners at levels exceeding the current minimal guidelines. However, this result may be due to the small sample size that lacks the statistical power to test for incremental changes across a range of high levels of training (Williams, 1997). In general, this study contributes to understanding the heterogeneity of blood lipids in young distance runners. The inter-relationships among TV, peak Vo_2, body fatness, and blood lipids appear to be complex. Although TV was not directly related to HDL, it may be related through its association with peak Vo_2 and body fatness. The relationship between TV and HDL may also be modulated by the level of HDL according to clinical cut-points. Finally, peak Vo_2 is an important predictor of HDL in young distance runners independent of body fatness. It is possible that the inter-relationships peak Vo2, body fatness and HDL is mediated through shared genes. Further study is warranted to explore the contribution of growth, maturation, genetics,

exercise training, and skeletal muscle and adipose tissue properties on lipoprotein metabolism during adolescence.

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REFERENCES

Al-Hazzaa HM, Sulaiman MA, Al-Matar AJ, Al-Mobaireek KF (1994) Cardiorespiratory fitness, physical activity patterns and coronary risk factors in preadolescent boys. Int J Sports Med 15:267-272.

Armstrong N, Simons-Morton B (1994) Physical activity and blood lipids in adolescents. Pediatr Exerc Sci 6:381-405.

Armstrong N, Williams J, Balding J, Gentle P, Kirby B (1991) Cardiorespiratory fitness, physical activity patterns, and selected coronary artery risk factor variables in 11- to 16-year-olds. Pediatr Exerc Sci 3:219-228.

Bard RL, Kaminsky LA, Whaley MH, Zajakowski S (1997) Evaluation of lipid profile measurements obtained from the Cholestech LDX analyzer. J Cardiopul Rehab 17:413-418.

Barr SI, Costill DL, Fink WJ, Thomas R (1991) Effect of increased training volume on blood lipids and lipoproteins in male collegiate swimmers. Med Sci Sports Exerc 23:795-800.

Baumgartner RN, Siervogel RM, Chumlea WC, Roche AF (1989) Associations between plasma lipoprotein cholesterols, adiposity and adipose tissue distribution during adolescence. Int J Obes 13:31-41.

Berg A, Keul J (1985) Influence of maximum aerobic capacity and relative body weight on the lipoprotein profile in athletes. Atherosclerosis 55:225-231.

Bouchard C, Malina RM, Perusse L (1997) Genetics of Fitness and Physical Performance.Champaign, IL: Human Kinetics.

Brown RC, Cox CM (1998) Effects of high fat versus high carbohydrate diets on plasma lipids and lipoproteins in endurance athletes. Med Sci Sports Exerc 30:1677-1683.

Casperson CJ, Nixon PA, DuRant RH (1998) Physical activity epidemiology applied to children and adolescents. Exerc Sci Sports Rev 26:341-403.

Despres J-P (1997) Visceral obesity, insulin resistance, and dyslipidemia: contribution of endurance exercise training to the treatment of the plurimetabolic syndrome. Exerc Sport Sci Rev 25:271-300.

Despres J-P, Bouchard C, Malina RM (1990) Physical activity and coronary heart disease risk factors during childhood and adolescents. Exerc Sport Sci Rev 18:243-261.

Freedman DS, Srinivasan SR, Harsha DW, Webber LS, Berenson GS (1989) Relation of body fat patterning to lipid and lipoprotein concentrations in childern and adolescents: the Bogolusa Heart Study. Am J Clin Nutr 50:930-939.

Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 18:499-502.

Guo S, Salisbury S, Roche AF, Chumlea WC, Siervogel RM (1994) Cardiovascular disease risk factors and body composition: a review. Nutr Rev 14:1721-1777.

Gutin B, Owens S (1996) Is there a scientific rationale supporting the value of exercise for the present and future cardiovascular health of children? the pro argument. Pediatr Exerc Sci 8:294-302.

Hickman TB, Briefel RR, Carroll MD, Rifkind BM, Cleeman JI, Maurer KR, Johnson CL (1998) Distributions and trends of serum lipid levels among United States children and adolescents ages 4-19 years: data from the Third National Health and Nutrition Examination Survey. Prev Med 27:879-890.

Katzmarzyk PT, Malina RM, Bouchard C (1999a) Physical activity, physical fitness, and coronary heart disease risk factors in youth: The Québec Family Study. Prev Med 29:555-562.

Katzmarzyk PT, Malina RM, Song TMK, Bouchard C (1999b) Physique, subcutaneous fat, adipose tissue distribution, and risk factors in the Québec Family Study. Int J Obes 23:476-484.

Katzmarzyk PT, Pérusse L, Bouchard C (1999c) Genetics of abdominal visceral fat levels. Am J Hum Biol 11:225-235.

Krauss RM (1989) Exercise, lipoproteins, and coronary artery disease. Circulation 79:1143-1145.

Kwiterovich PO (1989) Beyond Cholesterol: the John Hopkins Complete Guide for Avoiding Heart DiseaseBaltimore, MD: The John Hopkins Press.

Leddy J, Horvath P, Rowland J, Pendergast D (1997) Effect of a high or a low fat diet on cardiovascular risk factors in male and female runners. Med Sci Sports Exerc 29:17-25.

Lukaski HC, Bolonchuck WW, Klevay LM, Mahalko JR, Milne DB, Sandstead HH (1984) Influence of type and amount of dietary lipid on plasma lipid concentrations in endurance athletes. Am J Clin Nutr 39:35-44.

Macek M, Bell D, Rutenfranz J, Vavra J, Masopust J, Neidhart B, Schmidt K-H (1989) A comparison of coronary risk factors in groups of trained and untrained adolescents. Eur J Appl Physiol 58:577-582.

Malina RM (1990) Growth, exercise, fitness, and later outcomes. In C Bouchard, RJ Shephard, T Stephens, JR Sutton and BD McPherson (eds.): Exercise, Fitness, and Health: A Consensus of Current Knowledge. Champaign, IL: Human Kinetics, pp. 637-653.

Malina RM (1995) Anthropometry. In PJ Maud and C Foster (eds.): Physiological Assessment of Human Fitness. Champaign, IL: Human Kinetics, pp. 205-219.

Malina RM, Bouchard C (1991) Growth, Maturation, and Physical Activity.Champaign, IL: Human Kinetics.

Malina RM, Koziel S, Bielicki T (1999) Variation in subcutaneous adipose tissue distribution associated with age, sex, and maturation. Am J Hum Biol 11:189-200.

Matsudo SMM, Matsudo VKR (1994) Self-assessment and physician assessment of sexual maturation in Brazilian boys and girls: concordance and reproducibility. Am J Hum Biol 6:451-455.

Morrison JA, Laskarzewski PM, Rauh JL, Brookman R, Mellies M, Frazer M, Khoury P, deGroot I, Kelly K, Glueck CJ (1979) Lipids, lipoproteins, and sexual maturation during adolescence: the Princeton Maturation Study. Metabolism 28:641-649.

Nikkila EA, Taskinen M-R, Rehunen S, Harkonen M (1978) Lipoprotein lipase activity in adipose tissue and skeletal muscle of runners: relation to serum lipoproteins. Metabolism 27:1661-1671.

Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, Buchner D, Ettinger W, Heath GW, King AC, Kriska A, Leon AS, Marcus BH, Morris J, Paffenbarger RS, Patrick K, Pollock ML, Rippe JM, Sallis J, Wilmore JH (1995) Physical activity and health: A recommendation from the Centers of Disease Control and Prevention and the American College of Sports Medicine. JAMA 273:402-407.

Pérusse L, Rice T, Després JP, Rao DC, Bouchard C (1997) Cross-trait familial resemblance for body fat and blood lipids: familial correlations in the Quebec Family Study. Arterioscler Throm Vasc Biol 17:3270-3277.

Riopel DA, Boerth RC, Coates TJ, Hennekens CH, Miller WM, Weidman WH (1986) Coronary risk factor modification in children: exercise - A statement for physicians by the Committee on Atherosclerosis and Hypertension in Childhood of the Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 74:1189A-1191A.

Rotkis TC, Cote R, Coyle E, Wilmore JH (1982) Relationship between high density lipoprotein cholesterol and weekly running mileage. J Cardiac Rehab 2:109-112.

Sallis JF, Patrick K, Long BJ (1994) Overview of the International Consensus Conference on Physical Activity Guidelines for Adolescents. Pediatr Exerc Sci 6:299-301.

Sallis JF, Patterson TL, Buono MJ, Nader PR (1988) Relation of cardiovascular fitness and physical activity to cardiovascular disease isk factors in children and adults. Am J Epidemiol 127:933-941.

Smith BW, Metheny WP, Sparrow AW (1986) Serum lipid and lipoprotein profiles in age-group runners. In MR Weiss and D Gould (eds.): Sport for Children and Youths. Champaign, IL: Human Kinetics, pp. 269-273.

St.-Amand J, Prud'homme D, Moorjani S, Nadeau A, Tremblay A, Bouchard C, Lupien PJ, Després J-P (1999) Apolipoprotein E polymorphism and the relationships of physical fitness to plasma lipoprotein-lipid levels in men and women. Med Sci Sports Exerc 31:692-697.

Stefanik ML, Wood PD (1994) Physical activity, lipid and lipoprotein metabolism, and lipid transport. In C Bouchard, S R.J. and T Stephens (eds.): Physical Activity, Fitness, and Health. Champaign, IL: Human Kinetics, pp. 417-431.

Superko HR (1991) Exercise training, serum lipids, and lipoprotein particle: is there a change threshold? Med Sci Sports Exerc 23:677-685.

Suter E, Hawes MR (1993) Relationship of physical activity, body fat, diet, and blood lipid profile in youths 10-15 yr. Med Sci Sports Exerc 25:748-754.

Taimela S, Lehtimaki T, Porkka KV, Rasanen L, Viikari JS (1996) The effect of physical activity on serum total and low-density lipoprotein cholesterol concentrations varies with apolipoprotein E phenotype in male children and young adults: The Cardiovascular Risk in Young Finns Study. Metabolism 45:797-803.

Tanner JM (1962) Growth at Adolescence, 2nd edition. Oxford: Blackwell.

Tell GS (1985) Cardiovascular disease risk factors related to sexual maturation: the Oslo Youth Study. J Chron Dis 38:633-642.

Tell GS, Vellar OD (1988) Physical fitness, physical activity, and cardiovascular disease risk factors in adolescents: The Oslo Youth Study. Prev Med 17:12-24.

Thompson PD, Cullinane EM, Eshleman R, Kantor MA, Herbert PN (1984) The effects of high-carbohydrate and high-fat diets on the serum lipid and lipoprotein concentrations of endurance athletes. Am J Clin Nutr 33:1003-1010.

Tikkanen HO, Harkonen M, Naveri H, Hamalainen E, Elovainio R, Sarna S, Heikki Frick M (1991) Relationship of skeletal muscle fiber type to serum high density lipoprotein cholesterol and apolipoprotein A-I levels. Atherosclerosis 90:49-57.

Tolfrey K, Campbell IG, Jones AM (1999) Selected predictor variables and the lipid-lipoprotein profile of prepubertal girls and boys. Med Sci Sports Exerc 31:1550-1557.

Tolfrey K, Jones AM, Campbell IG (2000) The effects of aerobic exercise training on the lipid-lipoprotein profile of children and adolescents. Sports Med 29:99-112.

Tsopanakis C, Kotsarellis D, Tsopanakis AD (1986) Lipoprotein and lipid profiles of elite athletes in Olympic sports. Int J Sports Med 7:316-321.

Valimaki I, Hursti M-L, Pihlakoski L, Viikari J (1980) Exercise performance and serum lipids inrelation to physical activity in schoolchildren. Int J Sports Med 1:132-136.

van Lenthe FJ, van Mechelen W, Kemper HCG, Twisk JWR (1998) Association of a central pattern of body fat with blood pressure and lipoproteins from adolescence into adulthood. Am J Epidemiol 147:686-693.

Van Wieringen JC, Wafelbakker F, Verbrugge HP, de Haas JH (1971) Growth Diagrams 1965 Netherlands: Second National Survey on 0-24-year-oldsGroningen: Wolters-Noorhoff Publishing.

Williams PT (1990) Weight set-point theory predicts HDL-cholesterol levels in previously obese long-distance runners. Int J Obes 14:421-427.

Williams PT (1993) High-density lipoproteins and lipase activity in runners. Atherosclerosis 98:251-254.

Williams PT (1994) Lipoproteins and adiposity show improvement at substantially higher exercise levels than those currently recommended. Circulation 90:I-471 (Abstract).

Williams PT (1996) High-density lipoprotein cholesterol and other risk factors for coronary heart disease in female runners. N Engl J Med 334:1298-1303.

Williams PT (1997) Relationship of distance run per week to coronary heart disease risk factors in 8283 male runners. Arch Intern Med 157:191-198.

Williams PT (1998) Relationships of heart disease risk factors to exercise quantity and intensity. Arch Intern Med 158:237-245.

Williams PT, Wood PD, Haskell WL, Vranizan K (1982) The effects of running mileage and duration on plasma lipoprotein levels. JAMA 247:2674-2679.

Yataco A, Busby-Whitehead J, Drinkwater D, Katzel L (1997) Relationship of body composition and cardiovascular fitness to lipoprotein lipid profiles in master athletes and sedentary men. Aging 9:88-94.

Table 5.1. Characteristics young distance runners.

	Males (n=45)		Females (n=22)	
	Mean (SD)	Range	Mean (SD)	Range
Age (yrs)	16.9 (2.0)	10.4-19.4	15.5 (2.6)	9.6-18.4
Ht (cm)	173.9 (7.3)	149.2-185.1	161.1 (9.8)	132.7-178.1
Wt (kg)	61.7 (7.4)	39.9-76.3	50.1 (10.4)	27.0-71.1
SSF (mm)	40.7 (7.6)	25.0-55.5	58.3 (17.7)	32.5-99.0
SUM 3T (mm)	24.8 (5.8)	14.0-40.0	29.5 (9.4)	14.5-50.0
SUM 3E (mm)	15.8 (3.4)	8.0-27.0	18.8 (8.8)	16.0-49.0
TER (mm/mm)	1.60 (0.37)	0.70-2.48	1.05 (0.13)	0.85-1.29
Peak Vo_2 ($ml \cdot min^{-1}$)	4225.6 (597.2)	2262-5526	2869.8 (540.3)	1709-3725
Peak Vo_2 ($ml \cdot kg^{-1} min^{-1}$)	66.9 (5.8)	54.8-77.0	56.8 (5.3)	48.0-63.3
TV ($km \cdot wk^{-1}$)	47.7 (22.8)	15-88	35.2 (13.8)	15-60

See text for abbreviations.

Table 5.2. Blood lipids of young distance runners.

	Males (n=45)		Females (n=22)	
	Mean (SD)	Range	Mean (SD)	Range
TC	167.2 (30.2)	100-241	157.6 (18.0)	117-188
HDL	48.6 (13.7)	28-89	51.7 (11.1)	35-78
LDL	102.9 (26.4)	55-174	91.0 (17.0)	58-131
TG	83.2 (38.8)	45-188	75.1 (21.8)	50-149

See text for abbreviations.
Values expressed in mg/dl.

Table 5.3. Partial correlations, controlling for chronological age and pubertal stage, for training volume, peak Vo_2, body fatness, and blood lipids in young distance runners.

Males Blood Lipids	TV	Peak Vo_2	SSF	TER
HDL	.10	.41*	-.34*	-.01
LDL	.27	.36*	-.19	.07
logTG	-.11	.01	.22	-.04
Females **Blood Lipids**	**TV**	**Peak Vo_2**	**SSF**	**TER**
HDL	-.27	.41	-.27	-.60*
LDL	.17	-.15	.18	-.18
logTG	.09	.30	-.21	.16

TV, training volume; peak Vo_2, peak oxygen consumption; SSF, sum of six skinfolds; TER, trunk-to-extremity ratio.

*$p<0.05$

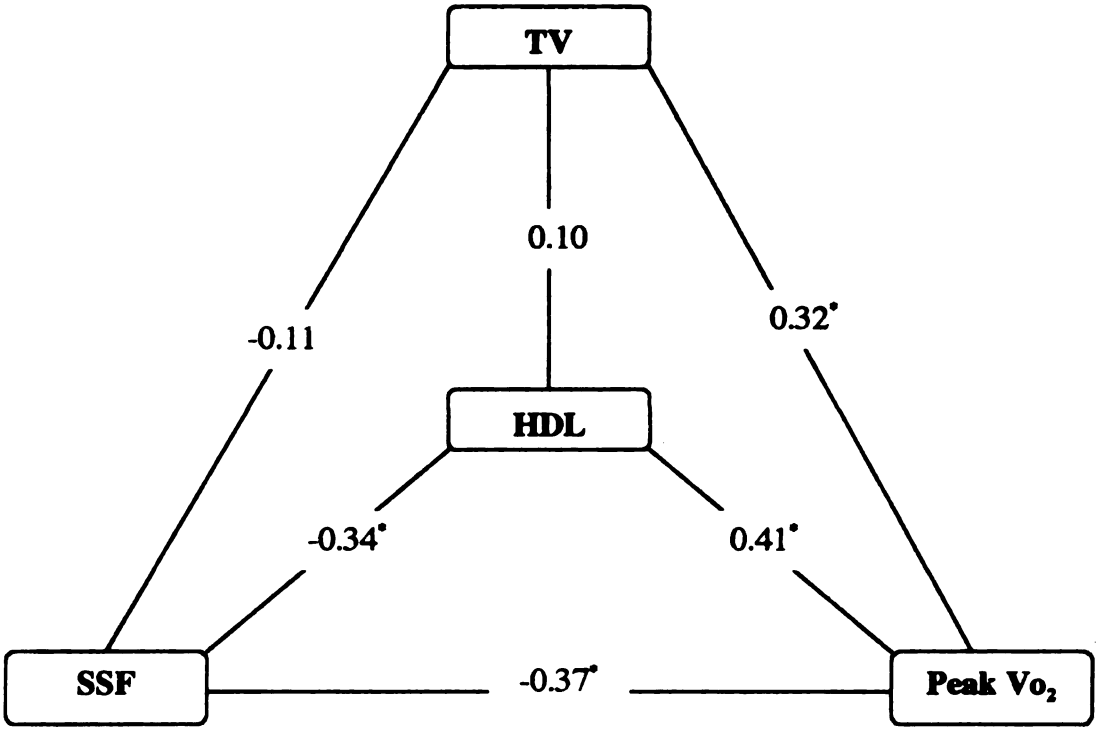

Figure 5.1a. Inter-relationships among training volume (TV), sum of six skinfolds (SSF), peak oxygen consumption (peak Vo_2), and high-density lipoprotein (HDL) in 45 young male distance runners 10 to 19 years of age. Values are partial correlation coefficients controlling for age and genital stage of pubertal development. * $p<0.05$.

