STUDIES IN SPORT, PHYSICAL EDUCATION AND HEALTH 11

HARRI SUOMINEN

EFFECTS OF PHYSICAL TRAINING IN MIDDLE-AGED AND ELDERLY PEOPLE

WITH SPECIAL REGARD TO SKELETAL MUSCLE, CONNECTIVE TISSUE, AND FUNCTIONAL AGING

UNIVERSITY OF JYVÄSKYLÄ, JYVÄSKYLÄ 1978

STUDIES IN SPORT, PHYSICAL EDUCATION AND HEALTH 11

HARRI SUOMINEN

EFFECTS OF PHYSICAL TRAINING IN MIDDLE-AGED AND ELDERLY PEOPLE

WITH SPECIAL REGARD TO SKELETAL MUSCLE, CONNECTIVE TISSUE, AND FUNCTIONAL AGING

ACADEMIC DISSERTATION TO BE PUBLICLY DISCUSSED, BY PERMISSION OF THE FACULTY OF PHYSICAL AND HEALTH EDUCATION OF THE UNIVERSITY OF JYVÄSKYLÄ, AUDITORIUM L-303, ON AUGUST 14, 1978, AT 12 O'CLOCK NOON

UNIVERSITY OF JYVÄSKYLÄ, JYVÄSKYLÄ 1978

EFFECTS OF PHYSICAL TRAINING IN MIDDLE-AGED AND ELDERLY PEOPLE

WITH SPECIAL REGARD TO SKELETAL MUSCLE, CONNECTIVE TISSUE, AND FUNCTIONAL AGING

STUDIES IN SPORT, PHYSICAL EDUCATION AND HEALTH 11

HARRI SUOMINEN

EFFECTS OF PHYSICAL TRAINING IN MIDDLE-AGED AND ELDERLY PEOPLE

WITH SPECIAL REGARD TO SKELETAL MUSCLE, CONNECTIVE TISSUE, AND FUNCTIONAL AGING

UNIVERSITY OF JYVÄSKYLÄ, JYVÄSKYLÄ 1978

URN:ISBN:978-951-39-7940-9
ISBN 978-951-39-7940-9 (PDF)
ISSN 0356-1070

ISBN 951-678-020-2
ISSN 0356-1070

Jyväskylässä 1978 Kirjapaino Oy Sisä-Suomi

CONTENTS

PREFACE

The present thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

I SUOMINEN, H., E. HEIKKINEN, H. LIESEN, D. MICHEL, and W. HOLLMANN. Effects of 8 weeks' endurance training on skeletal muscle metabolism in 56-70-year-old sedentary men. Europ. J. Appl. Physiol. 37: 173-180, 1977.

II SUOMINEN, H., E. HEIKKINEN, and T. PARKATTI. Effect of eight weeks' physical training on muscle and connective tissue of the m. vastus lateralis in 69-year-old men and women. J. Geront. 32: 33-37, 1977.

III SUOMINEN, H., E. HEIKKINEN, H. MOISIO, and K. VILJAMAA. Physical and chemical properties of skin in habitually trained and sedentary men. Brit. J. Dermat. 99: 147-154, 1978.

IV SUOMINEN, H., and E. HEIKKINEN. Enzyme activities in muscle and connective tissue of the m. vastus lateralis in habitually training and sedentary 33 to 70-year-old men. Europ. J. Appl. Physiol. 34: 249-254, 1975.

V SUOMINEN, H., E. HEIKKINEN, T. PARKATTI, S. FORSBERG, and A. KIISKINEN. Effects of "lifelong" physical training on functional aging in men. In: Third Nordic Congress of Gerontology, May 4-6, 1977, Turku, edited by I. Ruikka and L. Sourander. Scand. J. Soc. Med. 6: Suppl. 14, 1978.

This work was carried out at the Department of Public Health, University of Jyväskylä, during the years 1973-1978. Of the persons who have contributed to the different phases of my work, I wish to express my gratitude to:

Professor Eino Heikkinen, M.D., for having introduced me to this field and for his expert quidance, valuable critisism, and willing support throughout the whole investigation;

Professor W. Hollmann, M.D., and Dr. Heinz Liesen, M.D., for the opportunity to perform study I in fruitful collaboration

with the Institute for Sports-Medicine and Cardiology, German Sports University, Cologne;

Professor Esko Karvinen, Ph.D., and Professor Kari I. Kivirikko, M.D., for their advice and constructive critisism at the licenciate stage;

Professor Osmo Hänninen, M.D., and Associate Professor Ossi Laitinen, M.D., for their valuable comments on the manuscript;

My research associates Mr. Seppo Forsberg, Ph.Lic., Miss Anja Kiiskinen, Ph.D., Mr. Dirk Michel, M.D., and Mrs. Terttu Parkatti, M.Sc., for their valuable co-operation and skilled assistance;

Research engineers Mr. Hannu Moisio and the late Mr. Kari Viljamaa for advice on technological matters and constructing the various apparatus;

The whole laboratory staff of the Department of Public Health, especially Mr. Erkki Helkala, Mrs. Kaarina Huttunen, Mrs. Vuokko Kovanen, B.Sc., Miss Salme Moilanen, Mrs. Raija Nikkinen, Mrs. Eija Paanala, and Mrs. Kaija Raulo for their excellent technical assistance and contribution to a working atmosphere which made it a pleasure to carry out this investigation;

Mrs. Heljä Göös, Miss Leena Hakala, Miss Sinikka Hakonen, M.Sc., and Mrs. Irene Voutilainen for performing secretarial work, Mrs. Tuula Niemistö for drawing the figures, and Miss Raili Kakkonen and Mr. Matti Salmi, B.Sc., for taking the photographs;

Mr. Michael Freeman, B.A., and Mr. Richard Gayle, M.Sc., for revising the English of the manuscripts.

I should like also to thank the subjects who volunteered for different studies.

This work was financially supported by grants from the Finnish Research Council for Physical Education and Sport (Ministry of Education) and the Academy of Finland.

Finally I should like to thank the University of Jyväskylä for accepting this report for publication in its series "Studies in Sport, Physical Education and Health".

Jyväskylä, July 1978

Harri Suominen

1. INTRODUCTION

Physical training has been reported to result in increased performance in several functional capacities and physiological measurements (for ref. see Åstrand and Rodahl 1970, Hollmann 1972). Previous studies in sedentary young and middle-aged men have shown that maximal oxygen uptake, which is a commonly used measure of physical fitness, can be markedly increased through a relatively short-term (from a few weeks up to a few months) endurance-type training (Ekblom 1969, Ekblom et al. 1968, Saltin et al. 1968, 1969). Long-term effects of physical training, usually established by means of cross-sectional studies, have been attributed to superior cardiorespiratory function and body composition characteristics in active endurance athletes compared to untrained persons of corresponding ages (e.g. Costill and Winrow 1970, Cureton 1969, Grimby and Saltin 1966, 1971, Pollock et al. 1974, Shephard 1966, Wilmore et al. 1974).