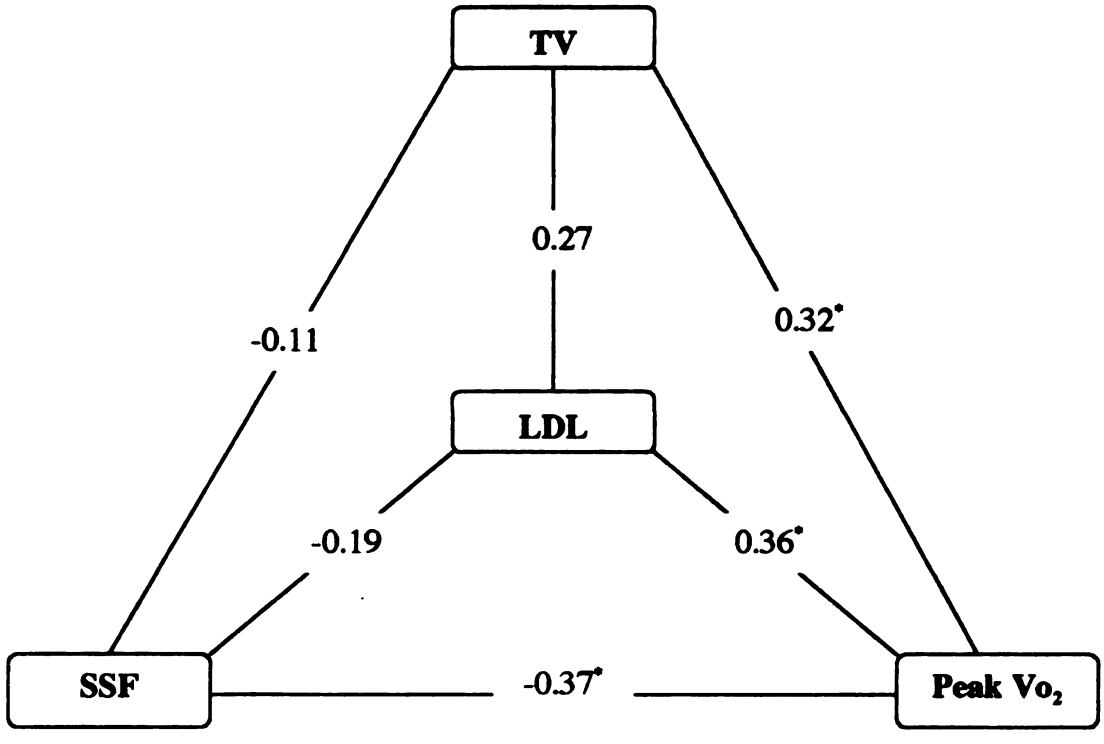

Figure 5.1b. Inter-relationships among training volume (TV), sum of six skinfolds (SSF), peak oxygen consumption (peak Vo_2), and low-density lipoprotein (LDL) in 45 young male distance runners 10 to 19 years of age. Values are partial correlation coefficients controlling for age and genital stage of pubertal development. * $p<0.05$.

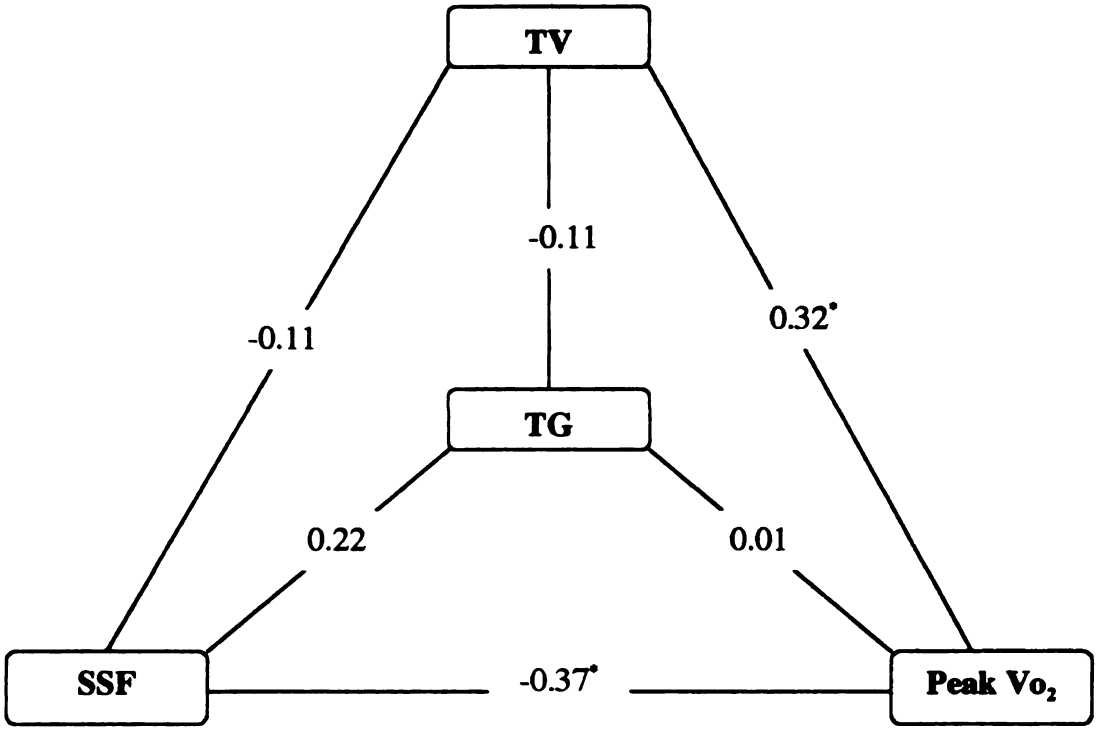

Figure 5.1c. Inter-relationships among training volume (TV), sum of six skinfolds (SSF), peak oxygen consumption (peak Vo_2), and triglycerides (TG) in 45 young male distance runners 10 to 19 years of age. Values are partial correlation coefficients controlling for age and genital stage of pubertal development. * $p<0.05$.

CHAPTER 6

REVIEW OF LITERATURE

PART II

INTRODUCTION

Peak oxygen consumption (Vo_2) can be defined as the maximal ability of the organism to uptake (via pulmonary respiration), deliver (via the cardiovascular system), and utilize (via the oxidative capacity of skeletal muscle) oxygen. Together, these processes govern the flow of oxygen from ambient air to the mitochondria through a series of structural barriers that can be considered the oxygen transport system (Weibel, 1984). Peak Vo_2 can be easily measured by a progressive, incremental exercise test that commences when additional power output fails to elicit any further increase in whole-body Vo_2.

The importance of peak Vo_2 can be viewed from auxological, physical performance, and health perspectives. From an auxological viewpoint, growth-related changes in peak Vo_2 may serve to indicate the structural (or quantitative) and functional (or qualitative) changes in the oxygen transport system. In terms of physical performance and health, peak Vo_2 is related to endurance performance (Coyle, 1995) and various chronic diseases (Blair et al., 1989), at least in adults.

Despite the relative ease of measurement of peak Vo_2, there is some controversy in the analysis and interpretation of growth-related changes in physiological capacity and performance. To provide a clear understanding of the growth-related changes in peak Vo_2, the confounding factor of growth-related changes in body dimensions must be appropriately controlled. The use of allometric scaling has recently received considerable attention within the field of pediatric exercise science (Armstrong and Welsman, 1994; Winter, 1996). The use of correctly scaled data has important implications regarding the understanding of growth-related changes in peak Vo_2, physiological differences between

adults and children, evaluation of youth athletes, and health-related fitness during childhood and adolescence.

Age-, sex-, and maturity-associated variation in absolute peak Vo_2 ($L \cdot min^{-1}$) and peak Vo_2 expressed per kg of body weight ($ml \cdot kg^{-1} \cdot min^{-1}$) in the general population is briefly reviewed. Extensive reviews have been published elsewhere (Armstrong and Welsman, 1994; Krahenbuhl et al., 1985; Malina and Bouchard, 1991; Rowland, 1996). Limited information on the age-, sex-, and maturity-associated variation in peak Vo_2 of young athletes is also critically examined. The basic principles of allometric scaling are presented to provide the reader with background of this concept prior to reviewing the growth-related changes in peak Vo_2 from an allometric perspective.

AGE-AND SEX-ASSOCIATED VARIATION IN PEAK Vo_2

Age- and sex-associated variation in peak Vo_2 are considered together since sex differences are apparent during the transition into puberty. Absolute peak Vo_2 generally increases with chronological age during the first two decades of life (Armstrong and Welsman, 1994; Krahenbuhl et al., 1985). The correlation between chronological age and absolute peak Vo_2 is moderately high from 8-16 yrs of age, r=0.75 and 0.53 in boys and girls, respectively (Armstrong and Welsman, 1994). The difference in the correlations between sexes can be attributed to the leveling of absolute peak Vo_2 in females during puberty and continued increase in boys. Data compiled by Krahenbuhl et al. (1985) indicate that average values for peak Vo_2 increase from about 1.0 $L \cdot min^{-1}$ at age 6 yrs to about 2.0 $L \cdot min^{-1}$ at 12 yrs; thereafter, sex differences become more apparent. By the age of 15 yrs, peak Vo_2 is 2.8 $L \cdot min^{-1}$ in boys and 2.0 $L \cdot min^{-1}$ in girls. Between 15 and

18 yrs of age, peak Vo_2 generally increases in boys and plateaus in girls. Mirwald and Bailey (1986) reported an average yearly increase of 11% in 8-16 yr old boys (n=75) and 8-13 yr old girls (n=22) followed longitudinally. The largest absolute increases occur between 13 and 14 yrs (332 $ml \cdot min^{-1}$) in boys and 11 and 12 yrs (271 $ml \cdot min^{-1}$) in girls.

When expressed per kg of body weight, peak Vo_2 remains stable in boys and declines in girls between 6-18 yrs (Armstrong and Welsman, 1994; Krahenbuhl et al., 1985). The average value in boys is approximately 52 $ml \cdot kg^{-1} \cdot min^{-1}$. The average value for an 8 yr old girl (50 $ml \cdot kg^{-1} \cdot min^{-1}$) is similar to that of an 8 yr old boy, but declines to 45 $ml \cdot kg^{-1} \cdot min^{-1}$ by age 12 yrs and 40 $ml \cdot kg^{-1} \cdot min^{-1}$ by age 16 yrs.

Why does absolute peak Vo_2 increase with chronological age? Why do sex differences emerge, particularly during puberty? Reasons for the age- and sex-associated variation in peak Vo_2 have not been as extensively investigated. Peak Vo_2 is ultimately determined by the flow of oxygen from the ambient air across a series of structural resistors, which include: ventilation, pulmonary gas diffusion across the alveolar-capillary membrane, the binding of oxygen to hemoglobin, cardiac and circulatory function, gas diffusion across the capillary-myocyte barrier, oxidative metabolism within skeletal muscle, and finally, skeletal muscle contraction. Structural and/or functional changes or differences at any of these sites could explain the age- and sex-associated variation in peak Vo_2. Although age-associated changes in physiological function with increasing body size and organ system development are evident, the specific adaptations remain poorly understood. Rowland (1990) addresses several important questions related to this dilemma: (1) Do age-related changes in peak Vo_2 occur as a continuum throughout the pediatric years, or only at critical points (such as puberty)? (2) How great is the inter-

individual variability in the rate of growth-related changes in peak Vo_2? (3) How important is the influence of physical activity or exercise training on growth-related changes in peak Vo_2?, (4) How significant are the contributions of functional changes compared to changes in body size? The last question is very difficult to address given ethical and methodological constraints in pediatric research.

Regardless of limitations in research design, the available information indicates that body size, specifically fat-free mass, accounts for a major portion of the variance in peak Vo_2 during childhood and adolescence (Eisenmann and Malina, in press; Rowland, 1996). Rowland (1996) suggests that because relative peak Vo_2 ($ml \cdot kg^{-1} \cdot min^{-1}$) remains stable in boys during the pediatric years, the increase in absolute peak Vo_2 during this same time period can be explained *solely* on the basis of dimensional (quantitative) changes in the oxygen transport system and peripheral muscle mass, without size-dependent functional (qualitative) changes. This conclusion is also based on the comparative analysis of the increase in absolute peak Vo_2, pulmonary (lung weight and vital capacity), and cardiac (left ventricular volume) parameters; all show about a 50% increase between 8 and 16 yrs. This hypothesis is supported by the early study of Asmussen and Heebøll-Nielson (1955). Although the authors hypothesized that both quantitative and qualitative changes occur during growth, the actual exponent for peak Vo_2 was very close to being proportional to the third power of the linear dimension (stature) or body mass (see section on allometric scaling). However, longitudinal studies that examine both structural and functional parameters of the oxygen transport system areneeded.

Sex differences in peak Vo_2 throughout childhood and adolescence have been primarily explained by differences in body composition (Armstrong and Welsman, 1994; Rowland, 1996). When peak Vo_2 is expressed per kg of fat-free mass, the sex difference is greatly reduced. However, a small difference still cannot be accounted; therefore other biological or socio-environmental factors apparently contribute to sex-associated variation in the phenotypic expression of peak Vo_2. During adolescence, hemoglobin concentration and habitual physical activity may also contribute to the sex difference in oxygen transport capacity. Although physical activity levels during adolescence decline moreso in females, Armstrong and Welsman (1994) argue that children and adolescents rarely experience levels of physical activity necessary to alter peak Vo_2.

MATURITY-ASSOCIATED VARIATION IN PEAK Vo_2

Variation in a biological variable can be considered relative to maturity status (skeletal age, pubertal stage), or relative to the timing of a given pubertal event (peak height velocity [PHV]), age at menarche). Subjects can also be grouped by timing, i.e., early, average, or late maturing. Using PHV requires longitudinal data throughout the adolescent growth spurt, whereas the other two approaches can be obtained by either a cross-sectional or longitudinal observations. Relatively limited information is available on the maturity-associated variation in peak Vo_2. In general, skeletal age and absolute peak Vo_2 are highly correlated (r=0.89) over a broad age range, 8-18 yrs, but are lower (r=0.40-0.60) within narrower age ranges. In contrast, relative peak Vo_2 is not significantly related to skeletal age (Malina and Bouchard, 1991).

Although some studies have used secondary sex characteristics to group subjects as "prepubertal", "pubertal", and/or "post-pubertal", few have considered peak Vo_2 within each maturity stage. Armstrong et al (1991) grouped subjects into sexual maturity stages, but did not account for variation in chronological age within and between maturity groups. This is important since even though youth may be in the same pubertal stage, chronological age per se can influence biological functions. In other words, a 12 yr old and 14 yr old in stage 3 of pubic hair are different. Another methodological limitation was the use of an average maturation score combining pubic hair and genital in boys, and pubic hair and breast, in girls. Allowing for there methodological limitations, absolute peak Vo_2 increased in both sexes whereas relative peak Vo_2 was relatively stable in both sexes across puberty. However, this study provided little insight into the understanding of the influence of maturation per se on peak Vo_2. In a subsequent study, Armstrong and colleagues (1998) enrolled sixth grade children in a longitudinal study. The design allowed for a sample within a narrow chronological age range (12 ± 0.4 yrs). Therefore, when subjects were grouped into maturity groups (pubic hair only), the effect of chronological age is limited. Results confirmed previous findings that absolute peak Vo_2 increased and relative peak Vo_2 remained relatively stable in both sexes across maturity groups within this narrow age range.

Among the longitudinal studies including peak Vo_2, several report increments but few use smoothing techniques or graphic or algebraic fitting procedures (Beunen and Malina, 1988). Armstrong and Welsman (1994) noted that the use of mathematical models to fit growth curves for peak Vo_2 should be interpreted with caution since a limited number of annual observations were considered in these studies. The available

data indicate that absolute peak Vo_2 shows a clear adolescent spurt in both sexes at the age of PHV (Beunen and Malina, 1988). Estimated peak velocities of absolute Vo_2 from the Saskatchewan Growth Study are 412 $ml \cdot min^{-1}$ and 284 $ml \cdot min^{-1}$ in boys and girls, respectively (Mirwald and Bailey, 1986). There is no clear change in relative peak Vo_2 during adolescence, but body size may confound this observation.

Maturity-associated variation can also be considered when adolescents are grouped as early, average, and late maturing based on an indicator of maturity status. In general, absolute peak Vo_2 is greater in early maturers and relative peak Vo_2 is greater in late maturers (Kemper and Verschuur, 1987; Malina et al., 1997). The differences in absolute peak Vo_2 reflects the greater body size of early maturers; in contrast, the smaller body size of late maturers may account for the greater relative peak Vo_2.

PEAK Vo_2 IN YOUNG ATHLETES

Comparisons between young athletes and the general population have been used to draw inferences about the influence of physical activity or exercise training on peak Vo_2. Allowing for potential genetic pre-disposition of athletes, some of the variation in peak Vo_2 can be explained by environmental factors and genotype-environmental interactions. It is also important to remember that child and adolescent athletes are often ill-defined so that comparability among studies may be questioned.

Table 6.1 provides a summary of cross-sectional studies of peak Vo_2 in child and adolescent athletes, while Figures 6.1 and 6.2 show age-associated variation in peak Vo_2 of young athletes followed longitudinally. In general, child and adolescent endurance athletes possess a superior peak Vo_2 compared to the general population.

Cross-sectional studies indicate the physiological profile of young athletes. Longitudinal studies of young athletes have mainly been conducted to determine the influence of intensive training on physiological measurements associated with endurance performance (Table 6.2). These studies ordinarily rely either on bi-annual or annual visits and continue from 2-8 years in 10-20 yr old youth. Only one longitudinal study included girls (Baxter-Jones et al., 1993). As in the general population, absolute peak Vo_2 increases with age, but results for relative peak Vo_2 are equivocal. Some studies show a stable pattern of development (Daniels et al., 1978) while others report an age-related increase in relative peak Vo_2 of young athletes (Murase et al., 1981; Paterson et al., 1987). The latter finding raises questions pertinent to the present study. Does the lack of an increase in weight-specific peak Vo_2 suggest that intensive training does not influence the developmental plasticity of peak Vo_2?, or is this observation confounded by the manner in which peak Vo_2 is expressed relative to body size?

Another relevant question is the following: Are the growth increments of peak Vo_2 greater in young athletes compared to the general population? Such a comparison would provide insight into the influence of intensive training during childhood and adolescence. However, genetic regulation of growth of the components of the oxygen transport system still cannot be dismissed. Only two longitudinal studies have reported the growth velocities of peak Vo_2 (Maingourd et al., 1994; Paterson et al., 1987). Maingourd et al. (1994) found that peak Vo_2 increased 309 $ml \cdot min^{-1} \cdot kg^{-1}$ prior to PHV and 433 $ml \cdot min^{-1} \cdot kg^{-1}$ after PHV in 11-15 yr old hockey players. Growth increments extrapolated from a figure in the study by Paterson et al. (1987) indicate that peak Vo_2 increased between 250-350 $ml \cdot min^{-1} \cdot yr^{-1}$ prior to PHV and between 450-500 $ml \cdot min^{-1} \cdot yr^{-1}$ at

PHV. Yearly increments estimated from the age-specific mean values of peak Vo_2 in Daniels et al. (1978) also suggest an increase of about 500 $ml \cdot min^{-1} \cdot yr^{-1}$ during the adolescent growth spurt. Compared to the 320 $ml \cdot min^{-1}$ increase in the general population of boys (Mirwald and Bailey, 1986), it appears that growth increments in peak Vo_2 of young athletes are greater during adolescence. However, increments have a disadvantage since the continuity of the developmental process is ignored and methodological inconsistencies may be introduced (Beunen and Malina, 1988). Future studies need to systematically address this issue.

Only the Training of Young Athletes (TOYA) study has examined maturity-associated variation in peak Vo_2 of young athletes grouped by sexual maturity status (Baxter-Jones et al., 1993). Subjects were grouped in pre- (stage 1), mid- (stages 2 and 3), and late- (stages 4 and 5) pubertal groups based on development of breasts in girls and genitalia in males. Absolute peak Vo_2 increased with advanced maturity status and relative peak Vo_2 remained stable in girls and increased in male swimmers and soccer players across maturity groups.

BASIC PRINCIPLES AND HISTORICAL BACKGROUND OF SCALING

The concept of scaling is a fundamental principle of engineering and a basic concept in the zoological sciences, particularly among comparative mammalian physiologists. Scaling is a cornerstone in the search for unifying principles among animals of differing body mass and shape (White, 1987). Engineers have long recognized that when the size of a structure is increased, three parameters could possibly

change - the dimensions, the materials, or the design of the structure. In animals, linear dimensions and body mass can easily be measured.

Principles of scaling are based on dimensionality theory, where surface area is proportional to the volume raised to the 2/3 power. Thus, as the volume of a body increases, its surface area does not increase in the same proportion, but rather as the 2/3 power of the volume. This argument holds only for an isometric body. Animals (and particularly growing animals), however, are not isometric, since certain proportions change in a regular fashion. Non-isometric scaling is referred to as allometric scaling (Schmidt-Nielsen, 1984).

A fundamental question related to scaling is, 'How should differences in body size be partitioned mathematically or statistically?' Several authors have addressed this question (Smith, 1984; Winter, 1996). Traditionally, exercise physiologists have expressed physiological measurements as a ratio standard (i.e., Vo_2 as $ml \cdot kg^{-1} \cdot min^{-1}$). Fifty years ago, Tanner (1949) addressed the theoretically fallacious and misleading practice of expressing physiological measurements per unit of body mass or per unit of surface area. Although acknowledged periodically thereafter, until recently the issue of scaling of Vo_2 has not been systematically addressed in humans. Nevertheless, the use of ratio standards remains common in exercise science.

How differences in body size can be partitioned mathematically or statistically may best be answered by the following three points of Packard and Boardman (1987) in a critical review of the use and misuse of ratios in ecological physiology:

> 1) Biologists were influenced by competent biometricians to use ratio standards to scale physiological data,

2) Ratios are easy to compute, and

3) It is hard to imagine that ratios can be misleading, because they are so easy to compute and comprehend.

Due to the theoretical and statistical limitations of the ratio standard, other statistical methods including linear regression, analysis of covariance (ANCOVA), allometric models, power functions, and multilevel modeling have recently gained attention in the exercise sciences (Armstrong and Welsman, 1994; Winter, 1996). The most widely used of these models is allometry. The allometric, or power function, equation has the general form $y = ax^b$ which describes the curvilinear relationship between a biological variables. In biological problems related to body size, the independent variable (x) is body mass (M_b) so that the allometric equation is expressed as, $y = a\ M_b{}^b$. In the present context, peak Vo_2 represents y, or the dependent variable.

Early studies of animals representing a wide range of animals from rodents to elephants indicated that a scaling factor of approximately 0.74 best describes the relationship between body size and resting metabolic rate (Brody, 1945; Kleiber, 1932). Taylor and Weibel (1981) used allometric scaling to compare the size of various structures in the oxygen transport system with peak Vo_2 in wild African and domestic mammals ranging from a 0.5 kg dwarf mongoose to a 263 kg Zebu cow. Findngs from this study were consistent with the theoretical models that peak Vo_2 scales to $M_b{}^{0.75}$.

When should allometry be used? Calder (1987) suggests that as useful as allometry may be, there is lack of a general consensus on principles of its application. To clarify the application of allometry, the following points have been emphasized by Schmidt-Nielson (1984).

- Allometric equations are descriptive; they are not biological laws.
- Allometric equations are useful for showing how a variable quantity is related to body size, all other things being equal.
- Allometric equations are valuable tools because they may reveal principles and connections that otherwise remain obscure.
- Allometric equations are useful as a basis for comparisons and can reveal deviations from a general pattern.
- Allometric equations are useful in estimating the expected magnitude of some variable for a given body size.
- Allometric equations cannot be used to extrapolate beyond the range of the data on which they are based.

ALLOMETRIC SCALING, BODY SIZE, AND PEAK VO_2

Peak Vo_2 increases as a function of body size throughout the animal kingdom. As noted above, peak Vo_2 in wild and domestic mammals scales approximately proportional to the theoretical value of $M_b^{0.75}$. In humans, the peak Vo_2 -body mass relationship also exists, particularly during growth and maturation. Given variation and change in body size and peak Vo_2 associated with growth and maturation, much of the attention on scaling peak Vo_2 for body size has been directed at children and adolescents. Table 6.3 provides a summary of reported scaling factors for peak Vo_2 in children and adolescents. Mean scaling factors for peak Vo_2 range from 0.27 to 1.09. An argument can be made that just as many scaling factors approximate $M_b^{1.0}$ as those that approximate the theoretical values of 0.67 and 0.75. This observation has led to the recommendation that

peak Vo_2 be expressed as a simple ratio standard in children and adolescents (Bar-Or, 1983). Nevill (1994) has explained this observation based upon the findings of Alexander et al. (1981), who demonstrated that larger mammals have a greater proportion of segmental muscle mass in relation to their total body mass, i.e., leg muscle mass is proportional to body mass$^{1.1}$. From an ontogenetic perspective, children may exhibit a disproportionate increase in muscle mass and, therefore, violate the assumption of the allometric model.

Until this point, the growth-related changes in peak Vo_2 have been considered in absolute terms and expressed as a ratio standard. Armstong and Welsman (1994) argue against the expression of peak Vo_2 as a ratio standard for growth-related comparisons, stating that it clouds the understanding of growth and maturational changes in the oxygen transport system. As noted earlier, peak Vo_2 expressed per unit body mass remains relatively stable during childhood and adolescence in boys and decreases with age in girls, particularly during adolescence. To explore the growth-related changes in peak Vo_2, Armstrong and colleagues (1994) have used various allometric scaling techniques. Adjusted means (ANCOVA controlling for body mass) for peak Vo_2 were similar between 10 and 15 year old boys (2.21 and 2.30 $L \cdot min^{-1}$, respectively). In a subsequent paper, a significant increase in peak Vo_2 from prepubertal to pubertal and adult males, and between prepubertal and pubertal girls was noted when data were fitted by linear and log-linear allometric models adjusted for body mass (Welsman et al., 1996). Adjusted means were similar between pubertal and adult females, suggesting that peak Vo_2 remains constant during this period. These results are intriguing, given past assumptions about growth-related changes in peak Vo_2. Recently, Armstrong et al. (1998) also

demonstrated a maturity-associated increase in peak Vo_2 in 12 year old boys and girls. Log-linear adjusted means increased from 2.01 to 2.30 $L \cdot min^{-1}$ in boys and 1.78 to 1.99 $L \cdot min^{-1}$ in girls grouped by stage of pubic hair development.

The preceding results are based on cross-sectional analyses. A longitudinal study of 11-14 yr old youth active in sport (track, wrestling, basketball) found that the peak Vo_2 -body size relationship varied with maturity status and sex (Beunen et al., 1997). In early and average maturing boys, peak Vo_2 increased at a slightly higher rate than expected from the increase in body mass, whereas in later maturing boys the increase was smaller than expected. In contrast, the increase of peak Vo_2 in girls active in sport (track, rowing) was generally unrelated to the increase in body mass or stature. There was also considerable inter-individual variation in scaling coefficients during early and mid-adolescence. These results, though limited to early and mid-adolescence, suggest sex- and maturity-associated variation in growth of the oxygen transport system.

A different interpretation of growth-related changes in peak Vo_2 of young athletes is also evident when peak Vo_2 is expressed per $kg^{-0.75}$ (Sjodin and Svedenhag, 1992), or when body size is controlled in multi-level modeling (Baxter-Jones et al., 1993). Although peak Vo_2 remained stable during adolescence in young distance runners when expressed as a ratio standard, peak Vo_2 expressed by the exponent 0.75 showed an increase from 161 to 186 $ml \cdot kg^{-0.75} \cdot min^{-1}$ (Sjodin and Svedenhag, 1992) . The increase in peak Vo_2 appeared to occur from 3 yrs before PHV to 6 months after PHV with a plateau occurring thereafter. In the TOYA study, peak Vo_2 increased after statistically controlling for age, stature, and body mass in males across pubertal status, and in girls from pre- to mid-puberty with no further increase between mid- and late-puberty (Baxter-

Jones et al., 1993). However, despite acclaimed usefulness in the interpretation of longitudinal data, the biological significance of the results derived from the multilevel modeling approach is difficult to interpret.

SCALING PEAK Vo_2: IMPLICATIONS FOR ENDURANCE PERFORMANCE AND HEALTH-RELATED FITNESS

The importance of scaling peak Vo_2 for differences in body size in the interpretation of growth-related changes in peak Vo_2 has been considered. An additional question is "What are the implications for endurance performance and health-related fitness?" The application of scaled peak Vo_2 to the interpretation of endurance performance and health-related fitness has received limited attention. Based on the various analyses and interpretations, the utility of allometric scaling may need to be considered in the context of the problem.

Svedenhag (1995) recently reviewed the implications of scaling peak Vo_2 and submaximal Vo_2 ($Vo_{2\ submax}$) for evaluations of the endurance athlete. The author suggested that whether peak Vo_2 and $Vo_{2\ submax}$ is scaled to $M_b^{1.0}$ or $M_b^{0.75}$ may influence the evaluation and the selection of a training program for an endurance athlete (Table 6.4). In this example, Runners A and B have an equivalent fractional utilization of Vo_2 ($\%Vo_2$) and similar performance levels. Based on the traditional ratio standard for $Vo_{2\ submax}$ and peak Vo_2 ($ml \cdot kg^{-1} \cdot min^{-1}$), Runner A has a better running economy but a lower peak Vo_2, whereas Runner B has a poorer running economy and a higher peak Vo_2. This may lead a coach or athlete to manipulate training in an attempt to improve upon the poorer functional capacity. In contrast, if values are expressed per unit $kg^{0.75}$, the

runners have similar values, or perhaps results contrary to the initial analysis. Thus, scaling $Vo_{2\ submax}$ and peak Vo_2 may influence the findings at evaluation and resultant training programs for endurance athletes. In contrast, Nevill (1997) suggested that the ratio standard provides the best predictor of weight-bearing athletic performance. Using a multiple log-linear regression, the best predictor of 5 km race performance in adults was almost exactly proportional to the ratio standard (Nevill et al., 1992).

When considering such physiological variables as peak Vo_2 in the context of risk factors, Nevill (1997) also noted the importance of partitioning the confounding effects of chronological age, body size, and biological maturity status. However, no study could be identified that specifically addressed the implication of scaled peak Vo_2 on the health-related fitness of either children or adults.

SUMMARY

Absolute peak Vo_2 is related to chronological age, biological age, and body size during childhood and adolescence, and increases by about 11% annually with the largest increase occurring near the time of PHV. Although limited by methodological and ethical constraints, it appears that quantitative increases in overall body size and the components of the oxygen transport system rather than qualitative changes in the functional properties of the components of the oxygen transport system explain growth-related changes in peak Vo_2. Sex-associated variation occurs due to differences in body composition, hematological, and perhaps, physical activity patterns. Sex differences are small prior to puberty, but increase greatly during adolescence. Future longitudinal

studies of children and adolescents, both athletes and non-athletes, need to consider both quantitative and qualitative changes in the oxygen transport system.

When expressed as a ratio standard, peak Vo_2 remains stable in boys and decreases in girls, particularly during adolescence. However, exercise scientists have been criticized for not recognizing the imperfections of ratio standards and for being unaware of alternative methods for partitioning the effects of body size in human studies (Winter, 1996). Therefore, current studies are exploring the use of allometric scaling in expressing peak Vo_2 during childhood and adolescence. However, it remains to be demonstrated if allometric scaling within a small magnitude of differences in body size warrants such statistical manipulation. According to Calder (1987), a small size range within a species obscures overall trends, patterns, and constraints of body size. Thus, scaling differences in body size within a small range of body size to understand variation in biological function may be of limited value. In contrast, others argue that scaling body size helps us to understand the growth and maturation of the oxygen transport system, its response to submaximal and maximal exercise (Armstrong and Welsman, 1994), its relationship to risk factors (Nevill, 1997), and the evaluation of endurance athletes (Svedenhag, 1995). The application of allometric scaling to the age-, sex-, and maturity-associated variation in peak Vo_2 of well-trained pediatric endurance athletes is limited. Part II of this dissertation examines this issue.

REFERENCES

Alexander RM, Jayes AS, Maloiy GMO, Wathuta EM (1981) Allometry of the leg muscles of mammals. J Zool 194:539-552.

Armstrong N, Welsman JR (1994) Assessment and interpretation of aerobic fitness in children and adolescents. Exerc Sport Sci Rev 22:435-476.

Armstrong N, Welsman JR, Kirby BJ (1998) Peak oxygen uptake and maturation in 12-yr olds. Med Sci Sports Exerc 30:165-169.

Armstrong N, Williams J, Balding J, Gentle P, Kirby B (1991) The peak oxygen uptake of British children with reference to age, sex and sexual maturity. Eur J Appl Physiol 62:369-375.

Asmussen E, Heebol-Nielsen K (1955) Dimensional analysis of physical performance and growth in boys. J Appl Physiol 7:593-603.

Bar-Or O (1983) Pediatric Sports Medicine for the Practitioner. New York: Springer-Verlag.

Baxter-Jones A, Goldstein H, Helms P (1993) The development of aerobic power in young athletes. J Appl Physiol 75:1160-1167.

Beunen GP, Malina RM (1988) Growth and physical performance relative to the timing of the adolescent spurt. Exerc Sci Sports Rev 16:503-540.

Beunen GP, Rogers DM, Woynarowska B, Malina RM (1997) Longitudinal study of ontogenetic allometry of oxygen uptake in boys and girls grouped by maturity status. Ann Hum Biol 24:33-43.

Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW (1989) Physical fitness and all-cause mortality: a prospective study of healthy men and women. JAMA 17:2395-2401.

Brody S (1945) Bioenergetics and Growth, with Special Reference to the Efficiency Complex in Domestic Animals.New York: Reinhold.