Since the application of the muscle biopsy technique in exercise related studies (Bergström 1962) several reports have been published about the effects of physical training on human skeletal muscle. In particular, the adaptation of aerobic and anaerobic muscle metabolism to endurance exercise in younger men is well documented. The typical results derived either from controlled training studies or the comparison between athletes and sedentary subjects consist of increased activity of oxidative enzymes, increased glycogen concentration, as well as decreased glycogen consumption and lactate concentration during submaximal exercise (Bergman et al. 1973, Björntorp et al. 1970, Gollnick et al. 1973, Holloszy 1975, Holloszy and Booth 1976, Holloszy et al. 1973, Holm and Schersten 1974, Karlsson et al. 1972, Kiessling et al. 1974, Morgan et al. 1971, Örlander et al. 1977, Saltin 1973, Saltin and Karlsson 1971, Saltin et al. 1974, 1976, Varnauskas et al. 1970). Endurance athletes are also known to have a distinct muscle fiber composition, viz. a greater proportion of slow twitch fibers compared to untrained persons (e.g. Costill et al. 1976, Gollnick et al. 1972, Rusko 1976, Vihko et al. 1975).

In view of the fact that numerous studies have dealt with the biochemistry of exercise, it is somewhat surprising that very little scientific data is available on the adaptation of connective tissues to physical exercise and training in human subjects. Yet the connective tissue, e.g. in bones, ligaments, tendons, muscles, and articular cartilage is the component of the locomotor system which, besides muscle tissue, is most susceptible to physical training. But evidence as to this has mainly been achieved by means of animal experiments (for recent reviews see Booth and Gould 1975, Heikkinen 1974, Kiiskinen 1976). The connective tissues in skeletal muscle and skin, which are, however, relatively easy to study in human subjects, have received little attention in exercise studies.

It has been suggested by Jablecki et al. (1973) that the activation of connective tissue cells is an important prerequisite to work-induced muscular growth. They found that during a compensatory hypertrophy of rat soleus muscle, the number of fibroblasts increases rapidly and that the majority of new RNA synthesis occurring during acute muscle growth is located in connective tissue, specifically in the fibroblasts and capillaries between muscle fibers. Another study on compensatory hypertrophy of rat plantaris muscle (Turto et al. 1974) showed that the activity of prolyl hydroxylase, which is an enzyme participating in the biosynthesis of collagen by hydroxylating proline residues in peptide precursors of collagen, increases significantly already 3 days after tenotomy. Previous experiments (Suominen and Heikkinen 1975, Heikkinen et al. unpublished data) have also demonstrated an increased prolyl hydroxylase activity and collagen turnover of the m. triceps surae and m. rectus femoris in mice after being trained on a treadmill for 4 weeks. The effects of endurance-type training on collagen in skeletal muscle remain, however, little understood.

As to skin as a connective tissue, slightly retarded metabolism of collagen in the skin of inactive mice and increased concentrations of hexosamines and nitrogen in the skin of physically active mice have been reported in the few studies carried out so far (Heikkinen and Vuori 1972, Kiiskinen and Heikkinen 1976).

Previous studies on the trainability of older people are somewhat contradictory. Benestad (1965) found no increase of aerobic work capacity in 70 to 81-year-old men after a 5-6 weeks' physical training program. Some later studies (e.g. Adams and deVries 1973, deVries 1970) have, however, suggested that the trainability of older people is better than previously assumed. Diverging opinions on the effects of training in older persons are largely due to the limited number of relevant investigations performed on those age groups. Contrary to the numerous reports on younger subjects, very little is known about the adaptation of skeletal muscle to endurance training in the elderly. This is particularly true with regard to elderly females.

At least some impairment of the trainability of various biological systems should be expected in view of the several structural and functional changes occurring in the body with aging. Cross-sectional studies have shown that after 25 to 30 years of age there is a gradual decline in most physiological functions of the body the average rate being about one percent yearly (deVries 1975, Kohn 1971, Shock 1962, Skinner 1973, Weg 1975, Weiss 1975). At rest many physiological parameters (blood pH, hemoglobine, and glucose, heart rate, etc.) appear relatively constant over the years (Åstrand 1968, Shock 1962, Weg 1975). Considerable differences between young and old individuals, however, occur when the organism is subjected to vigorous endogenous or exogenous stimuli (Skinner 1973). Aging is thus characterized by a reduced ability to adapt to and to recover from physiological stress. The greater the stress and the more control mechanisms involved, the smaller is the homeostatic and reserve capacity of an old organism compared to that of a younger one (Selye 1970, Shock 1968, 1974, Weg 1975).

In general, the age-related decline is greater in those performances requiring coordinated activities and the complex functioning of several organ systems. A considerable inter- and intra-individual variation is, however, typical of the age changes in physiology (Bourlière 1973, Ries et al. 1976, Weg 1975).

The typical changes in skeletal muscle with aging involve the loss of muscle mass and increase in fat and connective tissue (Bakerman 1969, Gutmann 1977). The specific activities of some of the enzymes of both aerobic and anaerobic energy metabolism have been reported to diminish with increasing age (Bass et al. 1975, Ermini 1976).

The effects of aging on various connective tissues are relatively well documented. Both collagen concentration and the amount of covalent crosslinks of collagen are known to increase while the collagen biosynthesis and the concentration of total ground substance glycosaminoglycans decrease with age in several mammalian tissues (Heikkinen 1973, Lindner 1972).

Moreover, aging is characterized by a considerable increase in morbidity. The probability of dying due to various diseases is progressively increased after 30 years of age (Strehler 1962). Among the diseases not directly affecting the mortality rates but markedly increasing with advancing age, diseases of the locomotor system are perhaps the most important.

Since physical training usually results in increased capacity to resist the physiological stress of exercise and since some effects of training, e.g. on the cardiovascular system are opposite to those of aging (c.f. Skinner 1970, 1973), one might assume that training could delay the changes normally seen with aging or even retard aging per se. Hardly any direct experimental evidence is, however, available to support this assumption although there are several reports concluding that training counteracts the age-related decrease in functional capacity or that active persons are physiologically "younger" compared to their sedentary counterparts (e.g. Bassey 1978, Dehn and Bruce 1972, Gore 1972, Hollmann et al. 1967, Kasch and Wallace 1976).

There are, however, many difficulties in determining the effects of physical training on aging. Aging and training are complex phenomena which are not easy to study in isolation. Both cross-sectional and long-term longitudinal training studies have their own problems: the cross-sectional approach is disadvantaged by the generation effect, the longitudinal approach by the changes in environment.

Some attempts have been made recently to develop methods for the assessment of "functional age" in man (for ref. see Heikkinen 1978). One of the approaches is based on the theory of a gradual decline of abilities. By using different physiological, psychophysiological (sensory, psychomotor, psychological) and, if possible, social tests which show high correlations to chronological age, it is possible to get estimates of "biological" or "functional" aging (Bourlière 1970, 1973, Comfort 1969, Corso 1971, Dirken 1972, Heikkinen et al. 1974, Hirayama 1969, Hollingsworth et al. 1965, Ries et al. 1976, Webster and Logie 1976). These tests can also be used to form indices of functional age (see e.g. Dirken 1972, Heikkinen et al. 1974, Hollingsworth et al. 1965, Ries et al. 1976, Webster and Logie 1976). Previous studies in athletes have, however, largely been limited to variables which are closely related to physical performance. Hence, the above strategy of aging as a totality (i.e. the attempt to obtain a multidimensional profile of functional age) has not been fulfilled in the various studies on the effects of physical training with regard to the aging process.

2. PURPOSE OF THE PRESENT INVESTIGATION

The present series of experiments was undertaken to gain further insight into the effects of endurance-type physical training at older ages by studying the trainability of various physiological systems in middle-aged and elderly people and by examining the relationships between training and functional aging. The overall aim of the investigation was to contribute to the better understanding of the connections between physical activity, functional capability, aging, and health.