Calder WA (1987) Scaling energetics of homeothermic vertebrates: an operational allometry. Ann Rev Physiol 49:107-120.

Coyle E (1995) Integration of the physiological factors determining endurance performance ability. Exerc Sport Sci Rev 23:25-63.

Daniels J, Oldridge N, Nagle F, White B (1978) Differences and changes in Vo2 among young runners 10 to 18 years of age. Med Sci Sports 10:200-203.

Daniels J, Oldridge N, Nagle F, White B (1978) Differences and changes in Vo2 among young runners 10 to 18 years of age. Med Sci Sports 10:200-203.

Eisenmann JC, Malina RM (in press) Body size and endurance performance. In RJ Shephard (ed.): Endurance in Sport. Oxford: Blackwell Science.

Kemper HCG, Verschuur R (1987) Longitudinal study of maximal aerobic power in teenagers. Ann Hum Biol 14:435-444.

Kleiber M (1932) Body size and metabolism. Hilgardia 6:315-353.

Krahenbuhl GS, Skinner JS, Kohrt WM (1985) Developmental aspects of maximal aerobic power in children. Exerc Sport Sci Rev 13:503-538.

Maingourd Y, Libert JP, Bach V, Jullien H, Tanguy C, Freville M (1994) Aerobic capacity of competitive ice hockey players 10-15 years old. Jap J Physiol 44:255-270.

Malina RM, Beunen G, Lefevre J, Woynarowska B (1997) Maturity-associated variation in peak oxygen uptake in active adolescent boys and girls. Ann Hum Biol 24:19-31.

Malina RM, Bouchard C (1991) Growth, Maturation, and Physical Activity. Champaign, IL: Human Kinetics.

Mirwald RL, Bailey DA (1986) Maximal Aerobic Power: A Longitudinal Analysis. London, Ontario: Sports Dynamics.

Murase Y, Kobayashi K, Kamei S, Matsui H (1981) Longitudinal study of aerobic power in superior junior athletes. Med Sci Sports Exerc 13:180-184.

Nevill AM (1994) The need to scale for differences in body size and mass: an explanation of Kleiber's 0.75 mass exponent. J Appl Physiol 65:110-117.

Nevill AM (1997) The appropriate use of scaling techniques in exercise physiology. Pediatr Exerc Sci 9:295-298.

Nevill AM, Ramsbottom R, Williams C (1992) Scaling physiological measurements for individuals of different body size. Eur J Appl Physiol 65:110-117.

Packard G, Boardman T (1987) The misuse of ratios to scale physiological data that vary allometrically with body size. In M Feder, A Bennet, W Burggren and R Huey (eds.): New Directions in Ecological Physiology. Cambridge: Cambridge University Press, pp. 216-236.

Rowland TW (1990) Developmental aspects of physiological function relating to aerobic exercise in children. Sports Med 10:255-266.

Rowland TW (1996) Developmental Exercise Physiology. Champaign, IL: Human Kinetics.

Schmidt-Nielsen K (1984) Scaling: Why is animal size so important? Cambridge: Cambridge University Press.

Sjodin B, Svedenhag J (1992) Oxygen uptake during running as related to body mass in circumpubertal boys: a longitudinal study. Eur J Appl Physiol 65:150-157.

Smith R (1984) Allometric scaling in comparative biology: problems of concept and method. Am J Physiol 246:R152-R160.

Svedenhag J (1995) Maximal and submaximal oxygen uptake during running: how should body mass be accounted for? Scand J Med Sci Sports 5:175-180.

Tanner JM (1949) Fallacy of per-weight and per-surface area standards, and their relation to spurious correlation. J Appl Physiol 2:1-15.

Taylor CR, Maloiy GMO, Weibel EW, Langman VA, Kamau JMZ, Seeherman HJ, Heglund NC (1981) III. Scaling maximum aerobic capacity to body mass: wild and domestic mammals. Respir Physiol 44:3-37.

Weibel E (1984) The Pathway for Oxygen: Structure and Function in the Mammalian Respiratory System. Cambridge: Harvard Press.

Welsman JR, Armstrong N, Nevill AM, Winter EM, Kirby BJ (1996) Scaling peak Vo2 for differences in body size. Med Sci Sports Exerc 28:259-265.

White F (1987) Scaling and structure-function relationships. Ann Rev Physiol 49:105-106.

Winter EM (1996) Importance and principles of scaling for size differences. In O Bar-Or (ed.): The Child and Adolescent Athlete. Oxford: Blackwell Science, pp. 673-679.

Table 6.1. Mean peak oxygen consumption (peak Vo_2) reported in cross-sectional studies of child and adolescent endurance athletes.

Study	N	Age (yrs)	Sex	Sport	Vo_{2max} ($ml \cdot kg^{-1} min^{-1}$)
Dill and Adams (1971)	6	17	M	Running	72.0
Vaccaro and Clarke (1978)	15	9-11	M	Swimming	55.4
Kobayashi et al. (1978)	4	17	M	Running	73.9
Mayers and Gutin (1979)	8	8-11	M	Running	56.6
Lehmann et al. (1981)	8	12	M	Running	60.3
Sundberg and Elovaino (1982)	12	12	M	Running	59.3
	12	16			66.4
Fario et al. (1989)	15	15-19	M	Cycling	75.5
Nudel et al. (1989)	16	8-17	M, F	Running	61.0
Cunningham (1989)	20	15	F	Running	62.1
Cunningham (1990)	12	16	F	Running	66.1
	12	16	M		74.6
Rowland et al. (1991)	10	11-13	M	Running	61.2

Adapted from Rowland (1996).

Table 6.2. Longitudinal studies of physiological capacity in child and adolescent endurance athletes.

Study	Subjects	Methods	Main findings
Daniels et al. (1978)	20 male middle distance runners; ages 10-18 yrs (mixed-longitudinal)	data collected every 6 months for 2-5 yrs	no change in relative peak Vo_2; decrease in submax Vo_2 with age
Murase et al. (1981)	11 Japanese male middle and long distance winners in the Jr. Championships; ages 14-21 yrs	annual visit for 5-7 yrs; 5 boys stopped training after 18 yrs of age	increase in relative peak Vo_2 (65 to 75 $ml \cdot kg^{-1} min^{-1}$)
Paterson et al. (1987)	18 boys involved in sport who were in the upper quartile of those tested in lab; age 11-15 yrs	annual visit for 5 yrs	increase in rel Vo_{2max} (61 to 68 $ml \cdot kg^{-1} min^{-1}$) and VT (34 to 42 $ml \cdot kg^{-1} min^{-1}$); VT/Vo_{2max} stable; when aligned to PHV, greatest increase in Vo_{2max} occurs at PHV, while VT stable
Sjodin and Svendenhag (1992)	8 trained and 4 untrained boys; age 12-20	every 6 months for 8 yrs	spurt in relative Vo_{2max} 6 months after PHV in trained group; decrease in submax Vo_2; increase in peak Vo_2 expressed per $kg^{-0.75}$
Baxter-Jones et al. (1993)	38 male and 39 females swimmers; ages 12-19 yrs (mixed-longitudinal)	annual visit for 3 yrs.; multi-level modelling	Peak Vo_2 increased when age and body size were controlled;
Maingourd et al. (1994)	11 ice hockey players; ages 10-15 yrs	annual visit for 6 yrs	Peak Vo_2 and VT positively correlated with PHV; Increments constant from yr to yr

Vo_2, oxygen consumption; VT, ventilatory threshold; PHV, peak height velocity

Table 6.3. Summary of scaling factors for peak Vo_2 in children and adolescents.

Study	N	Sex	Age (yrs)	Mode	M_b Exponent
Cross-sectional					
Åstrand (1952)	68	M, F	6-17	T	0.95^
Cooper et al. (1984)	58	M	6-17	C	1.09
	51	F			0.83
	109	M,F			1.01
Rogers et al. (1995)	25	M,F	7-10	T	0.47
	27	M,F	11-14		0.62
Welsman et al. (1997)	32	M, F	9-10	T	0.52
Armstrong et al. (1998)	212	M,F	12	T	0.65
Longitudinal					
Åstrand et al. (1963)	30	F	12-16		0.97#
Daniels et al. (1972)	14	M	10-15	T	1.07#
Klissouras (1972)	50*		7-13		0.88#
Bailey et al. (1978)	51	M	8-15	T	0.82^
Paterson et al. (1987)	18	M	11-15	T	1.02 1.19**
Sjodin & Svedenhag (1992)	8 (trained)	M	11-15	T	1.01
	4 (untrained)	M			0.78
Beunen et al. (1997)	47	M	11-14	C	0.80 (early + avg. maturers) 0.57 (late maturers)**
	31	F			0.27 (early + avg. maturers) 0.42 (late maturers)**

M_b, body mass; T, treadmill; C, cycle ergometer.
Table adopted from Rowland (1996).
#As estimated by McMiken (1976).
*25 sets of twins including 15 pairs of identical twins and 10 pairs of fraternal twins.
**Results of ontogenetic allometric scaling.
^As reported by Rowland (1996).

Table 6.4. A comparison of two elite distance runners of differing body mass and submaximal and peak Vo_2 based on simple ratio standard and allometric scaling.

			Vo_2 submax		Peak Vo_2	
	Mass (kg)	FU (%)	$ml \cdot kg^{-1} \cdot min^{-1}$	$ml \cdot kg^{-0.75} \cdot min^{-1}$	$ml \cdot kg^{-1} \cdot min^{-1}$	$ml \cdot kg^{-0.75} \cdot min^{-1}$
Runner A	80	75	55.5	166	74.0	221
Runner B	50	75	61.5	164	82.0	218

Adopted from Svedenhag (1995).
FU, fractional utilization (Vo_2 submax/peak Vo_2).

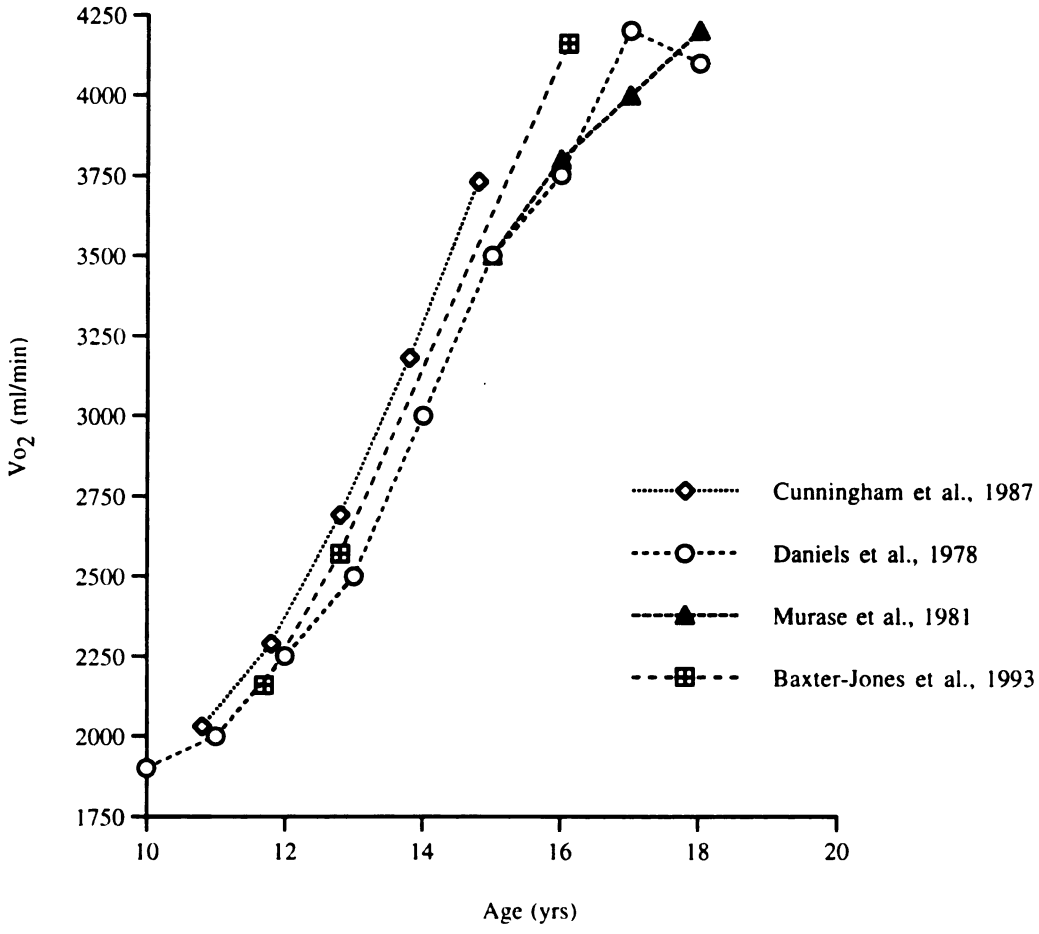

Figure 6.1. Longitudinal studies of absolute peak Vo2 in male athletes.

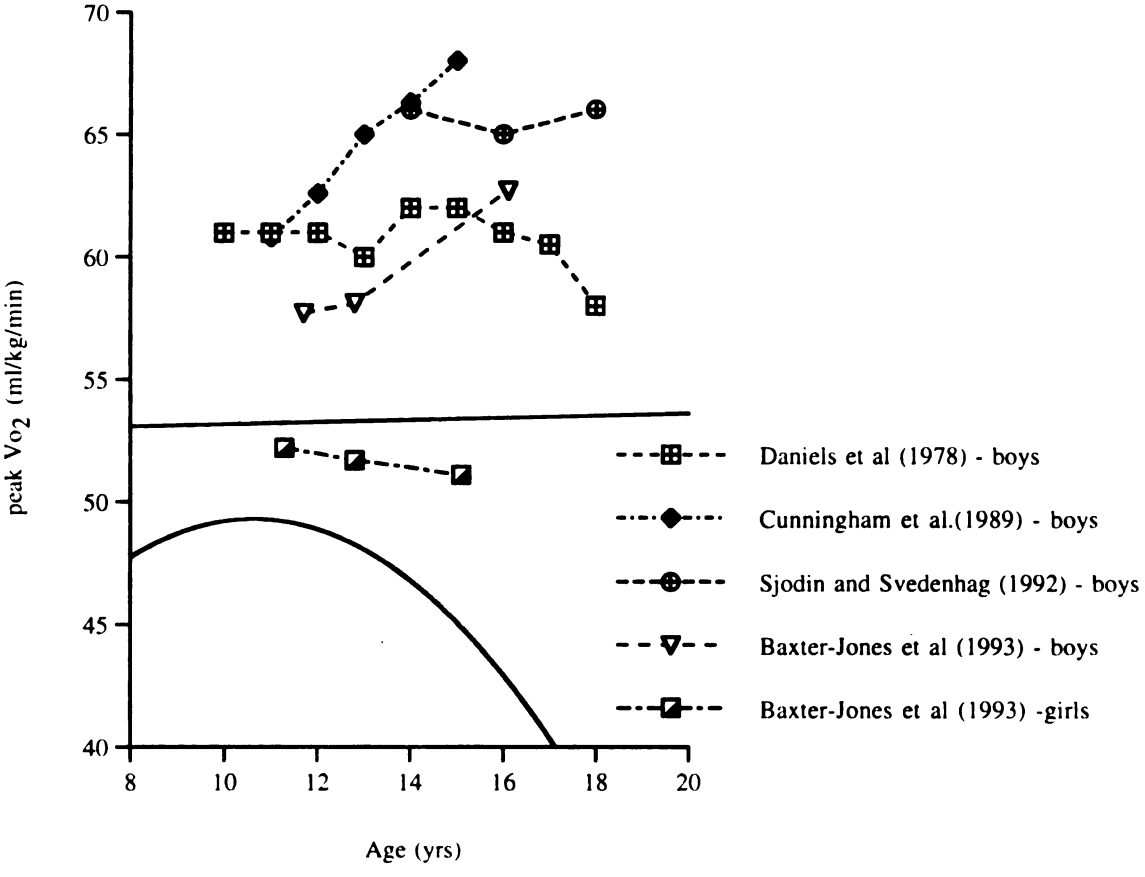

Figure 4. Longitudinal studies of relative peak Vo2 in young athletes. Solid lines represent age-related changes in the general population.

CHAPTER 7

SCALING PEAK Vo_2 TO BODY MASS IN YOUNG MALE AND FEMALE DISTANCE RUNNERS

ABSTRACT

This study examined age- and sex-associated variation in peak Vo_2 of young male and female distance runners from an allometric scaling perspective. Subjects were from two separate studies of 9-19 yr old distance runners from the mid-Michigan area, one conducted between1982-1986 (Young Runners Study I, YRS I) and the other in 1999-2000 (Young Runners Study II, YRS II). Data from 27 males and 27 females from YRS I and 48 males and 22 females from the YRS II were included, and a total of 139 and 108 measurements of body size and peak Vo_2 in males and females, respectively, were available. Subjects were divided into whole year age groups. A 2x9 (sex x age group) ANOVA was used to examine differences in peak Vo_2. Intra-individual ontogenetic allometric scaling was determined in 20 males and 17 females measured annually for 3-5 years. Allometric scaling factors were calculated using linear regression of log-transformed data. Results indicated that 1) absolute peak Vo_2 increases with age in boys and girls, 2) relative peak Vo_2 ($ml \cdot kg^{-1} min^{-1}$) remains stable until age 15 when it increases in boys and decreases in girls, 3) relative peak Vo_2 ($ml \cdot kg^{-0.75} min^{-1}$) increases throughout the age range in boys and increases in girls until age 15 yrs, and 4) peak Vo_2 adjusted for body mass ($ml \cdot min^{-1}$) increases with age in boys and girls. The overall mean cross-sectional scaling factor was 1.01 ± 0.03 (SE) in boys and 0.85 ± 0.05 (SE) in girls. Significant age x sex interactions and significant scaling factors between sexes identifies the progressive divergence of peak Vo_2 between adolescent male and female distance runners. Mean ontogenetic allometric scaling factors were 0.81 (0.71-0.92, 95% CI) and 0.61 (0.50-0.72, 95% CI) in males and females, respectively (p=0.002). There was considerable variation in individual scaling factors (0.51-1.31 and 0.28-0.90 in males and

females, respectively). The results suggest that the interpretation of growth-related changes in peak Vo_2 of young distance runners is dependent upon the manner of expressing peak Vo_2 relative to body size and/or the statistical technique employed.

INTRODUCTION

During growth and maturation, absolute peak Vo_2 ($ml \cdot min^{-1}$) increases as a function of body size (Armstrong and Welsman, 1994; Krahenbuhl et al., 1985). A major question related to this observation is, "Are the growth-related improvements in physiological capacity a function of increasing body size or qualitative changes in the structural and functional capacity independent of body size or both?" (Rowland, 1990; Winter, 1996). To provide answers to this question, the potentially confounding effect of variation in body size must be appropriately partitioned.

Age- and sex-associated variation in peak Vo_2 has been extensively studied in the general population (Armstrong and Welsman, 1994; Krahenbuhl et al., 1985). Several cross-sectional studies have characterized the physiological profile of young endurance athletes, but longitudinal studies of the development of peak Vo_2 in young athletes, especially females, are rather limited (Baxter-Jones et al., 1993; Beunen et al., 1997; Daniels et al., 1978; Maingourd et al., 1994; Murase et al., 1981; Paterson et al., 1987; Sjodin and Svedenhag, 1992). These studies generally include small sample sizes and are limited to a narrow age range (i.e., 11-15 yrs), and therefore, do not describe the growth-related changes in peak Vo_2 across the entire adolescent period. Longitudinal studies are important to identify individual and population growth patterns. Thus, there is a need for analyses of longitudinal data examining the age- and sex-associated variation of peak Vo_2 in young athletes from various sports.

Traditionally and conventionally, peak Vo_2 is expressed as a ratio standard, or per kg of body mass ($ml \cdot kg^{-1} \cdot min^{-1}$). When expressed as the simple ratio standard, peak Vo_2 remains stable in boys and declines in females during adolescence (Krahenbuhl et al.,

1985). By expressing peak Vo_2 in this manner, it is assumed that peak Vo_2 is "normalized" and the influence of body mass is removed. However, the theoretical and statistical limitations of the ratio standard have been widely addressed, yet largely ignored (Tanner, 1949; Winter, 1996). Therefore, alternate statistical models, including analysis of covariance (ANCOVA), allometric scaling, and multilevel modeling have been used to create a "size-free" expression of peak Vo_2. The mathematical model that is widely used to create a "size-free" variable is allometry. Besides the calculation of cross-sectional allometric scaling factors, intra-individual, or ontogenetic, scaling factors can be calculated from longitudinal records. Ontogenetic allometry refers to differential growth in the individual growth process (Gould, 1966). Few studies have employed ontogenetic allometry to examine growth-related changes of peak Vo_2 in young athletes (Beunen et al., 1997; Paterson et al., 1987; Sjodin and Svedenhag, 1992).

The purpose of this study is to examine age- and sex-associated variation of peak Vo_2 in competitive young distance runners from an allometric scaling perspective.

METHODS

Design

Subjects are from two separate studies of young distance runners from the mid-Michigan area conducted at the Institute for the Study of Youth Sports at Michigan State University. The first study (Young Runners Study I, YRS I) was an inter-disciplinary, mixed-longitudinal assessment of intensive training and competition on "elite" young distance runners between 1982 and 1986 (Seefeldt, 1986). The second study (Young Runners Study II, YRS II) was a cross-sectional study of the association between training

volume and blood cholesterol that included the measurement of peak Vo_2. Data sets were pooled for the cross-sectional analysis to create a larger sample for age group comparisons. Differences in subject inclusion criteria, treadmill protocol, and exercise testing systems between the two studies are recognized. However, subjects from both studies were highly trained based on training history, race performance, and peak Vo_2. Previous studies have also shown that minimal differences in peak Vo_2 occur due to treadmill protocol (speed and incline, continuous versus discontinuous) (Paterson et al., 1981; Skinner et al., 1971) and exercise testing systems (automated versus non-automated) (Jones, 1984). The former has specifically been addressed in adolescent distance runners (Rivera-Brown et al., 1994). Only data from the YRS I was used for the ontogenetic allometric analysis.

Subjects

YRS I. Runners between the ages of 8 and 15 years, who consistently placed within the top five finishers of road races of 10 km or more by age and sex, were identified and contacted for the study. Race results were obtained from a statewide running publication, *Michigan Runner*, between May and August 1981. Of the runners contacted (response rate unknown), 27 males and 27 females agreed to participate in the study. Subjects entered the study at 8.0 to 15.7 years of age and were followed annually. Twenty males and 17 females were followed at approximately annual intervals for 3 to 5 years. The remaining subjects (7 boys and 10 girls) participated in either 1 or 2 annual visits. Each age and sex group included only one observation per subject, thus the subjects were treated as independent in each age group. A total of 99 and 84 annual

measurements were available for males and females, respectively. Parental consent and child assent was obtained prior to the study. The study was approved by the Michigan State University Committee for Research Involving Human Subjects.

YRS II. Forty-eight males and 22 females, 10-19 years of age, agreed to participate in the study. Eligible subjects participating on local Michigan junior or senior high school cross-country teams or local track clubs during Fall,1999 and Spring, 2000 were invited to participate. Administrators of the various organizations (i.e., camps, schools) were contacted and given information about the study. A brief description of the study was provided to athletes participating on interscholastic teams and track clubs. Information about the study was also provided at local road races and running facilities, and in the local newspaper. Due to the primary objective of the study being the investigation of blood cholesterol the following exclusion criteria were indicated: current smoking, excessive alcohol intake, current use of blood cholesterol lowering and anti-hypertensive medication, anabolic steroid use, hepatic, renal, and thyroid disease. In addition, subjects who had trained less than 30-40 weeks per year or non-consecutively during the past 3 consecutive months were also excluded to ensure a sample engaged in regular participation in long distance running. Parental consent and child assent was obtained prior to the study. The study was approved by the Michigan State University Committee for Research Involving Human Subjects.

Anthropometry.

YRS I. Chronological age was calculated as the difference between observation date and birthdate, and expressed as a decimal age. Anthropometry was conducted by

two experienced anthropometrists according to standard procedures (Weiner and Lourie, 1969). Stature was measured with a fixed stadiometer. The subject stood erect, without shoes and with weight distributed evenly between both feet, heels together, arms relaxed at the sides, and the head in the Frankfort horizontal plane . Body mass was measured with the subject attired in gym shorts and T-shirt without shoes on a balance beam scale. Measurements were conduced between early morning and mid-afternoon. Intra- and/or inter-observer reliabilities were not reported.

YRS II. Chronological age was calculated as the difference between observation date and birthdate, and expressed as a decimal age. Stature and body mass were measured according to the procedures of the International Biology Program (Weiner and Lourie, 1969). Stature was measured with a fixed stadiometer. The subject stood erect, without shoes and with weight distributed evenly between both feet, heels together, arms relaxed at the sides, and the head in the Frankfort horizontal plane. Body mass was measured with the subject attired in gym shorts and T-shirt without shoes on a balance beam scale. The stadiometer and scale were calibrated periodically during the study. Intra-observer reliability was conducted on a small sub-sample by the principal investigator (JCE). The intra-class correlation coefficient was 0.99 for both stature and body mass, whereas the intra-observer technical errors of measurement were 0.42 cm for stature and 0.08 kg for body mass.

Measurement of maximal oxygen consumption.

YRS I. An intermittent progressive treadmill protocol consisting of 3 minute work intervals and 3 minute rest intervals until volitional exhaustion was used to determine

peak Vo_2. The protocol began with a warm-up at 6 mph and 0% grade. Foolowing the warm-up, the grade was increased to 5%. Speed increased 1 mph and grade increased 1% in each subsequent stage until volitional exhaustion. Expired gases were collected using the Douglas bag method. Gas concentrations were analyzed with Beckman oxygen and carbon dioxide analyzers within two minutes after collection. Gas volumes were measured with a Parkinson-Cowan CD2 dry gas meter. Prior to testing, expired gas volumes were calibrated with a 3-L syringe and gas concentrations were calibrated with standard gases of known concentrations. Heart rate was monitored using a commercial electrocardiogram. End of test criteria were established by volitional exhaustion, HR $\geq$90% of age-predicted maximum, respiratory exchange ratio >1.0, and a plateau in Vo_2 (defined by an increase in Vo_2 of <2.0 $ml \cdot kg^{-1} \cdot min^{-1}$ with increasing workload). Two of the latter three criteria must have been met for a subject to be included in the analysis.

YRS II. A maximal exercise test was conducted on a motorized treadmill to exhaustion in an air-conditioned laboratory (20-22 degrees C, relative humidity 45-60%). The treadmill protocol was determined by the subject's estimated 5 km race pace. Subjects walked/jogged at a speed of 3 mph and 4.5 mph for 1 min each. This initial warm-up period was followed by 4 minute stages at 6, 7.5, and 8 mph (depending on estimated 5 km race pace) and then increased in grade of 2.5% every minute until exhaustion or test termination. Expired gases were collected for the measurement of oxygen consumption (Vo_2), carbon dioxide production (VCo_2), and minute ventilation. Expired gases were continually sampled and averaged every 20 seconds via the open circuit method using a metabolic cart (Gould 2900; Dayton, OH). Expired gas volumes were measured with a flow probe anemometer and expired gas concentrations were

measured by electronic analyzers. Prior to testing, expired gas volumes were calibrated with a 3-L syringe and gas concentrations were calibrated with standard gases of known concentrations. Heart rate was continually monitored by pulse telemetry (Polar Advantage). End of test criteria were established by volitional exhaustion, HR ≥90% of age-predicted maximum, respiratory exchange ratio >1.0, and a plateau in Vo_2 (defined by an increase in Vo_2 of <2.0 $ml \cdot kg^{-1} \cdot min^{-1}$ with increasing workload). Two of the latter three criteria must have been met to be included in the analysis.

Statistical analysis.

Subjects were divided into whole year age groups (i.e., 11.0 to 11.99), except for the youngest age group in both sexes, which consisted of subjects 9.0 to 10.99 years, and the oldest age group in girls that consisted of subjects 17.0 to 19.49 years. Descriptive statistics were calculated by age and sex groups for absolute peak Vo_2 and relative peak Vo_2 expressed per $kg^{1.0}$ and per $kg^{0.75}$. The exponent 0.75 is common in the allometric literature and is based on both theoretical and statistical evidence. A 2x9 (sex x age group) ANOVA was used to examine differences in peak Vo_2. Paired post hoc differences were examined by the Scheffé test. The allometric analysis was applied to the entire group for each sex (i.e., scaling factor for all boys and all girls) and to each age- and sex-specific group (i.e., scaling factor for 14 yr old girls, etc.).

Allometric scaling. Prior to allometric analysis, the relationship between body mass and peak Vo_2 was initially checked for linearity after Tanner (1949). In this procedure, the Pearson correlation coefficient (r) between body mass and absolute peak Vo_2 was compared with the ratio of the coefficient of variation (CV) for the two variables

$((SD_x/X_x)/SD_y/X_y)$. If r is approximately equal to the CV, a linear relationship is indicated and the simple ratio standard ($ml \cdot kg^{-1} \cdot min^{-1}$) is appropriate. Conversely, if these two terms are not similar a linear relationship does not exist and the simple ratio standard is inappropriate.

The allometric relationship between body size and peak Vo_2 is based on the general allometric equation,

$$y = ax^b \qquad \text{(Equation 1)}$$

where Y = absolute peak Vo_2; x = body mass, b = scaling factor; and a = proportionality constant. The statistical approach to allometry is to use a logarithmic transformation as follows:

$$\log Y = b \cdot \log Mb + \log a \qquad \text{(Equation 2)}$$

where b is the slope of the linear regression line on a double logarithmic plot. The slope is calculated by regression analysis, where b in the regression output is equal to the scaling factor and the inverse log of log a is equivalent to the constant (a) in Equation 1. Analysis of covariance (ANCOVA) of log-transformed data was used to confirm the allometric analysis and generate adjusted means for age- and sex-specific groups.

Ontogenetic allometry. Individual (ontogenetic) scaling factors were calculated for individual longitudinal records for subjects who were assessed annually for 3 to 5 years. Of the 27 males and 27 females enrolled in YRS I, 20 males and 17 females were considered in the present analysis. A least squares linear regression was carried out for the records of each subject on the double logarithmic transformations of peak Vo_2 and body mass. Individual regressions were checked for goodness of fit by examining the multiple r value and the p value from the ANOVA. Sex-specific means and standard

deviations of the ontogenetic allometric scaling factors were calculated. The difference was examined by an independent t-test.

Regression diagnostics. Residuals (predicted - observed peak Vo_2) were converted to absolute values and correlated with the predictor variable (log body mass) to examine the data for heteroscedasticity. Pearson correlations were also calculated between the simple ratio standard and the common power function ratio ($ml \cdot kg^{-0.75} \cdot min^{-1}$) as a diagnostic test. In this case, if the influence of body size has been removed, the correlation should not be different from zero (Batterham et al., 1997)

RESULTS

Age- and sex-specific anthropometric and peak Vo_2 values are reported in Tables 7.1 and 7.2. Stature reaches a plateau at 17 yrs in boys and 15 yrs in girls. Body mass progressively increases across age in both sexes. Prior to 14 yrs, girls are taller and heavier than boys, thereafter, boys are taller and heavier than girls. Mean statures for both males and females approximate the medians of U.S. reference values (Hamill et al., 1977) and mean body mass for both males and females is somewhat below the reference medians. Stature and mass also maintain their position relative to the reference values across age (Eisenmann et al., 1999).

Means for absolute peak Vo_2 ($ml \cdot min^{-1}$) increase with age in both sexes ($p<0.05$). Absolute differences between the sexes are small (134-186 $ml \cdot min^{-1}$) prior to 14 yrs, when the differences increase sharply in each age group and reach a mean difference of 1000-1500 $ml \cdot min^{-1}$ in the oldest age groups ($p<0.05$).

There is no significant age-related trend for peak Vo_2 expressed as the simple ratio standard ($ml \cdot kg^{-1} \cdot min^{-1}$) ($p>0.05$). Means of relative peak Vo_2 remain stable in boys between 9-15 yrs (61-63 $ml \cdot kg^{-1} \cdot min^{-1}$), but increase in the older age groups (65-67 $ml \cdot kg^{-1} \cdot min^{-1}$). In girls, means for relative peak Vo_2 remain stable between 9-15 yrs of age (55-58 $ml \cdot kg^{-1} \cdot min^{-1}$) and decrease in the oldest age groups (52-53 $ml \cdot kg^{-1} \cdot min^{-1}$). Sex differences vary between 5-7 $ml \cdot kg^{-1} \cdot min^{-1}$ prior to 16 yrs and increase to 12-15 $ml \cdot kg^{-1} \cdot min^{-1}$ in the oldest age groups ($p<0.005$). When peak Vo_2 is expressed to the theoretical value of body mass 0.75, it increases significantly with age ($p<0.05$). A plateau is evident in males between 14-16 yrs, and there are two instances of a decline in age-specific means in females, one at 13 yrs and the other in the oldest age groups. Similar to absolute values, sex differences are small prior to15 yrs, and then increase ($p<0.05$ at all age groups).

Peak Vo_2 adjusted for body mass also shows a significant age-related increase ($p<0.05$). The largest differences in adjusted means occur in the youngest and oldest age groups (600-750 $ml \cdot min^{-1}$). Mean differences between 12-15 yrs of age are 410-475 $ml \cdot min^{-1}$, and there is a significant age group x sex interaction in adjusted means ($p=0.001$).

Results of the cross-sectional allometric analysis are shown in Table 7.3. Overall, body mass exponents are 1.01 ± 0.03 (SE) and 0.85 ± 0.05 (SE) in boys and girls, respectively. The adjusted r^2 is 0.89 in boys and 0.75 in girls. Age-specific scaling factors are closer to the theoretical values of 0.67 and 0.75 in boys, but do not fit the model closely and in two age groups are not significantly different from zero. In girls, three of the eight age-specific models are not significantly different from zero. The

significant models have scaling factors between 0.53 and 0.89. In general, the age-specific models fit better in males than females. The cumulative effect of multiple age groups on the overall scaling factor is also shown in Table 7.3. Although age-specific scaling factors differ from those calculated for the entire sample, this may be due to small age-specific sample sizes and a lack of variation in body mass and peak Vo_2 within age-specific groups. Scaling factors begin to approximate the overall sex-specific scaling factor when multiple age groups are considered.

The computation of Tanner's "special circumstance" (Tanner, 1949) and other diagnostic results are reported in Table 7.4. Body mass is significantly related to absolute peak Vo_2 in males (r= 0.95) and females (r=0.87). As a group, there is a similarity between r (body mass and absolute peak Vo_2) and CV for boys. Age-specific calculations produce divergent ratios, especially in girls, suggesting a non-linear relationship. As a group, the correlations between the simple ratio standard and body mass are 0.07 and -0.41 in boys and girls, respectively. Correlations between scaled peak Vo_2 and body mass are 0.71 and 0.03 in boys and girls, respectively. Correlations between absolute residuals and log body mass are 0.07 and -0.11 in boys and girls, respectively. Age-specific correlations vary between the sexes with coefficients approaching zero in some age groups when peak Vo_2 is expressed per unit body mass 0.75. Correlations do not approach zero in any age group in females.