More specifically, the objects of the present work may be summarized as follows:

1. to determine the effects of a short-term endurance-type physical training program on physical performance and selected variables representing the aerobic and anaerobic energy metabolism of skeletal muscle in elderly men and women (I,II),
2. to elucidate the effects of "lifelong" endurance training on functional capability and selected variables of the aerobic and anaerobic energy metabolism of skeletal muscle in middle-aged and elderly men (IV,V),
3. to determine the effects of endurance training on selected biochemical and physical variables of connective tissue in skeletal muscle and skin in middle-aged and elderly people (II,III,IV,V), and
4. to study the effects of habitual endurance training on functional aging, viz. the changes occurring with age in several anthropometric, physical, physiological, psychophysiological, and biochemical properties (III,V).

3. RESEARCH METHODS

3.1. Subjects and experimental design

The description of the subjects and experimental design in the different studies is schematically presented in Table 1.

From the two short-term studies carried out to study the trainability of elderly people, the first (I) was performed in collaboration with the Institute for Sports-Medicine and Cardiology in Cologne. Study II was a part of a larger gerontological research project for which the basic population was composed of an age cohort of 66-year-old persons living in the town of Jyväskylä in 1971 (see Heikkinen and Käyhty 1977). A similar 8 weeks' supervised physical training program was conducted in both studies I and II. With the exception of some of the men in study II, the subjects had not participated in regular physical activity for at least 20 years.

To study the effects of "lifelong" physical training, a series of cross-sectional studies was carried out. Twenty-nine middle-aged and elderly male volunteers from the local orienteers and long-distance runners were initially selected for study III. The trained subjects were matched according to age with 29 healthy male volunteers, who had either no previous experience of physical training or at least had not participated in regular physical activity for several years. Both the trained and sedentary men were invited to the laboratory altogether three times. The first call included the initial experiment of study III. The second call one year later comprised study IV, the additional experiment of study III as well as the initial experiment of study V. After two more years, the third call finally included the additional experiment of study V.

In addition to physical activity, the subjects' occupation, length of education, living habits, etc. were established by means of a questionnaire before the experiments. As to these results, only the observations of the cross-sectional studies

(III-V) will be briefly reported here.

More detailed information on the subjects and experimental design are given in the original reports referred to.

Table 1. Subjects and experimental design in studies I-V

Study	Subjects			Experimental design
	Category	Age	n	
I	Sedentary men	56-70	31	Eight weeks' physical training program comprising 3-5 one-hour periods for walking-jogging, swimming, gymnastics, and ball games per week
II	Sedentary men Sedentary women	69 69	19 14	Eight weeks' physical training program comprising 3-5 one-hour periods for walking-jogging, swimming, gymnastics, and ball games per week
III	Endurance athletes Sedentary men Endurance athletes Sedentary men	32-69 31-68 34-70 33-68	29 29 21 21	Cross-sectional study with an additional experiment one year later, "lifelong" physical training comprising running and cross-country skiing at an average of 50 km per week
IV	Endurance athletes Sedentary men	34-70 33-68	23 23	Cross-sectional study, "lifelong" physical training comprising running and cross-country skiing at an average of 50 km per week
V	Endurance athletes Sedentary men Endurance athletes Sedentary men	34-70 33-68 41-72 39-70	22 22 14 14	Cross-sectional study with an additional experiment two years later, "lifelong" physical training comprising running and cross-country skiing at an average of 50 km per week

3.2. Test procedures and analytical methods

The variables investigated in the different studies together with references to the methods used are listed in Table 2. Most of the anthropometric, physiological, and psychophysiological measurements were performed in study V. The biochemical analyses of skeletal muscle and its connective tissue were carried out in studies I, II, IV, and V. Study III was specifically aimed at the physical and chemical properties of skin.

The detailed description of the tests, measurements and analytical methods is presented in each original publication (I-V).

3.3. Statistical methods

Standard procedures were used to calculate means, standard deviations (SD), standard errors (SE), and method errors (C.V. = coefficient of variation for duplicate determinations). The correlation coefficients (Pearson r) as well as least squares' regression lines were also determined, primarily when the relationships between age and the different variables were studied. A weighed sum index of "functional age" was determined as a multiple linear regression function of the most age-dependent physiological and psychophysiological variables (Dirken 1972, Webster and Logie 1976). The statistical significances were calculated by Student's t-test (2P) for correlating or non-correlating means and for correlation and regression coefficients.

Table 2. Research variables with reference to studies I-V and methods used

Variables	Studies	Methods/references	C.V.[1]
Anthropometric and physical:			
Body height	I,II,III,IV,V		
Total body weight	I,II,III,IV,V		
Skeletal weight	V	von Döbeln 1966	
Fat-free weight	V	von Döbeln 1959	
Body fat	V	Durnin & Rahaman 1967	
Skin			
- Biopsy wet weight	III	Medial brachium, 4 mm punch, Mettler H20T	
- Biopsy dry weight	III	Drying at +95°C for 24 h, Mettler H20T	
- "Elastic stiffness"	III	Ventral forearm, in vivo "diaphragm method"	4.7
- "Elastic efficiency"	III	Ventral forearm, in vivo "diaphragm method"	5.7
Physiological:			
Maximal oxygen uptake	I	Hollmann & Hettinger 1976	
Predicted maximal oxygen uptake	II,IV,V	Åstrand 1954, Lange Andersen et al. 1971	
Vertical velocity	V	Margaria et al. 1966	
Isometric grip strength	V	Electric dynamometer	
"Dynamic" grip strength	V	Electric dynamometer, ΣF/min	
Vital capacity	V	Spengler Spiromètre, Mijnhardt Volutest VT 1	
Maximal breathing capacity	V	Mijnhardt Volutest VT 1	
Systolic blood pressure	V	Auscultation technique	
Diastolic blood pressure	V	Auscultation technique	
Patellar reflex time	V	Komi et al. 1973	
Psychophysiological:			
Simple reaction time	V	Light stimulus, index finger	
Balance	V	One-foot standing, eyes closed	
Vibratory perception	V	Ankle, Heikkinen et al. 1974	
Auditory perception	V	4000 Hz, Maico Hearing Instruments	
Manipulative dexterity	V	Purdue pegboard test	
Digit symbol test	V	Heikkinen et al. 1974	

Table 2 (continued)

Variables	Studies	Methods/references	C.V.[1]
Biochemical and histochemical:			
Skeletal muscle		Vastus lateralis, needle biopsy technique	
- Fiber composition	II,V	Dubowitz & Brooke 1973, Padykula & Herman 1955	13.1
- Glycogen	I	Hyvärinen & Nikkilä 1962	2.4
- Lactate	I	Biochemica Test Combination, Boehringer/Mannheim	3.9
- "Anaerobic" enzymes:			
Creatine phosphokinase (CPK)	I,IV	Biochemica Test Combination, Boehringer/Mannheim	2.9
Hexokinase (HK)	I,IV	Silberberg et al. 1970	4.5
Phosphofructokinase (PFK)	V	Kemp 1975	6.0
Lactate dehydrogenase (LDH)	I,II,IV	Biochemica Test Combination, Boehringer/Mannheim	2.8
- "Aerobic" enzymes:			
Isocitrate dehydrogenase (ICDH)	V	Dohm et al. 1973, Plaut 1969	7.0
Succinate dehydrogenase (SDH)	I,IV	Earl & Korner 1965, Green et al. 1955	5.5
Malate dehydrogenase (MDH)	I,II,IV	Biochemica Test Combination, Boehringer/Mannheim	3.5
- Collagen:			
Hydroxyproline	V	Kivirikko et al. 1967	3.3
Soluble collagen	V	0.45 M NaCl, Heikkinen 1968	3.3
Prolyl hydroxylase	II,IV	Kivirikko & Prockop 1967	7.4
- Nitrogen	V	Minari & Zilversmit 1963	3.0
- Total soluble protein	V	0.45 M NaCl, Heikkinen 1968	3.0
Skin		Medial brachium, punch biopsies	
- Hydroxyproline	III	Woessner 1961	1.1
- Hexosamine	III	Gatt & Berman 1966	3.0
- Nitrogen	III	Minari & Zilversmit 1963	5.5
- Soluble collagen	III	0.5 M acetic acid, Heikkinen 1968	3.6
- Total soluble protein	III	0.5 M acetic acid, Heikkinen 1968	6.6
Serum		Medial antecubital vein	
- Cholesterol	V	Pearson et al. 1953	1.5
- Triglycerides	V	Biochemica Test Combination, Boehringer/Mannheim	7.5