In general, the intra- individual (ontogenetic) linear regression shows a better fit in boys than girls. In boys, 4 of 20 scaling factors are not significantly different from zero ($p>0.10$). Logarithmically transformed peak Vo_2 and mass are highly related ($r>0.85$) in all but one male subject. In contrast, scaling factors are significantly different

from zero in 6 of 17 females. The relationship between logarithmically transformed peak Vo_2 and mass is high ($r > 0.85$) in 8 females, and moderate (0.40-0.85) in 7 others. Based on a combination of the correlation coefficients and least squares regression model, one male and two female subjects were eliminated from the analysis.

Ontogenetic scaling factors show considerable variation (range, 0.51-1.31 and 0.29-0.90 in males and females, respectively). Five males exhibit scaling factors ≥ 0.99. The mean (95% confidence interval) ontogenetic scaling factors are 0.81 (0.71-0.92) and 0.61 (0.50-0.72) in males and females, respectively ($p=0.002$ between group differences).

DISCUSSION

This study examined age- and sex-associated variation in peak Vo_2 of 9-19 yr old distance runners and provides unique information from three perspectives. First, previous studies are generally limited to a relatively narrow age range (i.e., 11-15 yrs), and therefore, do not describe growth-related changes in peak Vo_2 across the entire adolescent period. Second, only one longitudinal study (Baxter-Jones et al., 1993) has included females across a broad age range in childhood and adolescence. No study has included young distance runners of both sexes 9 to 19 years. Third, this study used allometric scaling techniques to interpret the age- and sex-associated variation in peak Vo_2 of young distance runners.

The observed values for absolute and relative peak Vo_2 expressed per unit body mass in this sample of young distance runners are similar to those previously reported in longitudinal studies of young endurance athletes (Figures 7.1 and 7.2). Relative peak Vo_2 in females is somewhat lower than the cross-sectional data of Massachusetts cross-

country runners (mean = 66 $ml \cdot kg^{-1} min^{-1}$) (Cunningham, 1990), but higher than the maturity-grouped values of swimmers (mean = 51-52 $ml \cdot kg^{-1} min^{-1}$) in the Training of Young Athletes (TOYA) mixed-longitudinal study (Baxter-Jones et al., 1993).

The pattern of development of relative peak Vo_2 in males is similar to that reported by Daniels et al. (1978) until the age of 16 yrs, when a divergent pattern occurs between studies. In the present sample, there is an increase in relative peak Vo_2 whereas there is a decrease in Daniels et al. (1978). Previous studies have also reported an age-related increase in relative peak Vo_2 of young athletes (Murase et al., 1981; Paterson et al., 1987). The typical pattern of development in the general population of normal, healthy boys is a steady value of approximately 52 $ml \cdot kg^{-1} min^{-1}$ (Krahenbuhl et al., 1985). The age-related increase has led some investigators to suggest an influence of exercise training on peak Vo_2 during growth and maturation (Murase et al., 1981).

Less information is available on the age-related trend in female athletes. In the general population of normal, healthy females, relative peak Vo_2 decreases during adolescence (Krahenbuhl et al., 1985). In the only study that reported age (maturity)-specific values, relative peak Vo_2 remains stable at about 52 $ml \cdot kg^{-1} min^{-1}$ in pre-, mid-, and late-pubertal swimmers (Baxter-Jones et al., 1993). Results from the present study show a relatively stable pattern between the ages of 9-15 yrs of age at 55-58 $ml \cdot kg^{-1} min^{-1}$ before decreasing in the oldest age groups to 52-53 $ml \cdot kg^{-1} min^{-1}$. More evidence is needed to establish if the age-related decline of peak Vo_2 in adolescent females is attenuated with exercise training.

Many authors have argued the interpretation of the growth-related changes in peak Vo_2 on the basis of theoretical and statistical limitations of the simple ratio standard

(Armstrong and Welsman, 1994; Baxter-Jones et al., 1993; Sjodin and Svedenhag, 1992; Winter, 1996). Therefore, alternate statistical models, including allometric scaling, ANOVA, and multilevel modeling, have been used in an attempt to create a "size-free" expression of peak Vo_2. The use of alternate models has resulted in different interpretations of growth-related changes in peak Vo_2. For example, Sjodin and Svedenhag (1992) showed an increase in peak Vo_2 expressed per body mass$^{0.75}$ from 3 yrs before peak height velocity until 1 yr after peak height velocity in 8 male distance runners. Others have shown an increase in scaled peak Vo_2 in the general population of normal, healthy boys (Kemper and Verschuur, 1987; Rogers et al., 1995; Rowland et al., 1997; Welsman et al., 1996). Armstrong and colleagues (Armstrong and Welsman, 1994; Armstrong et al., 1998; Welsman et al., 1996) have used adjusted means produced from ANCOVA (controlling for body mass) to explore age- and growth-related changes in peak Vo_2 of normal, healthy children and adolescents. The results generally indicate an increase in adjusted means across age- and maturity-groups in males, but an increase in adjusted means from prepuberty to puberty and similar values between pubertal and young adulthood in females. The results suggest that peak Vo_2 remains constant from late adolescence into young adulthood in females.

Recently, multilevel modeling has been applied to investigate the growth-, maturity-, and training-related changes in peak Vo_2 (Baxter-Jones et al., 1993; Winter, 1996). Multilevel modeling attempts to partition the independent and multiplicative effects of age, body size and composition, pubertal status, and exercise training on a dependent variable (e.g., peak Vo_2). Studies using multilevel modeling have demonstrated size-independent effects of sex and maturity on peak Vo_2 (Armstrong et al.,

1999; Baxter-Jones et al., 1993). Results from the TOYA study indicate that peak Vo_2, controlling for age and body size, increases with pubertal status in male and female athletes, although an increase between mid- and post-pubescent groups in males is not evident in females (Baxter-Jones et al., 1993). The results are intriguing, given past assumptions about growth-related changes in peak Vo_2. However, despite acclaimed usefulness in the interpretation of longitudinal data, the biological significance of the results derived from the multilevel modeling approach is difficult to interpret.

Sex differences in peak Vo_2 during growth and maturation are well documented in the general population of normal, healthy children and adolescents (Armstrong and Welsman, 1994; Krahenbuhl et al., 1985). Less information is available on age-specific differences of young athletes due to the lack of longitudinal studies of female athletes and the narrow age ranges reported in cross-sectional studies. A significant age x sex group interaction in the present study indicates a progressive divergence in peak Vo_2. Age-specific differences in absolute peak Vo_2 are slight (134-186 $ml \cdot min^{-1}$) prior to age 14 yrs when the difference increases sharply in each age group until reaching a mean difference of 1000-1500 $ml \cdot min^{-1}$in the oldest age groups. Similar to absolute values, sex differences are reduced prior to 15 yrs, and then increase sharply when peak Vo_2 is expressed per unit body $mass^{1.0}$ or body $mass^{0.75}$. The mean ontogenetic scaling factor was significantly different between male and female adolescent distance runners, which is consistent with the literature. The difference in scaling factors probably reflects variation in the rate of change in peak Vo_2 with body mass.

Mean cross-sectional scaling factors are 1.01 in males and 0.85 in females. These values are similar to those reported for body mass and peak Vo_2 in cross-sectional

analyses of longitudinal data of other male athletes (McMiken, 1976; Paterson et al., 1987) and cross-sectional analysis of 6-17 yr old males and females (Cooper et al., 1984). However, mean scaling factors reported in the literature show considerable variability (Eisenmann and Malina, in press). Age-specific scaling factors in this study show considerable disparity with estimates for the total sample (Table 7.4). In boys, age-specific scaling factors range from 0.52-0.90 and most conform to the theoretical values of 0.67 and 0.75. In girls, age-specific scaling factors range from -0.09 to 1.41. In both sexes, age-specific scaling models do not represent a good fit as indicated by adjusted r^2 values and non-significant log-linear regression models. This observation probably reflects the small range of body size within an age group (Calder, 1987), small age-specific sample sizes, confounding influences of biological maturity status (Beunen et al., 1997), and differences in body composition, especially among females. Indeed, when multiple age groups were considered, scaling factors began to approximate the overall sex-specific scaling factor.

Table 7.5 provides a summary of longitudinal studies utilizing ontogenetic scaling. The mean ontogenetic scaling factor of 0.81 in males is considerably less than previous studies of highly trained adolescent athletes (Paterson et al., 1987; Sjodin and Svedenhag, 1992). In contrast, similar results have been obtained for active boys in the Saskatchewan Growth Study (Beunen et al., in review) and early and late maturing boys training in Polish sports schools (track, wrestling, or basketball) (Beunen et al., 1997). The mean scaling factor in the present study is actually higher than that in late maturing boys from the Polish sports schools. The subjects in the study by Rowland et al. (1997) were described as "physically active and inclined towards sports participation" (p. 264)

based on a parental description. However, only one was engaged in regular aerobic training (swimming). An explanation for such a high ontogenetic scaling factor (1.10) in this sample is unknown. Interestingly, the average cross-sectional exponent was only 0.53.

The mean ontogenetic scaling factor in female distance runners is higher than maturity-grouped girls from Polish sports schools (track or rowing) (Beunen et al., 1997) and lower than recreational sport participants (Rowland et al., 1997). Ontogenetic scaling factors in 10 of 16 female distance runners are not significantly different from zero, indicating that the growth of peak Vo_2 is not related to growth in body mass. The lack of fit in female runners also reflects a plateau or decline in peak Vo_2 with age (Beunen et al., 1997) as typically observed in female adolescents. Therefore, the higher scaling factor found by Rowland et al. (1997) may be due to age-associated variation, as the mean age at entry in their study was 9.2 yrs whereas most of the female subjects in the present study entered at 12-14 yrs of age.

Previous studies also show considerable variability in individual scaling factors (Table 7.5). The range in male distance runners (0.51-1.31) is similar with that reported in the Saskatchewan Growth Study (0.56-1.18) (Beunen et al., in review). Sjodin and Svedenhag (1992) show a range from approximately 0.85-1.20 in young male distance runners aligned to peak height velocity. The range in female distance runners (0.29-0.90) is similar to that reported for active girls (0.18-1.11) (Rowland et al., 1997).

It has been suggested that variability in scaling exponents is due to factors other than body mass including: individual variation in geometric similarity, changes in the ratio of leg muscle mass to body mass, differences in physical activity and/or training

level, and individual differences in rates of development of size-independent factors such as skeletal muscle oxidative enzyme capacity or myocardial contractility (Rowland et al., 1997). The last mentioned factors would suggest that qualitative changes in the functional capacity of specific sub-components of the oxygen transport system also contribute to the growth-related changes in peak Vo_2. Genotype may also contribute to the variability in the phenotypic expression of peak Vo_2. Familial aggregation for peak Vo_2 in the sedentary state and the peak Vo_2 response to exercise training has been demonstrated in the HERTIAGE Study (Bouchard et al., 1998; Bouchard et al., 1999). The identification of genes and mutations responsible for the heterogeneity of peak Vo_2 are currently under investigation. Early evidence suggests that muscle-specific creatine kinase (Rivera et al., 1997; Rivera et al., 1999), Na^+-K^+-ATPase (Rankinen et al., 2000), and angiotensin converting enzyme (Gayagay et al., 1998) are possible candidate genes. Future cross-sectional and longitudinal studies examining allometric relationships between body mass and peak Vo_2 may benefit from the identification of specific candidate genes associated with peak Vo_2.

The observed variability in the ontogenetic scaling factors may be related to maturity-associated variation in body mass and peak Vo_2. Given the individuality of timing and tempo of maturation, year-to-year changes in body mass and peak Vo_2 may have been masked by maturity effects. Maturity-associated variation in peak Vo_2 has been recently estimated using various statistical models (Armstrong et al., 1998; Baxter-Jones et al., 1993; Beunen et al., in review; Beunen et al., 1997). Peak Vo_2 increases at a slightly higher rate in early and average maturing males than expected from the increase in body mass (Beunen et al., in review; Beunen et al., 1997). In one study, the increase is

smaller than expected in later maturing boys (Beunen et al., 1997). In the present sample of distance runners, differences in biological maturity were evident as determined by skeletal age estimated from the hand-wrist x-ray obtained on the first visit. The mean difference between chronological age and skeletal age was -0.52 in 12 males and -0.57 in 10 females. Unfortunately, an insufficient number of subjects were available for the analysis of skeletal maturity. Future studies should consider maturity-associated variation in peak Vo_2.

A scaling factor less than unity indicates that the conventional simple ratio standard ($ml \cdot kg^{-1} min^{-1}$) is erroneous. This tenet has theoretical, statistical, and empirical grounds. Theoretically, dimensionality theory predicts that metabolic rate should relate to body mass by a scaling exponent of 0.67. McMahon (1973) has proposed the 'elastic similarity' model suggesting that elastic criteria impose limits on biological proportions and metabolic rates. Based on this model the theoretical value is 0.75. Early studies on a wide range of animals from rodent to elephant indicated that a scaling factor of approximately 0.74 best describes the relationship between body size and resting metabolic rate (Brody, 1945; Kleiber, 1932). Taylor and colleagues (1981) found that peak Vo_2 scaled approximately to 0.75in wild African and domestic mammals ranging from 0.5 kg (dwarf mongoose) to 263 kg (Zebu cattle). Statistically, Tanner (1949) addressed the fallacious and misleading practice of expressing physiological measurements per unit of body mass or per unit of surface area.

When expressed per $kg^{-0.75}$ a different interpretation of the growth-related changes in peak Vo_2 of young athletes is evident. Although peak Vo_2 remains relatively stable during adolescence in young male distance runners when expressed as a ratio standard, it

increases when expressed per $kg^{-0.75}$. This finding confirms previous results across a narrower age range (Sjodin and Svedenhag, 1992). In females, peak Vo2 expressed per $kg^{-0.75}$ increases from 9 to 15 yrs and then shows a decline.

Most important to this study is the identification of an appropriate model to interpret growth-related changes in peak Vo_2 of young distance runners, and children and adolescents in general. Several authors argue that peak Vo_2 should be expressed in accordance with theoretical values according to dimensionality theory (i.e, $ml \cdot kg^{0.67} \cdot min^{-1}$ or $ml \cdot kg^{0.75} \cdot min^{-1}$) (Armstrong and Welsman, 1994; Heil, 1997; Katch, 1973; Nevill, 1994; Rogers et al., 1995; Svedenhag, 1995). The first step in the investigation of appropriate scaling procedures should involve the calculation of Tanner's "special circumstances (Batterham et al., 1997). If r is equal, or approximately equal, to the ratio of the coefficient of variations, a linear relationship is evident and the simple ratio standard ($ml \cdot kg^{-1} \cdot min^{-1}$) is appropriate. Conversely, if these two terms are not similar, a linear relationship does not exist and the appropriate power function ratio should be calculated. Other regression diagnostics used in this study (i.e., correlations between residuals, simple and power function ratios, and body mass) were used to examine if the influence of body mass was removed (i.e., the correlation should not be different from zero if the influence of body mass has been removed) (Batterham et al., 1997; Welsman et al., 1996). Based on these criteria, the simple ratio standard could be empirically justified in males, while the power function ratio could be empirically justified in females (Table 7.3). Other authors (Bar-Or, 1983; Batterham et al., 1999) have also concluded that the mass exponent for peak Vo_2 is close to unity.

In conclusion, the results of this study suggest that the interpretation of growth-related changes in peak Vo_2 of young distance runners is dependent upon the expression of peak Vo_2 relative to body size and/or the statistical technique employed. Considerable variability in individual growth patterns in scaled peak Vo_2 points to the fact that determining a single scaling factor is difficult and may actually be problematic given the genetic, environmental, and genetic-environmental interactions that influence peak Vo_2. The most appropriate means of normalizing peak Vo_2 for body size still remains problematic (Rowland, 1998; Rowland et al., 1997). Exercise scientists have been criticized for not recognizing the imperfections of ratio standards and being unaware of alternative methods for partitioning the effects of body size in human studies (Winter, 1996). However, it remains to be demonstrated that allometric scaling among a small magnitude of variation in body size warrants such statistical manipulation. According to Calder (1987), small size ranges within a species obscure overall trends, patterns, and constraints of size. Thus, scaling differences in body size among a small range of body size to understand variation in biological function may be of limited value. In contrast, others argue that scaling body size helps us to understand the growth and maturation of the oxygen transport system, and its response to submaximal and maximal exercise (Armstrong and Welsman, 1994). To solve the problem of the structural and functional consequences of changes in size or scale among growing and maturing children and adolescents, pediatric exercise scientists should perhaps collaborate with comparative mammalian physiologists for whom the statistical tool of allometry has been central for many years.

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REFERENCES

Armstrong N, Welsman JR (1994) Assessment and interpretation of aerobic fitness in children and adolescents. Exerc Sport Sci Rev 22:435-476.

Armstrong N, Welsman JR, Kirby BJ (1998) Peak oxygen uptake and maturation in 12-yr olds. Med Sci Sports Exerc 30:165-169.

Armstrong N, Welsman JR, Nevill AM, Kirby BJ (1999) Modeling growth and maturation changes in peak oxygen uptake in 11-13 yr olds. J Appl Physiol 87:2230-2236.

Bar-Or O (1983) Pediatric Sports Medicine for the Practitioner.New York: Springer-Verlag.

Batterham AM, George KP, Mullineaux DR (1997) Allometric scaling of left ventrcular mass by body dimensions in males and females. Med Sci Sports Exerc 29:181-186.

Batterham AM, Vanderburgh PM, Mahar MT, Jackson AS (1999) Modeling the influence of body size on Vo_2peak: effects of model choice and body composition. J Appl Physiol 87:1317-1325.

Baxter-Jones A, Goldstein H, Helms P (1993) The development of aerobic power in young athletes. J Appl Physiol 75:1160-1167.

Beunen G, Baxter-Jones A, Mirwald RL, Thomis M, Lefevre J, Malina RM, Bailey DA (in review) Intra-individual allometric development of aerobic power in 8 to 16 year-old boys: association with maturity level and activity level.

Beunen GP, Rogers DM, Woynarowska B, Malina RM (1997) Longitudinal study of ontogenetic allometry of oxygen uptake in boys and girls grouped by maturity status. Ann Hum Biol 24:33-43.

Bouchard C, Daw EW, Rice T, Pérusse L, Gagnon J, Province MA, Leon AS, Rao DC, Skinner JS, Wilmore JH (1998) Familial resemblance for Vo_2max in the sedentary state: the HERITAGE family study. Med Sci Sports Exerc 30:252-258.

Bouchard C, Ping A, Rice T, Skinner JS, Wilmore JH, Gagnon J, Pérusse L, Leon AS, Rao DC (1999) Familial aggregation of Vo_2max response to exercise training: results from the HERITAGE Family Study. J Appl Physiol 87:1003-1008.

Brody S (1945) Bioenergetics and Growth, with Special Reference to the Efficiency Complex in Domestic Animals. New York: Reinhold.

Cooper DM, Weiler-Ravell D, Whipp BJ, Wasserman K (1984) Aerobic parameters of exercise as a function of body size during growth in children. J Appl Physiol 56:628-634.

Cunningham LN (1990) Physiologic comparison of adolescent female and male cross-country runners. Pedatr Exerc Sci 2:313-321.

Daniels J, Oldridge N, Nagle F, White B (1978) Differences and changes in Vo2 among young runners 10 to 18 years of age. Med Sci Sports 10:200-203.

Eisenmann JC, Haubenstricker JL, Seefeldt VD, Malina RM (1999) Growth status and estimated growth rates of competitive young distance runners. Med Sci Sports Exerc 31 (Suppl.):S169 (Abstract).

Eisenmann JC, Malina RM (in press) Body size and endurance performance. In RJ Shephard (ed.): Endurance in Sport. Oxford: Blackwell Science.

Gayagay G, Yu B, Hambly B, Boston T, Hahn A, Celermajer DS, Trent R (1998) Elite endurance athletes and the ACE I allele - the role of genes in athletic performance. Hum Genet 103:48-50.

Gould SJ (1966) Allometry and size in ontogeny and phylogeny. Biol Rev 41:587-640.

Hamill PVV, Johnson CL, Reed RB, Roche AF (1977) NCHS growth curves for children birth-18 years, United States.: Vital and Health Statistics.

Heil DP (1997) Body mass scaling of peak oxygen uptake in 20- to 79-yr-old adults. Med Sci Sports Exerc 29:1602-1608.

Jones NL (1984) Evaluation of a microprocessor-controlled exercise testing system. J Appl Physiol 57:1312-1318.

Katch VL (1973) Use of the oxygen/body weight ratio in correlational analyses: spurious correlations and statistical considerations. Med Sci Sports 5:253-257.

Kemper HCG, Verschuur R (1987) Longitudinal study of maximal aerobic power in teenagers. Ann Hum Biol 14:435-444.

Kleiber M (1932) Body size and metabolism. Hilgardia 6:315-353.

Krahenbuhl GS, Skinner JS, Kohrt WM (1985) Developmental aspects of maximal aerobic power in children. Exerc Sport Sci Rev 13:503-538.

Maingourd Y, Libert JP, Bach V, Jullien H, Tanguy C, Freville M (1994) Aerobic capacity of competitive ice hockey players 10-15 years old. Jap J Physiol 44:255-270.

McMahon T (1973) Size and shape in biology. Science 179:1201-1204.

McMiken DF (1976) Maximum aerobic power and physical dimensions of children. Ann Hum Biol 3:141-147.

Murase Y, Kobayashi K, Kamei S, Matsui H (1981) Longitudinal study of aerobic power in superior junior athletes. Med Sci Sports Exerc 13:180-184.

Nevill AM (1994) The need to scale for differences in body size and mass: an explanation of Kleiber's 0.75 mass exponent. J Appl Physiol 65:110-117.

Paterson DH, Cunningham DA, Donner A (1981) The effect of different treadmill speeds on the variability of Vo_{2max} in children. Eur J Appl Physiol 47:113-122.

Paterson DH, McLellan TM, Stella RS, Cunningham DA (1987) Longitudinal study of ventilation threshold and maximal O2 uptake in athletic boys. J Appl Physiol 62:2051-2057.

Rankinen T, Pérusse L, Borecki I, Chagnon YC, Gagnon J, Leon A, Skinner JS, Wilmore JH, Rao DC, Bouchard C (2000) The Na^+-K^+-ATPase alpha2 gene and trainability of cardiorespiratory endurance: the HERITAGE Family Study. J Appl Physiol 88:346-351.

Rivera MA, Dionne FT, Simoneau J-A, Pérusse L, Chagnon M, Chagnon Y, Gagnon J, Leon AS, Rao DC, Skinner JS, Wilmore JH, Bouchard C (1997) Muscle-specific creatine kinase gene polymorphism and Vo_2max in he Heritage Family Study. Med Sci Sports Exerc 29:1311-1317.

Rivera MA, Pérusse L, Simoneau J-A, Gagnon J, Dionne FT, Leon AS, Skinner JS, Wilmore JH, Province M, Rao DC, Bouchard C (1999) Linkage between a muscle-specific CK gene marker and Vo_2max in the HERITAGE Family Study. Med Sci Sports Exerc 31:698-701.

Rivera-Brown AM, Rivera MA, Frontera WR (1994) Achievement of Vo_{2max} in adolescent runners: effects of testing protocol. Pediatr Exerc Sci 6:236-245.

Rogers DM, Olson BL, Wilmore JH (1995) Scaling for the Vo2-to-body size relationship among children and adults. J Appl Physiol 79:958-967.

Rowland TW (1990) Developmental aspects of physiological function relating to aerobic exercise in children. Sports Med 10:255-266.

Rowland TW (1998) The case of the elusive denominator. Pediatr Exerc Sci 10:1-5.

Rowland TW, Vanderburgh PM, Cunningham L (1997) Body size and the growth of maximal aerobic power in children: a longitudinal analysis. Pediatr Exerc Sci 9:262-274.

Seefeldt VD (1986) Elite young runners: an interdisciplinary perspective. In M Weiss and D Gould (eds.): Sport for Children and Youths. Champaign, IL: Human Kinetics, pp. 213-284.

Sjodin B, Svedenhag J (1992) Oxygen uptake during running as related to body mass in circumpubertal boys: a longitudinal study. Eur J Appl Physiol 65:150-157.

Skinner JS, Bar Or O, Bergsteinova V, Bell CW, Royer D, Buskirk ER (1971) Comparison of continuous and intermittent tests for determining maximal oxygen intake in children. Acta Paediatr Scand 217:24-28.

Svedenhag J (1995) Maximal and submaximal oxygen uptake during running: how should body mass be accounted for? Scand J Med Sci Sports 5:175-180.

Tanner JM (1949) Fallacy of per-weight and per-surface area standards, and their relation to spurious correlation. J Appl Physiol 2:1-15.

Taylor CR, Maloiy GMO, Weibel EW, Langman VA, Kamau JMZ, Seeherman HJ, Heglund NC (1981) III. Scaling maximum aerobic capacity to body mass: wild and domestic mammals. Respir Physiol 44:3-37.

Weiner JS, Lourie JA (1969) Human Biology: A Guide to Field Methods. Oxford: Blackwell Science.

Welsman JR, Armstrong N, Nevill AM, Winter EM, Kirby BJ (1996) Scaling peak Vo2 for differences in body size. Med Sci Sports Exerc 28:259-265.

Winter EM (1996) Importance and principles of scaling for size differences. In O Bar-Or (ed.): The Child and Adolescent Athlete. Oxford: Blackwell Science, pp. 673-679.

Table 7.1. Age-specific values for body size and peak Vo2 in male distance runners. Mean, standard deviation, and range are provided for all variables except adjusted means for peak Vo_2.

Age group	n	Ht (cm)	Wt (kg)	Peak Vo_2 ($ml \cdot min^{-1}$)	Adjusted Peak Vo_2 ($ml \cdot min^{-1}$)	Peak Vo_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	Peak Vo_2 ($ml \cdot kg^{-75} \cdot min^{-1}$)
Boys							
9-10	13	137.8 (7.2) 125.6-150.1	31.2 (4.4) 25.9-39.9	1943.0 (224.2) 1450-2269	2723.6	62.7 (6.1) 53.5-72.8	147.6 (12.6) 125.8-167.9
11	12	143.5 (6.9) 131.0-156.6	33.5 (4.4) 24.5-39.2	2113.3 (285.3) 1670-2670	2797.8	63.6 (7.1) 52.5-73.8	152.3 (15.6) 124.6-176.5
12	14	150.0 (7.7) 134.7-164.8	39.3 (7.2) 25.9-53.0	2469.1 (442.7) 1830-3659	2880.4	63.3 (6.3) 52.0-70.7	157.6 (14.2) 136.0-186.2
13	16	155.5 (8.0) 139.5-170.9	43.4 (7.0) 28.8-55.0	2625.5 (487.2) 1920-3790	2820.9	60.8 (7.2) 45.5-71.6	158.4 (21.0) 123.8-195.9
14	20	162.1 (9.8) 143.3-178.4	48.6 (10.2) 31.0-63.2	3071.3 (658.9) 1960-4380	3021.8	63.5 (5.2) 50.1-74.5	166.7 (14.5) 136.2-195.4
15	16	170.7 (8.3) 150.8-183.8	57.3 (11.0) 36.9-85.9	3642.5 (614.6) 2200-4633	3100.7	62.7 (6.3) 53.9-77.1	178.8 (19.8) 146.9-211.8
16	14	174.1 (5.0) 163.0-179.9	60.1 (6.9) 46.8-73.4	3884.2 (443.0) 3070-4583	3238.0	64.8 (5.0) 53.5-72.3	179.5 (12.8) 147.3-196.6
17	20	175.9 (5.0) 166.0-184.7	63.1 (4.7) 55.4-71.5	4248.6 (372.3) 3671-5022	3405.3	67.5 (5.6) 58.1-78.1	177.8 (21.7) 144.1-212.0
18	14	176.2 (6.1) 165.8-185.1	65.3 (7.0) 51.9-76.3	4386.6 (655.2) 3270-5482	3404.6	67.3 (8.0) 44.1-75.5	191.0 (22.7) 129.5-215.5
Total	139						

Table 7.2. Age-specific values for body size and peak Vo_2 in female distance runners. Mean, standard deviation, and range are provided for all variables except adjusted means for peak Vo_2.

Age group	n	Ht (cm)	Wt (kg)	Peak Vo_2 ($ml \cdot min^{-1}$)	Adjusted Peak Vo_2 ($ml \cdot min^{-1}$)	Peak Vo_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	Peak Vo_2 ($ml \cdot kg^{-.75} \cdot min^{-1}$)
Girls							
9-10	9	144.4(6.9) 132.7-152.4	32.5(4.8) 25.6- 38.3	1809.9(182.2) 1490-2050	2105.5	56.3 (6.6) 47.0-65.7	133.8 (12.5) 115.6-154.9
11	11	148.6 (6.5) 136.4-156.6	33.8 (7.0) 22.9-45.5	1946.3 (361.9) 1170-2460	2206.1	57.9 (5.2) 47.5- 63.8	138.9 (12.5) 111.8-155.4
12	15	153.8 (5.4) 144.5-160.4	40.1 (5.3) 48.9-68.0	2283.0 (276.3) 1866-2890	2379.9	57.1 (5.3) 48.9-68.0	146.9 (12.0) 122.5-165.6
13	17	158.3 (6.1) 149.4-170.0	45.0 (6.4) 36.5-57.7	2441.2 (221.0) 2080-2870	2410.3	54.8 (6.3) 42.4-65.7	141.5 (13.2) 117.0-61.6
14	14	161.3 (6.4) 153.7-175.1	47.7 (4.8) 40.6-54.3	2688.6 (277.3) 2020-3040	2567.0	56.9 (8.4) 39.8-68.7	151.1 (21.6) 106.3-183.8
15	11	162.6 (7.9) 151.4-179.1	50.4 (5.4) 43.5-61.0	2838.3 (274.3) 2352-3360	2625.4	56.2 (7.0) 45.5-68.1	151.9 (15.2) 125.6-176.4
16	12	165.3 (8.4) 156.9-181.2	54.6 (7.3) 46.2-65.1	2854.8 (308.5) 2480-3460	2541.3	54.3 (6.8) 39.5-60.0	141.1 (19.0) 110.2-158.0
17-18	16	163.2 (8.4) 152.2-182.1	55.5 (5.9) 48.9-66.7	2894.7 (389.0) 2100-3535	2647.3	51.8 (6.4) 41.0-63.0	139.2 (16.7) 113.0-167.9
Total	108						

Table 7.3. Age- and sex-specific proportionality coefficients (a) and allometric scaling factors (b) in young distance runners.

Age group	a	b	Multiple r	Adjusted r^2	b^1
Boys					
9-10	5.36 (0.65)	0.64 (0.19)	.71	.46	-
11	5.41 (0.83)	0.64 (0.23)	.65	.36	0.67 (0.09)
12	5.11 (0.52)	0.73 (0.14)	.84	.68	0.78 (0.08)
13	4.89 (0.69)	0.79 (0.18)	.75	.53	0.80 (0.07)
14	4.54 (0.34)	0.90 (0.09)	.93	.86	0.77 (0.15)
15	4.67 (0.60)	0.87 (0.15)	.85	.70	0.92 (0.09)
16	5.07 (0.84)	0.78 (0.20)	.77	.55	0.94 (0.04)
17	6.18 (1.05)	0.52 (0.25)*	.46	.16	0.99 (0.03)
18	5.36 (1.48)	0.72 (0.34)*	.51	.20	-
Total	4.12 (0.12)	1.01 (0.03) (95 CI, 0.96-1.03)	.95	.89	
Girls					
9-10	6.01 (0.68)	0.43 (0.19)*	.64	.32	-
11	4.46 (0.14)	0.88 (0.14)	.89	.79	0.76 (0.12)
12	5.18 (0.71)	0.69 (0.19)	.70	.45	0.82 (0.08)
13	6.46 (0.57)	0.35 (0.15)	.53	.23	0.75 (0.06)
14	8.26 (1.29)	-0.09 (0.32)*	.09	-0.08	0.77 (0.06)
15	6.91 (1.09)	0.26 (0.28)*	.30	-0.01	0.78 (0.06)
16	7.36 (1.28)	0.14 (0.32)*	.19	-0.12	0.78 (0.05)
17+	2.40 (1.15)	1.41 (0.28)	.72	.50	-
Total	4.58 (0.18)	0.85 (0.05) (95 CI, 0.76-0.94)	.87	.75	

b^1, cumulative scaling factor when an additional age group is considered (i.e., 9-10 yr plus 11 yr; 9-10 yr, 11 yr plus 12 yr, etc.).
Values are mean (SE). *p>0.05

Table 7.4. Diagnostic criteria for the relationships between peak Vo_2 and body size.

Age group	CV	R1	R2	R3
Boys				
9-10	1.22	0.73	-0.51	-0.21
11	0.97	0.63	-0.44	-0.14
12	1.02	0.83	-0.45	0.04
13	0.87	0.71	-0.26	0.17
14	0.98	0.92	-0.25	0.41
15	1.14	0.81	-0.28	0.55
16	1.01	0.78	-0.34	0.00
17	0.85	0.48	-0.42	-0.04
18	0.72	0.54	-0.21	0.00
Total	0.90	0.93	0.07	0.71
Girls				
9-10	1.47	0.62	-0.74	-0.53
11	1.11	0.88	-0.33	.021
12	1.09	0.75	-0.40	-0.09
13	1.57	0.51	-0.74	-0.57
14	0.97	-0.09	-0.75	-0.68
15	1.11	0.35	-0.65	-0.64
16	1.24	0.24	-0.74	-0.47
17+	0.53	0.73	0.31	0.43
Total	1.08	0.87	-0.41	0.03

CV, ratio of coefficient of variation; R1, correlation coefficient between body mass and absolute peak Vo_2; R2, , correlation coefficient between body mass and relative peak Vo_2; R3, , correlation coefficient between body mass and scaled peak Vo_2.

Table 7.5. Summary of allometric ontogenetic scaling factors in children and adolescents.