[1] Coefficient of variation (%) for duplicate determinations

4. RESULTS

A schematic presentation of the effects of both short-term (8 weeks') and "lifelong" endurance-type training in middle-aged and elderly people with regard to the variables investigated in the different studies is shown in Table 3 which summarizes the statistically significant differences between before and after training in studies I and II as well as between habitually trained and sedentary men in studies III-V. The detailed quantitative results of the different variables are given in each original report.

As to the 8 weeks' program, the most pronounced changes after training appeared in maximal oxygen uptake and aerobic enzyme activity of skeletal muscle. The mean improvement in maximal oxygen uptake was about 11% both when a direct (I: Fig. 1) and an indirect (II: Table 1) method was used. Compared to the men, the female subjects in study II showed similar or, as in muscle MDH and PH activity (II: Tables 2 and 3), even greater training effects. The male subjects had, however, higher LDH and MDH activities both before and after training, whereas the percentages of slow twitch (ST) fibers were nearly the same in the two groups (II: Table 2). The enzyme activities were lower following an acute ergometer exercise before as well as after the training period (I: Table 1).

In agreement with the 8 weeks' program, the cross-sectional studies also demonstrated the most significant differences between habitually trained and sedentary men in the variables representing physical performance and aerobic capacity of skeletal muscle. When expressed in ml/kg·min, the mean maximal oxygen uptake in the trained group was more than 40% higher than that observed in the control group (IV: Table 1; V: Table 2). In contrast with the effects of the 8 weeks' training in study I, the athletes had lower muscle LDH activity compared to the untrained men (IV: Table 2). Besides the ordinary training effects in anthropometric and physiological properties, the two

Table 3. Effects of 8 weeks' and "lifelong" endurance training in middle-aged and elderly people with regard to variables investigated in studies I-V

8 weeks' training	"Lifelong" training
After training/before training	Habitually trained/sedentary men
Anthropometric and physical variables:	
	- lower total body weight (III,IV,V) - higher biopsy weight, "elastic stiffness", and "elastic efficiency" of skin (III)
Physiological variables:	
- higher maximal oxygen uptake (I,II)	- higher maximal oxygen uptake (IV, V), vertical velocity (V), and maximal breathing capacity (V) - lower systolic and diastolic blood pressure (V) - faster patellar reflex time (V)
Biochemical and histochemical variables:	
- higher muscle glycogen concentration (I) - lower muscle lactate production during submaximal work (I) - higher muscle CPK (I), LDH (I), SDH (I), and MDH (I,II) activity - higher PH activity of muscle connective tissue (II)	- higher percentage number of slow twitch (ST, type I) muscle fibers (V) - lower proportion of glycolytic (type IIB) fibers among fast twitch (FT) muscle fibers (V) - lower muscle LDH activity (IV) - higher muscle ICDH (V), SDH (IV), and MDH (IV) activity - higher PH activity of muscle connective tissue (IV) - higher contents of hydroxyproline and nitrogen per skin surface area (III) - lower serum triglyceride concentration (V)

groups also differed with regard to some of the connective tissue variables. In accord with study II, the muscle PH activity was significantly higher for the trained versus the sedentary subjects (IV: Fig. 1). The physical and chemical properties of skin also showed differences between the physically active and control groups (III: Tables 2 and 3).

The "best" physiological and psychophysiological variables for the multiple regression analysis of "functional age" were selected on the basis of their age-dependency and relative heterogeneity. There were six distinct variables which showed significant correlations to chronological age with at least 42 subjects (see V: Table 5 for maximal oxygen uptake, vital capacity, systolic blood pressure, vibratory as well as auditory perception, and digit symbol test). The intercorrelations of the selected variables are listed in Table 4. The final multiple linear regression equation was: Index of functional age = 69.51 - 2.27 maximal oxygen uptake (l/min) - 3.68 vital capacity (l) + 0.0092 systolic blood pressure (mmHg) + 0.736 vibratory perception (U) + 0.128 auditory perception (dB) - 0.148 digit symbol test (digits). The multiple correlation of these variables was .850, accounting for about 72% of the observed total variance.

Table 4. Intercorrelations of different variables of "functional age". Both trained and sedentary subjects are included (n = 44)

	$\dot{V}O_2max$	Vital cap.	Syst. BP	Vibr. perc.	Aud. perc.	Digit symb.
Chronological age	-.551	-.687	.463	.552	.617	-.478
Maximal oxygen uptake		.498	-.430	-.265	-.343	.192
Vital capacity			-.298	-.426	-.399	.356
Systolic blood pressure				.397	.415	-.287
Vibratory perception					.280	-.152
Auditory perception						.380
Digit symbol test						

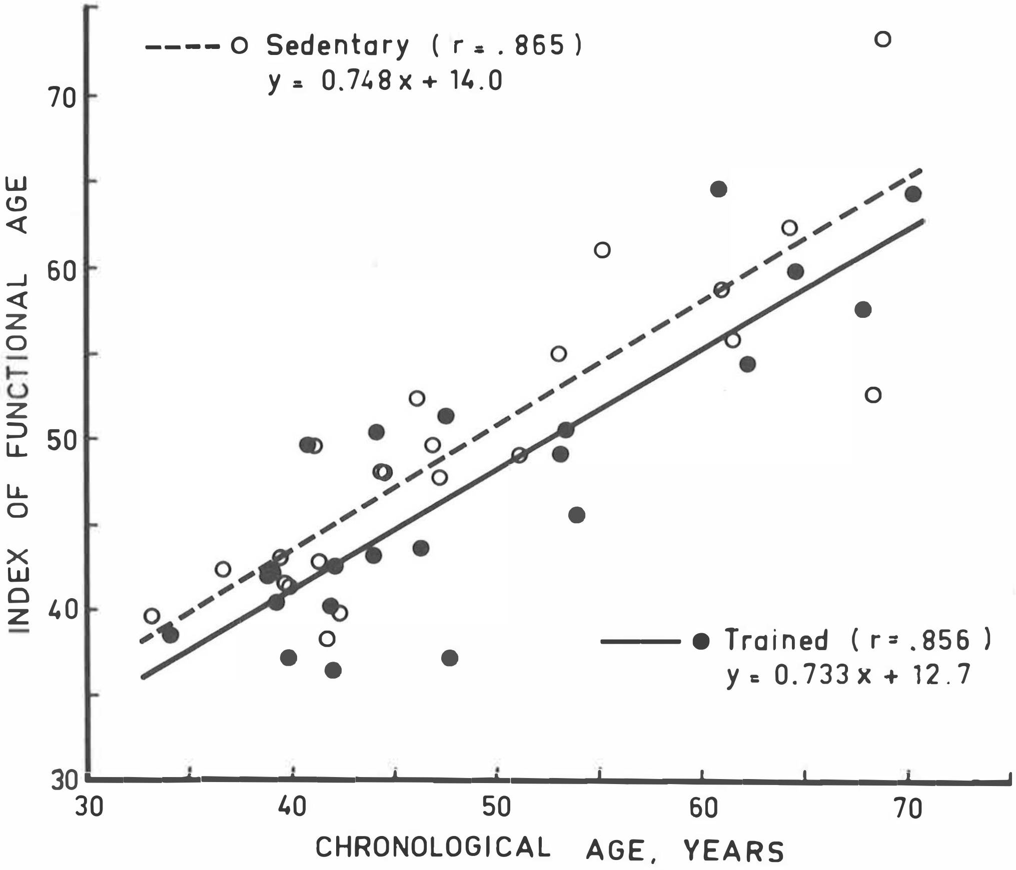

Figure 1. Comparison of chronological age and index of functional age (weighed sum of selected physiological and psychophysiological variables, see text) in habitually trained and sedentary men (n = 22 pairs)

The effect of "lifelong" endurance training on functional aging is summarized in Figure 1 which shows the comparison of chronological age and index of functional age in habitually trained and sedentary men. Although the mean "functional age" of the trained men tended to be slightly younger compared to that of the untrained men (47.4 ± 8.5 vs. 49.7 ± 8.6), the slopes of age regression were parallel for the two groups. In some of the variables influenced by training, the regression lines were rather steeper for the athletes (V: Figs. 1 and 2).

Among the biochemical variables, only total soluble protein and some of the aerobic and anaerobic enzymes of skeletal muscle showed significant age-dependency (see IV: Table 3; V: Table 5, Fig. 2). The age-related decreases of soluble protein and LDH activity as well as increases of ICDH activity were similar for both groups. Neither the trained nor the control subjects showed any significant age regressions for the connective tissue variables investigated in the cross-sectional studies.

The relation between chronological age and the different variables in habitually trained and sedentary men can be seen in greater detail in original reports III-V.

The results of the questionnaire (V) showed that except for being non-smokers, the physically active men did not significantly differ from the control subjects in respect to other living habits (alcohol consumption, quality of diet, etc.), length of education, or occupational status.

5. DISCUSSION AND CONCLUSIONS

The results presented above show that the trainability of elderly men and women does not greatly differ from that of younger people if compared on a percentage basis. This is in agreement with the recent results of, e.g. Adams and deVries (1973) and deVries (1970). The relative improvement of maximal oxygen uptake in the present investigation was of the same magnitude as previously observed among young and middle-aged persons after corresponding training programs (Ekblom et al. 1968, Flint et al. 1974, Saltin et al. 1969).

The increased aerobic enzyme activity of skeletal muscle after the 8 weeks' program also agrees with earlier studies in younger subjects (Bergman et al. 1973, Gollnick et al. 1973, Morgan et al. 1971, Örlander et al. 1977, Varnauskas et al. 1970). This result further demonstrates the enhanced aerobic capacity of elderly people after endurance-type training. According to previous reports (e.g. Holloszy et al. 1971, Morgan et al. 1971), the glycolytic capacity of skeletal muscle does not usually increase in response to endurance training. In one of our two training studies (see I: Table 1), some of the anaerobic enzymes also showed increased activities after training. The increases in the LDH and CPK activities were, however, minor compared to those in the aerobic enzymes and may therefore simply be part of an activated energy metabolism of muscle among sedentary persons during relatively acute physical training which also included anaerobic phases, e.g. the ball games. Similar effects of short-term training on muscle LDH activity have also been observed by Kiessling et al. (1974) and Örlander et al. (1977).

Moreover, the increased resting values for muscle glycogen concentration during the training period, the mean glycogen consumption during exercise, as well as the training-induced reduction in muscle lactate production during the equal ergometer exercise were similar to those earlier observed in young and middle-aged men (Holm and Schersten 1974, Karlsson et al. 1972, Saltin and Karlsson 1971, Saltin et al. 1974). The mean percentage of ST fibers of the m. vastus lateralis in both men and women was also about the same as earlier reported in untrained young and middle-aged persons (Costill et al. 1976, Gollnick et al. 1972).

As could be expected on the basis of the previous literature referred to in the introduction, the habitually trained endurance athletes had superior values in some functional capacities when compared to the sedentary men in the cross-sectional studies. Higher maximal oxygen uptake, maximal breathing capacity, and aerobic enzyme activity of skeletal muscle, in addition to lower body weight, blood pressure, and serum triglyceride concentration in the trained versus the untrained men are all in accord with earlier results (e.g. Costill et al. 1976, Gollnick et al. 1972, Grimby and Saltin 1966, Shephard 1966). The differences between the two groups in the anthropometric characteristics were not, however, as pronounced as previously reported by Pollock et al. (1974) and Wilmore et al. (1974). The results of the present investigation also failed to show significant training effects in the psychophysiological measurements (see V: Table 3), although the recent results of Vanfraechem and Vanfraechem (1977) suggest that a relatively high level of physical activity is connected with an increased performance in some psychomotor tests in aged persons.

Together with the high activity in the aerobic enzymes (ICDH, SDH, MDH), a decreased LDH activity of skeletal muscle was observed in the athletes. Although contrary to some short-term training effects mentioned above, this result agrees with other studies of a similar nature (e.g. Karlsson et al. 1975, Kiessling et al. 1974). Besides the duration of endurance training, this disparity may be explained by the differences in muscle fiber composition (c.f. Essen et al. 1975), which is usually regarded as an inherited characteristic. Among the differences between the two groups in muscle fiber composition (V: Table 4), the lower percentage of IIB fibers and higher percentage of IIA fibers among the subgroups of FT fibers in the trained versus untrained men are apparently due to the effect of endurance training (see Andersen and Henriksson 1977). The high amount of ST fibers in physically active men indicates, however, that people undergoing endurance training, are at least partly selected on the basis of inherited structural and functional properties. The results on maximal oxygen uptake, the upper limit of which is also influenced by heredity (Klissouras 1972), further suggest that the marked differences between trained and sedentary persons in aerobic capacity reflect differences in both physical activity and hereditary factors.

The adaptability of connective tissues to physical training observed in the animal studies (see Booth and Gould 1975, Heikkinen 1974, Kiiskinen 1976) is supported by the present results obtained from skeletal muscle and skin. The increased PH activities both after 8 weeks' training in study II and in physically active men in study IV show that endurance training also affects the collagen metabolism in human skeletal muscle. It is possible that the turnover of muscle collagen in endurance athletes is continuously faster than that in sedentary men of corresponding ages, even in the absence of a difference in the collagen solubility and concentration values between the two groups. The importance of a possible increased collagen turnover for an elderly person remains, however, to be elucidated.

The results of study III show that physical training also affects the properties of human skin. It could be assumed that skin to a certain degree reflects the training-induced changes in the connective tissues of, e.g. the locomotor system which is directly loaded in physical work. It is also possible that even skin adapts to increased physiological stress by increasing its mass and strengthening its structure. The mechanisms of the observed hypertrophy and high "elastic efficiency" of skin in physically active men as with the role of hormonal factors, etc., could not, however, be clarified in the present investigation.