Study	Subjects	Mean scaling factor	Range
Sjodin and Svedenhag (1995)	8 trained distance runners	1.01	0.85-1.20
	4 untrained	0.78	0.60-0.85
Paterson et al (1989)	18 male athletes	1.19	
Beunen et al. (1997)	Early/average maturing males (n=16)	0.80	
	Late maturing males (n=31)	0.54	
	Early/average maturing females (n=21)	0.27	
	Late maturing females (n=10)	0.42	
Beunen et al. (in review)	Total (n=73)	0.86	0.56-1.18
	Early maturers (n=11)	0.85	
	average maturers (n=52)	0.85	
	Late maturers (n=10)	0.80	
	Inactive (n=12)	0.79	
	Average (n=47)	0.86	
	Active (n=14)	0.87	
Rowland et al. (1997)	11 males	1.10	0.75-1.74
	9 females	0.78	0.18-1.11
Present study	20 male distance runners	0.81	0.51-1.31
	16 female distance runners	0.61	0.29-0.90

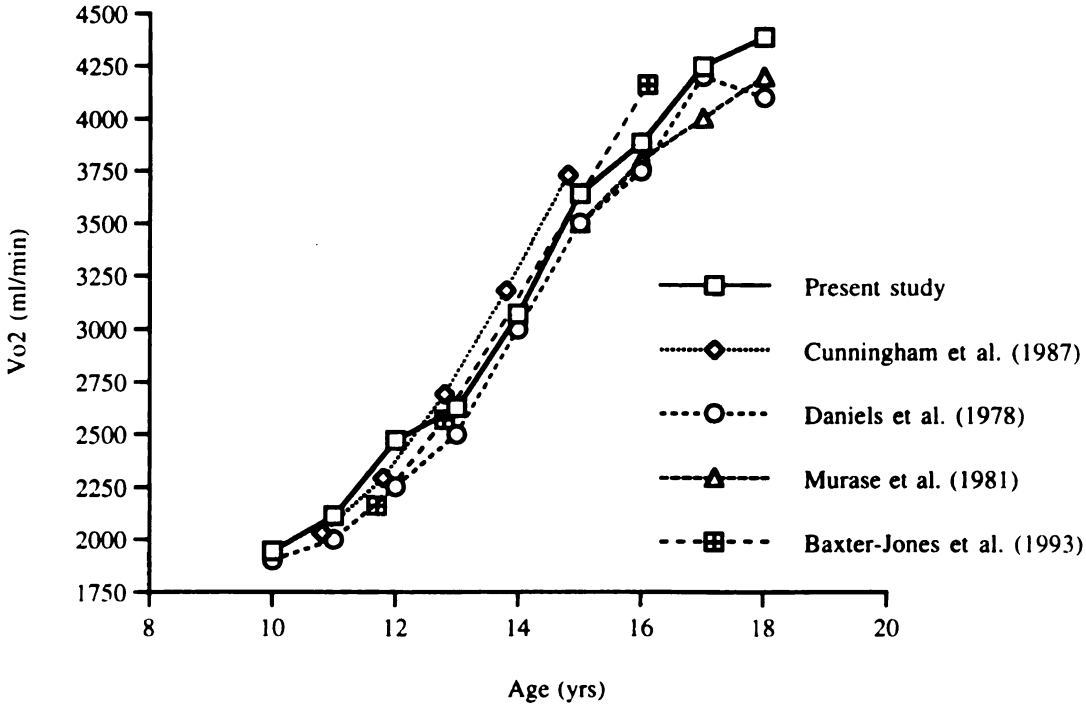

Figure 7.1. Longitudinal studies of absolute peak Vo2 in male athletes.

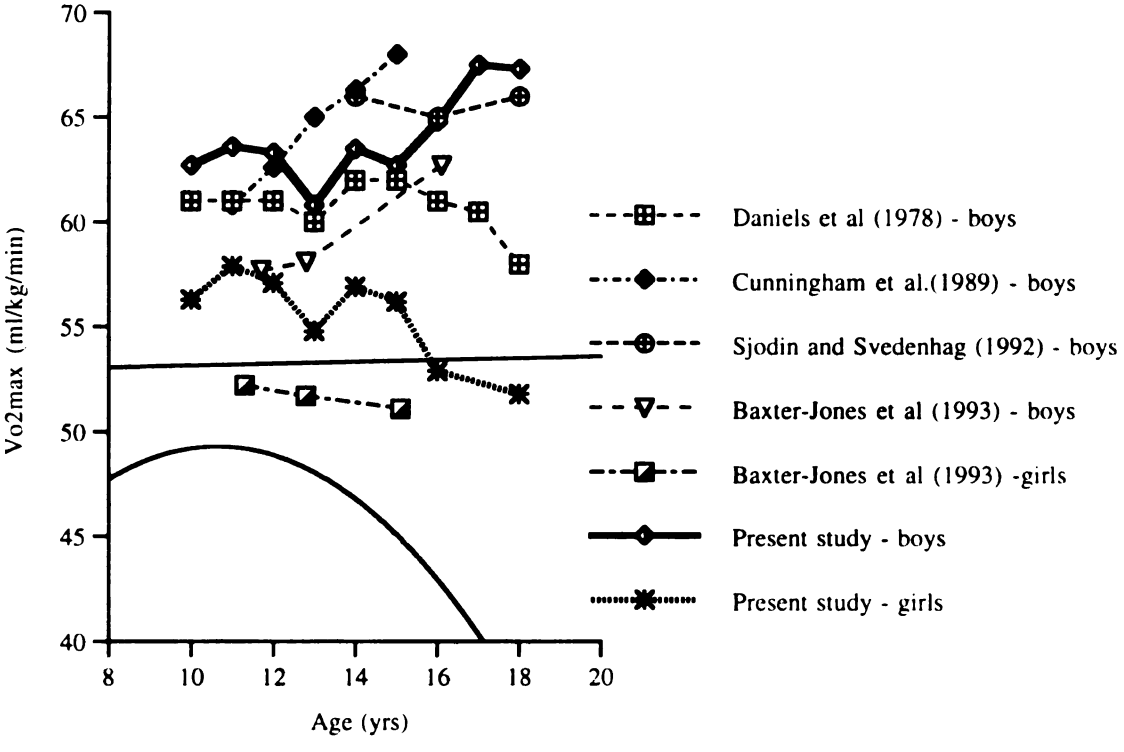

Figure 7.2. Longitudinal studies of relative peak Vo2 in young athletes. Solid lines represent age-related changes in the general population.

CHAPTER 8

SUMMARY AND RECOMMENDATIONS

This dissertation focuses on blood lipids and peak Vo_2 in young male and female distance runners. The studies are based on two independent samples of young distance runners from the mid-Michigan area. Both studies were supported in part by the Institute for the Study of Youth Sports. The mixed-longitudinal cohort of the Young Runners Study I (YRS I) (1982-1986) included 27 males and 27 females. Twenty males and 18 females were followed annually for 3 to 5 years, and the remaining subjects were followed for 1 or 2 years. A total of 99 and 84 observations were available for analysis. This study formed the basis for age-specific analyses of blood lipids and peak Vo_2. During 1999-2000, a cross-sectional study (Young Runners Study II, YRS II) was undertaken to specifically address the dose-response relationship between training volume and blood lipids, specifically high-density lipoprotein (HDL), in young distance runners. This sample included 48 males and 22 females.

Age- and sex-associated variation in blood lipids of 9 to 18 yr olds from the YRS I were initially described (Chapter 3). The development of blood lipids in young distance runners appears to be similar to the general population - TC and LDL remain stable, HDL declines during adolescence (especially in males), and TG increases with age. One of the major study hypothesis was that the decline in HDL during male adolescence would be attenuated in young distance runners given the high levels of exercise training. The lack of the attenuation may lend to the robustness of normal growth and maturation, including genes, hormones, and fat distribution, on the development of HDL in males regardless of exercise training. This sample also did not display a superior blood lipid profile compared to age- and sex-specific reference values for United States youth, except for higher HDL in male and female runners prior to age14 yrs. Unlike

anthropometric and functional capacity variables, there was considerable variability in blood lipids, including dyslipidemic values. These results were also supported by the findings from the YRS II (Chapter 4).

Heterogeneity in blood lipids among young distance runners was considered in Chapter 5. Determinants included training volume (km per wk), peak oxygen consumption (peak Vo_2, $ml \cdot kg^{-1} min^{-1}$), and body fatness. YRS II was originally designed to address the dose-response relationship between training volume and blood lipids. Young distance runners were identified as a "special exposure group" to test the hypothesis that physical activity at levels greater than the current recommendations would result in accrued health benefits as shown in adults. Results did not indicate that increased weekly running distance was related to blood lipids in young distance runners. TV may be indirectly related with HDL through its relationship with peak Vo_2 in males. A unique finding was the differential relationships between TV and HDL when the entire sample was grouped according to modified clinical cut-points. Specifically, TV was significantly related to HDL in subjects with HDL<45 mg/dl ($r=0.40$, $p<0.05$). This finding supports the notion that increased levels of training do not influence lipoprotein metabolism when blood lipids are already desirable during childhood and adolescence.

The complex inter-relationships between body fatness, peak Vo_2, and HDL were further explored. Partial correlations indicate that the association between peak Vo_2 and HDL remained significant after controlling for the concomitant variation in SSF and explained 9% of the variance in HDL. The association between SSF and HDL did not remain significant after controlling for the concomitant variation in peak Vo_2. This finding would suggest that skeletal muscle properties are an important factor in

determining HDL in young well-trained distance runners, although the influence of adipose tissue cannot be dismissed.

The role of genes, peak Vo_2, and body fatness in the modulation of elevated blood lipid levels has also been indicated. The correlation between parental BMI and measures of fatness and blood lipids in adolescent distance runners were positive. Therefore, it is possible that blood lipids in adolescent distance runners are moderated by the genetic contribution of body fatness and/or the pleiotropy (shared genes) of body fatness and blood lipids. It is also possible that shared environmental factors (i.e., dietary intake) could contribute to the relationship between parental fatness, offspring fatness and blood lipids.

The results from Part I indicate that the phenotypic expression of blood lipids in young distance runners is influenced by multiple factors. The contribution of growth, maturation, genetics, and skeletal muscle and adipose tissue properties on lipoprotein metabolism during adolescence are definitely as important, if not more important, than exercise training.

Part II examined the usefulness of allometric scaling as a tool in the interpretation of age- and growth-related changes in peak Vo_2. As expected, an age-related increase in absolute peak Vo_2 occurred in both sexes with sex differences emerging during adolescence. However, the ability to "standardize" peak Vo_2 for comparative purposes is important to understanding the growth of the oxygen transport system, and its relationship with health-related fitness variables and endurance performance. When expressed per unit body mass, peak Vo_2 ($ml \cdot kg^{-1} min^{-1}$) remains stable until age 15 when it increases in boys, and decreases in girls. In contrast, relative peak Vo_2 ($ml \cdot kg^{-0.75} min^{-1}$)

increases throughout the age range in boys and increases in girls until age15 yrs, and peak Vo_2 adjusted for body mass ($ml \cdot min^{-1}$) increases with age in boys and girls. Allometric scaling factors varied by analytical methods. The overall mean cross-sectional scaling factor was 1.01 ± 0.03 (SE) in boys and 0.85 ± 0.05 (SE) in girls. Mean ontogenetic allometric scaling factors were 0.81 and 0.61 in males and females, respectively. Thus, it was concluded that the interpretation of growth-related changes in peak Vo_2 of young distance runners was dependent upon the manner of expressing peak Vo_2 relative to body size and/or the statistical technique employed.

The results from Part II do not answer the question, "What is the most appropriate means of normalizing peak Vo_2 for body size?". Rather, the results point out the fact that the problem still remains. Pediatric exercise physiologists are confronted with the dilemma of accounting for differences in body size and functional capacity during growth and maturation. To understand the development of the oxygen transport system (and other functional capacities) first requires an understanding of human growth and maturation. In order to understand the functional consequences of a change in body size also requires an understanding of allometry and more recently, advanced statistical techniques such as multilevel modeling. Although exercise scientists have been criticized for not recognizing the imperfections of ratio standards and being unaware of alternative methods for partitioning the effects of body size in human studies, it remains to be demonstrated that allometric scaling among a small magnitude of variation in body size warrants such statistical manipulation. Thus, scaling differences in body size among a small range of body size to understand variation in biological function may be of limited value. To solve the problem of the structural and functional consequences of changes in

size or scale among growing and maturing children and adolescents, pediatric exercise scientists should collaborate with comparative mammalian physiologists for whom the statistical tool of allometry has been central for many years.

RECOMMENDATIONS FOR FUTURE RESEARCH

An exciting part of science is the continuing cycle of research. Although this dissertation has added insight into the influence of growth, maturation, and exercise training on blood lipids and peak Vo_2 in young distance runners, it has also served as a catalyst for future studies.

- In general, future research should examine the complex inter-relationships between growth, maturation, genetics, exercise training, skeletal muscle and adipose tissue properties and lipoprotein metabolism.
- A "pure" longitudinal or mixed-longitudinal study of blood lipids is warranted. Such a study would re-examine if exercise training attenuates the decline in HDL during male adolescence, and if it does not - why? Measurements of sexual maturity, sex hormones, and body fatness (including visceral fatness) should be included to identify possible biological mechanisms.
- Familial resemblance of aerobic fitness, body fatness, and blood lipids may prove to also explain some of the variation in the blood lipid phenotype. The measurement of these variables on parents of young distance runners would be valuable. Furthermore, the identification of apolipoprotein E phenotypes may also prove beneficial in examining the inter-relationships between exercise training, peak Vo_2, body fatness, and blood lipids.

- What is the time course of the development of high levels of HDL in adult endurance athletes? A longitudinal study of collegiate distance runners may add insight into this question.
- The blood lipid profile in large samples and elite samples of sport-specific youth have not been explored, nor has the prevalence of dyslipidemia in youth athletes been adequately addressed. In young distance runners, it would be interesting to study national competitors.
- Investigations of the HDL and LDL sub-classes and apolipoproteins would add to our understanding of lipoproteins in young athletes.
- Measurement issues, such as day-to-day variation, need to be addressed. Perhaps, 2-3 measurements over a short time period should be averaged to represent the "true" blood lipid phenotype.
- The measurement of training volume also requires attention. Perhaps, estimates based on longer time periods are more appropriate. Training intensity should also be included in the derivation of training volume. Dietary information should also be included in future studies.
- The maturity-associated variation in blood lipids has yet to be established in highly trained youth endurance athletes.
- Prospective training studies examining the exercise training response in young athletes who possess dyslipidemic values are necessary.
- It is important for biostatisticians to communicate the biological relevance of multi-level modeling in the interpretation of growth- and training-related changes in peak Vo_2 and other physiological parameters.

- Appropriate animal models need to be developed to explore the growth- and training-related changes in the oxygen transport system, including the structure-function relationships in lung, heart, blood, and skeletal muscle.

APPENDIX A

SELF-REPORTED TRAINING VOLUME

TRAINING HISTORY

Name:_____

With the assistance of a parent, guardian, and/or coach, please indicate your training history below.

	March	April	May	June	July	Aug	Sept	Oct
What was the average number of **DAYS PER WEEK** that you trained?								
What was the average number of **MILES PER WEEK** that you trained?								
What percent of your training was **light** ?								
What percent of your training was **moderate**?								
What percent of your training was **heavy**?								

Personal best 5km time _____

APPENDIX C

CONSENT FORM

Informed Consent Form

Influence of intensive training on blood cholesterol
in young distance runners

Heart disease occurs in adults, but some children have high levels of blood pressure and cholesterol that may cause heart disease. Regular physical activity has beneficial effects on heart disease in adults. However, the effects of physical activity on cholesterol in children is not clear. Since sports are important to daily physical activity in kids, this study will show how important it is to be active in youth sports.

We are studying the effects of running mileage and cardiovascular fitness on blood cholesterol levels in young distance runners 10-18 yrs of age. To be in the study, runners must have been training for the previous 3 months or more. Participation in the study will include measurement of body size, blood pressure, blood cholesterol, cardiovascular fitness, self-assessed sexual maturity status, medical history, and physical activity. Body size measurements Ml] include height, weight, and fatness. Body fatness will be measured on the arm, back, stomach, and leg by a small pinch of the skin. Blood pressure will be measured with a cuff around the arm. Blood cholesterol will be measured by a small fingerprick. Sexual maturity will be assessed by yourself in a private setting by choosing illustrations that look most like you- Cardiovascular fitness, a good predictor of endurance performance, will be measured by a best effort on a treadmill. Testing will be conducted in the morning following a period in which you cannot eat for 12 hours. Food will be provided immediately following the measurement of blood cholesterol. We ask that the parent or guardian assist in completing the medical history and physical activity questionnaires. All information will be confidential and shared with the subject. Testing will take about 1 1/2 hours in the Human Energy Research Laboratory at Michigan State University.

There are minor risks involved in the testing. The risks of participation are no greater than completing a medical exam or physical fitness test. I may experience slight physical discomfort during the measurement of body fatness, blood pressure, and blood cholesterol. I may feel uneasy about assessing my own sexual maturity. During the exercise test, I may become tired and faint. However, the exercise test will be like running during practice or a race- I understand that participation is voluntary and I may choose not to participate at all, refuse to participate in certain tests, or discontinue participation at any time without penalty. Every effort will be made to protect me from having harmful problems during the testing. Pregnant women should not participate in the study. I understand that if I am injured as a result of my participation in this research project, Michigan State University will provide emergency medical care if necessary. I further understand that if my injury is not caused by negligence of MSU I am personally responsible for the expense of this emergency care and any other medical expenses incurred as a result of my injury.

The benefits of my participation in this study. include receiving information about my body size, blood pressure, blood cholesterol, and cardiovascular fitness the day of testing and a complete copy of my information in the mail. I will also be mailed a summary of the results of this study upon completion.

If you or your parents have any questions about the study, you may contact the following individuals:

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or

David Wright, Ph.D., Chair
University Committee on Research Involving Human Subjects
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Michigan State University
(517) 355-2180
UCRIHS@pilot.msu.edu

I have been provided information about this study and have had the opportunity to ask questions about this study. I agree to participate in this study by signing my name on the line below.

Parent/Guardian _____ Date _____

Subject _____ Date _____

Note: This form must be signed by BOTH the athlete and the parent/guardian to give consent for the athlete to participate in the study. Please remember to bring this form on the date of testing.