The effects of "lifelong" endurance training on functional aging were more closely estimated on the basis of the age regressions of the most age-dependent physiological and psychophysiological variables in physically active and sedentary men. Although the trained subjects showed a considerably higher capacity in some physiological functions (e.g. in maximal oxygen uptake, V: Fig. 1) at all ages, there was little difference between the two groups in the slope of the decrease in these functions with age. This result, which is in agreement with the findings of other cross-sectional studies, suggests that the trained persons have merely changed positions on the age regression curve related to average values (c.f. Skinner 1973). When the different physiological and psychophysiological variables were combined to an index of functional age, i.e. when more "total" aging was considered, the differences between physically active and sedentary men were only minor (Figure 1). Consequently, the differences between trained and untrained persons in mean "functional age" largely depend on the proportion of work-physiological variables in the test battery.

The age-related decline of the functions influenced by physical training is, however, still a controversial question. It is difficult to differentiate to what extent the decline is due to aging itself and to what extent it is due to decreased physical activity usually associated with advancing age. Some longitudinal studies (Dehn and Bruce 1972, Hollmann 1965, Kasch and Wallace 1976, Robinson et al. 1975) have suggested a significantly smaller annual decrement in maximal oxygen uptake for physically active versus untrained individuals. Unfortunately, the subjects in those studies were not followed for a sufficient period of time in view of the fact that maximal oxygen uptake in sedentary persons can easily be improved by 10 to 20%, which may compensate at least 10 years' average decrement. Therefore, only extremely long-term and well-controlled longitudinal studies would give the answer whether the rate of aging of, e.g. the cardiorespiratory system is really influenced by habitual endurance training.

As mentioned earlier, aging is a multidimensional phenomenon, the factors related to it being difficult to isolate. Recent observations show that functional age may be influenced by several living habits, occupational factors, length of education, etc. (Exton-Smith 1972, Heikkinen et al. 1974, 1975). Although there were no major differences between the two groups in educational and occupational parameters in the present study, their contribution should not be underestimated. Moreover, the limitations of the cross-sectional approach, particularly together with the small number of subjects and the indirect nature of one of the main variables (maximal oxygen uptake) have to be taken into consideration in interpreting the present findings and relating them to larger populations.

Although it can be concluded from the observations of this investigation that the aging process itself is not retarded by even "lifelong" physical training, there are, however, training effects which are contrary to the effects of aging and which may be beneficial for human well-being. Better physical performance capacity, activated and strengthened connective tissues, and reduced number of risk factors associated with coronary heart disease (c.f. the smoking habits, blood pressures, serum triglyceride concentrations, and body weights between the two groups of study V) in habitually active people may well contribute to a better life in old age, delay some of the degenerative changes of the locomotor system, and together with other positive health habits, even restrain premature death in present-day industrialized society which favours monotonous and stressful work but, however, physically inactive life. The results of the present investigation also show that still at a relatively advanced age, it is possible to start physical training and to achieve training effects that compare with younger persons and that may be of advantage to health. Further studies, particularly those of a prospective nature are, however, needed to elucidate the connections between physical activity, aging, and health, and the possiblities and consequences of physical training in every-day life in old age which is clearly more complex and problematic than a controlled research situation.

TIIVISTELMÄ

Tutkimuksessa selvitettiin kestävyystyyppisen liikunnan vaikutuksia keski-ikäisillä ja sitä vanhemmilla henkilöillä erityisesti luurankolihaksen, sidekudoksen ja "funktionaalisen" vanhenemisen osalta. Tavoitteena oli syventää näkemystä fyysisen aktiivisuuden, toimintakykyisyyden, vanhenemisen ja terveyden yhteyksistä tutkimalla

1. lyhyehkön kestävyystyyppisen liikuntaharjoittelun vaikutusta vanhenevien miesten ja naisten fyysiseen suorituskykyyn sekä luurankolihaksen aerobista ja anaerobista energia-aineenvaihduntaa kuvastaviin muuttujiin (I,II),
2. "elinikäisen" kestävyysharjoittelun vaikutusta keski-ikäisten ja sitä vanhempien miesten toimintakykyisyyteen sekä eräisiin luurankolihaksen aerobisen ja anaerobisen energia-aineenvaihdunnan muuttujiin (IV,V),
3. kestävyysharjoittelun vaikutusta luurankolihaksen ja ihon sidekudoksen biokemiallisiin ja fysikaalisiin muuttujiin keski-ikäisillä ja sitä vanhemmilla ihmisillä (II,III,IV,V) sekä
4. säännöllisen kestävyysharjoittelun vaikutusta funktionaaliseen vanhenemiseen, ts. muutoksiin, joita tapahtuu iän mukana useissa antropometrisissa, fysiologisissa, psykofysiologisissa ja biokemiallisissa muuttujissa (III,V).

Lyhyehkön kestävyystyyppisen harjoittelun vaikutuksia selvitettiin kahdessa eri osatutkimuksessa, joista ensimmäisessä (I) oli tutkittavina 31 56-70-vuotiasta aiemmin harjoittelematonta miestä sekä toisessa (II) 33 69-vuotiasta eläkeläistä (19 miestä ja 14 naista). Tutkittavat osallistuivat 8 viikon pituiseen johdettuun liikuntaharjoitteluun, joka sisälsi kävely-hölkkää, uintia, voimistelua ja palloilua yhteensä 3-5 kertaa viikossa. "Elinikäisen" fyysisen harjoittelun vaikutusten selvittämiseksi suoritettiin sarja poikittaistutkimuksia (III,IV,V), joihin valittiin alunperin 29 32-69-vuotiasta jatkuvasti harjoittelevaa (juoksua ja hiihtoa keskimäärin 50 km viikossa) kestävyysurheilijaa sekä yhtä monta vastaavanikäistä harjoittelematonta miestä.

Tutkittavien maksimaalinen hapenkulutus lisääntyi merkitsevästi 8 viikon harjoitteluperiodin jälkeen. Muutos oli keskimäärin n. 11 % sekä suoraan (I) että epäsuorasti (II) mitattuna. Luurankolihaksen (m. vastus lateralis) glykogeenikonsentraatio, tutkittujen "aerobisten" entsyymien (SDH, MDH) sekä I tutkimuksessa myös eräiden "anaerobisten" entsyymien (CPK, LDH) aktiivisuudet lisääntyivät merkitsevästi. Lihaksen maitohapon tuotto submaksimaalisessa kuormituksessa väheni harjoittelun vaikutuksesta. Energia-aineenvaihdunnan entsyymien ohella myös kollageenisynteesiin osallistuvan prolyylihydroksylaasin (PH) aktiivisuus lisääntyi. Naisten harjoitusvaste oli samanlainen tai eräiden muuttujien osalta jopa suurempi kuin miesten. Miehillä oli naisiin verrattuna suuremmat LDH- ja MDH-aktiivisuudet hitaasti supistuvien (ST) lihassäikeiden prosentuaalisen lukumäärän ollessa kuitenkin molemmilla samaa suuruusluokkaa. Entsyymiaktiivisuudet vähenivät akuutissa kuormituksessa sekä ennen harjoittelua että sen jälkeen.

Poikittaistutkimusten tulosten mukaan kestävyysurheilijoilla oli harjoittelemattomiin verrattuna yli 40 % parempi maksimaalinen hapenkulutus, suurempi juoksunopeus ja maksimaalinen hengityskapasiteetti, alhaisempi ruumiinpaino, seerumin triglyseridikonsentraatio, systolinen ja diastolinen verenpaine sekä nopeampi patellaarirefleksiaika. Koeryhmällä todettiin myös suurempi ST (tyyppi I)-lihassäikeiden prosentuaalinen lukumäärä, pienempi glykolyyttisten (IIB) säikeiden osuus nopeasti supistuvista (FT) säikeistä sekä suuremmat aerobisten entsyymien (ICDH, SDH, MDH) aktiivisuudet kuin kontrolliryhmällä. Anaerobisten entsyymien aktiivisuudet olivat samansuuruisia molemmissa ryhmissä tai jopa alhaisempia (LDH) harjoitelleilla miehillä. Urheilijoilla oli harjoittelemattomiin verrattuna lisäksi kohonnut lihaksen sidekudoksen PH-aktiivisuus, suurempi ihon hydroksiproliini- ja typpipitoisuus pinta-alayksikköä kohti sekä suurempi ihon biopsianäytteiden paino, ihon "elastinen jäykkyys" ja "kimmoisuuden hyötysuhde". Psykomotorisissa, psykologisissa sekä aistien toimintaa mittaavissa testeissä ei sen sijaan havaittu merkitseviä eroja tutkittujen ryhmien välillä.

"Elinikäisen" kestävyysharjoittelun vaikutusta funktionaaliseen vanhenemiseen tarkasteltiin lähemmin eri muuttujien ikäregressioiden avulla. Vaikka fyysisesti aktiivisilla henkilöillä oli merkitsevästi korkeammat arvot eräissä fysiologisissa funktioissa (esim. maksimaalisessa hapenkulutuksessa), tutkittujen ryhmien välinen ero pysyi samana tai jopa pieneni iän lisääntyessä. Kun kronologiseen ikään voimakkaimmin korreloivista fysiologisista ja psykofysiologisista muuttujista laskettiin "funktionaalisen iän" painotettu summaindeksi, harjoitelleiden ja harjoittelemattomien väliset erot jäivät sekä keskiarvojen että ikäregressioiden suhteen vähäisiksi.

Tutkimuksen tulokset osoittavat, että vielä suhteellisen vanhallakin iällä voidaan aloittaa liikuntaharjoittelu ja saada aikaan fyysisen suorituskyvyn sekä lihasten energia-aineenvaihdunnan, erityisesti aerobisen kapasiteetin paraneminen, joka ei oleellisesti poikkea nuoremmilla henkilöillä aikaisemmin todetuista adaptaatiomuutoksista. Kestävyystyyppistä liikuntaa pitkäjänteisesti harrastavien fyysinen toimintakykyisyys ja luurankolihasten aerobinen kapasiteetti pysyvät jatkuvasti vastaavanikäisten harjoittelemattomien keskimääräistä tasoa korkeammalla. Fyysinen harjoittelu aktivoi luurankolihaksessa myös sen sidekudoksen aineenvaihduntaa. Jopa iho näyttäisi hypertrofioituvan ja mekaanisesti lujittuvan harjoituksen vaikutuksesta. Vaikka tutkimustulokset viittaavat siihen, että eri funktioiden heikkenemistä iän mukana, ts. vanhenemisprosessia sinänsä ei voida estää edes elinikäisen kestävyysharjoittelun avulla, monet liikunnan vaikutukset ovat kuitenkin vastakkaisia vanhenemismuutoksille. Yhdessä muiden positiivisten terveystottumusten kanssa lisääntyneellä fyysisellä aktiivisuudella saattaa olla huomattava merkitys vanhenevien ihmisten hyvinvoinnille esimerkiksi tuki- ja liikuntaelimistön rappeutumismuutoksia sekä eräitä sydän- ja verisuonisairauksien riskitekijöitä ajatellen.

REFERENCES

ADAMS, G. M., and H. M. deVRIES. Physiological effects of an exercise training regimen upon women aged 52 to 79. J. Geront. 28: 50-55, 1973.

ANDERSEN, P., and J. HENRIKSSON. Training induced changes in the groups of human type II skeletal muscle fibres. Acta Physiol. Scand. 99: 123-125, 1977.

ÅSTRAND, P.-O. Experimental Studies of Physical Working Capacity in Relation to Age and Sex. Copenhagen: Munksgaard, 1952.

ÅSTRAND, P.-O. Physical performance as a function of age. JAMA 205: 105-109, 1968.

ÅSTRAND, P.-O., and K. RODAHL. Textbook of Work Physiology. New York: McGraw-Hill, 1970.

BAKERMAN, S. Aging Life Processes. Springfield Il: Charles C. Thomas, 1969.

BASS, A., E. GUTMANN, and V. HANZLÍKOVÀ. Biochemical and histochemical changes in energy supply-enzyme pattern of muscles of the rat during old age. Gerontologia 21: 31-45, 1975.

BASSEY, E. J. Age, inactivity and some physiological responses to exercise. Gerontology 24: 66-77, 1978.

BENESTAD, A. M. Trainability of old men. Acta Med. Scand. 178: 321-327, 1965.

BERGMAN, H., P. BJÖRNTORP, T.-B. CONRADSON, M. FAHLEN, J. STENBERG, and E. VARNAUSKAS. Enzymatic and circulatory adjustment to physical training in middle-aged men. Europ. J. Clin. Invest. 3: 414-418, 1973.

BERGSTRÖM, J. Muscle electrolytes in man. Determination by neutron activation analysis on needle biopsy specimens. A study on normal subjects, kidney patients and patients with chronic diarrhoea. Scand. J. Clin. Lab. Invest. Suppl. 68, 1962.

BJÖRNTORP, P., M. FAHLÉN, J. HOLM, T. SCHERSTEN, and W. SZOSTAK. Determination of succinic oxidase activity in human skeletal muscle. Scand. J. Clin. Lab. Invest. 26: 145-150, 1970.

BOOTH, F. W., and E. W. GOULD. Effects of training and disuse on connective tissue. In: Exercise and Sport Sciences Reviews, edited by J. H. Wilmore and J. F. Keogh. New York: Academic Press, 1975, p. 83-112.

BOURLIERE, F. The Assessment of Biological Age in Man. Public Health Papers 37. Geneva: WHO, 1970.

BOURLIÈRE, F. Ecology of human senescense. In: Textbook of Geriatric Medicine and Gerontology, edited by J. Brocklehurst. Edinburgh: Churchill Livingstone, 1973, p. 60-73.

COMFORT, A. Test-battery to measure ageing-rate in man. Lancet 2: 1411-1415, 1969.

CORSO, J. F. Sensory processes and age effects in normal adults. J. Geront. 26: 90-105, 1971.

COSTILL, D. L., J. DANIELS, W. EVANS, W. FINK, G. KRAHENBUHL, and B. SALTIN. Skeletal muscle enzymes and fiber composition in male and female track athletes. J. Appl. Physiol. 40: 149-154, 1976.

COSTILL, D. L., and E. WINROW. Maximal oxygen intake among marathon runners. Arch. Phys. Med. 51: 317-320, 1970.

CURETON, T. K. The physiological effects of exercise programs on adults. Springfield Il: Charles C. Thomas, 1969.

DEHN, M. M., and R. A. BRUCE. Longitudinal variations in maximal oxygen intake with age and activity. J. Appl. Physiol. 33: 805-807, 1972.

deVRIES, H. A. Physiological effects of an exercise training regimen upon men aged 52 to 88. J. Geront. 25: 325-336, 1970.

deVRIES, H. A. Physiology of exercise and aging. In: Aging. Scientific Perspectives and Social Issues, edited by D. S. Woodruff and J. E. Birren. New York: van Nostrand Company, 1975, p. 257-276.

DIRKEN, J. (ed.). Functional Age of Industrial Workers. Groningen: Wolters-Noordhoff, 1972.

DOHM, G. L., R. L. HUSTON, E. W. ASKEW, and H. L. FLESHOOD. Effects of exercise, training, and diet on muscle citric acid cycle enzyme activity. Can. J. Biochem. 51: 849-854, 1973.

DUBOWITZ, V., and M. H. BROOKE (eds.). Muscle Biopsy: A Modern Approach. London: W. B. Saunders, 1973.

DURNIN, J. V. C. A., and M. M. RAHAMAN. The assessment of the amount of fat in the human body from measurements of skinfold thickness. Brit. J. Nutr. 21: 681-689, 1967.

EARL, D. C. N., and A. KORNER. The isolation and properties of cardiac ribosomes and polysomes. Biochem. J. 94: 721-734, 1965.

EKBLOM, B. Effect of physical training on oxygen transport system in man. Acta Physiol. Scand. Suppl. 328, 1969.

EKBLOM, B., P.-O. ÅSTRAND, B. SALTIN, J. STENBERG, and B. WALLSTRÖM. Effects of training on circulatory response to exercise. J. Appl. Physiol. 24: 518-528, 1968.

ERMINI, M. Ageing changes in mammalian skeletal muscle. Biochemical studies. Gerontology 22: 301-316, 1976.

ESSEN, B., E. JANSSON, J. HENRIKSSON, A. W. TAYLOR, and B. SALTIN. Metabolic characteristics of fibre composition in skeletal muscle. Acta Physiol. Scand. 95: 153-165, 1975.

EXTON-SMITH, A. N. Physiological aspects of aging: relationship to nutrition. Am. J. Clin. Nutr. 25: 853-859, 1972.

FLINT, M. M., B. L. DRINKWATER, and S. M. HORWATH. Effects of training on women's response to submaximal exercise. Med. Sci. Sports 6: 89-94, 1974.

GATT, R., and E. R. BERMAN. A rapid procedure for the estimation of amino sugars on a micro scale. Anal. Biochem. 15: 167-171, 1966.

GOLLNICK, P. D., R. B. ARMSTRONG, B. SALTIN, C. W. SAUBERT IV, W. L. SEMBROWICH, and R. E. SHEPHERD. Effect of training on enzyme activity and fiber composition of human skeletal muscle. J. Appl. Physiol. 34: 107-111, 1973.

GOLLNICK, P. D., R. B. ARMSTRONG, C. W. SAUBERT IV, K. PIEHL, and B. SALTIN. Enzyme activity and fiber composition in skeletal muscle of untrained and trained men. J. Appl. Physiol. 33: 312-319, 1972.

GORE, I. Y. Physical activity and aging - a survey of Soviet literature. III. The character of physical activity; training and longitudinal results. Geront. Clin. 14: 78-85, 1972.

GREEN, D. E., S. MII, and P. M. KOHOUT. Studies on the terminal electron transport system. I. Succinic dehydrogenase. J. Biol. Chem. 217: 551-567, 1955.

GRIMBY, G., and B. SALTIN. A physiological analysis of physically well-trained middle-aged and old athletes. Acta Med. Scand. 179: 513-526, 1966.

GRIMBY, G., and B. SALTIN. Physiological effects of physical training. Scand. J. Rehab. Med. 3: 6-14, 1971.

GUTMANN, E. Muscle. In: Handbook of the Biology of Aging, edited by C. E. Finch and L. Hayflick. New York: van Nostrand Company, 1977, p. 445-469.

HEIKKINEN, E. Transformations of rat skin collagen. Acta Physiol. Scand. Suppl. 317, 1968.

HEIKKINEN, E. Ageing of interstitial collagen. In: Frontiers of Matrix Biology, Vol. 1. Ageing of Connective Tissues - Skin, edited by L. Robert. Basel: Karger, 1973, p. 107-129.

HEIKKINEN, E. Liikunnan vaikutus sidekudoksiin. Duodecim 90: 475-486, 1974.

HEIKKINEN, E. Assessment of functional aging. In: Lectures on Gerontology, Vol. 1, edited by A. Viidik. London: Academic Press, 1978, in press.

HEIKKINEN, E., A. KIISKINEN, B. KÄYHTY, M. RIMPELÄ, and I. VUORI. Assessment of biological age. Methodological study in two Finnish populations. Gerontologia 20: 33-44, 1974.

HEIKKINEN, E., and B. KÄYHTY. Gerontological aspects of physical activity - motivation of older people in physical training. In: Guide to Fitness After Fifty, edited by R. Harris and L. J. Frankel. New York: Plenum Press, 1977, p. 191-205.

HEIKKINEN, E., B. SEPPÄNEN, and M. RIMPELÄ. Biological age, health, and health-risk indicators among 25-57-year-old men in two parts of Finland. Scand. J. Soc. Med. 3: 105-110, 1975.

HEIKKINEN, E., and I. VUORI. Effect of physical activity on the metabolism of collagen in aged mice. Acta Physiol. Scand. 84: 543-549, 1972.

HIRAYAMA, H. Some physical functions of aging people in an agricultural village. Acta Med. Nagasaki 13: 187-210, 1969.

HOLLINGSWORTH, J. W., A. HASHIZUME, and S. JABLON. Correlations between tests of aging in Hiroshima subjects - an attempt to define "physiologic age". Yale J. Biol. Med. 38: 11-26, 1965.

HOLLMANN, W. Körperliche Training als Prävention von Herz-Kreislauf-Krankheiten. Stuttgart: Hippogrates-Verlag, 1965.

HOLLMANN, W. (ed.). Zentrale Themen der Sportmedizin. Berlin-Heidelberg-New York: Springer-Verlag, 1972.

HOLLMANN, W., B. GRÜNEWALD, and C. BOUCHARD. Die Alternsbedingte Reduction der kardio-pulmonalen Kapazität und ihre Begegnung durch ein Minimal-Trainingsprogram. Arbeitsmed. Sozialmed. Arbeitshyg. 3: 88-92, 1967.

HOLLMANN, W., and Th. HETTINGER. Sportmedizin - Arbeits- und Trainingsgrundlagen. Stuttgart-New York: Schattauer, 1976.

HOLLOSZY, J. O. Adaptation of skeletal muscle to endurance exercise. Med. Sci. Sports 7: 155-164, 1975.

HOLLOSZY, J. O., and F. W. BOOTH. Biochemical adaptations to endurance exercise in muscle. Ann. Rev. Physiol. 38: 273-291, 1976.

HOLLOSZY, J. O., P. A. MOLÉ, K. M. BALDWIN, and R. L. TERJUNG. Exercise induced enzymatic adaptations in muscle. In: Limiting Factors of Physical Performance, edited by J. Keul. Stuttgart: Georg Thieme, 1973, p. 66-80.

HOLLOSZY, J. O., L. B. OSCAI, P. A. MOLÉ, and I. J. DON. Biochemical adaptations to endurance exercise in skeletal muscle. In: Muscle Metabolism During Exercise. Advances in Experimental Medicine and Biology, Vol. 11, edited by B. Pernow and B. Saltin. New York: Plenum Press, 1971, p. 51-61.

HOLM, J., and T. SCHERSTEN. Metabolic changes in skeletal muscles after physical conditioning and in peripheral arterial insufficiency. Försvarsmedicin 10: 71-82, 1974.

HYVÄRINEN, A., and E. A. NIKKILÄ. Specific determination of blood glucose with o-toluidine. Clin. Chim. Acta 7: 140-143, 1962.

JABLECKI, C. K., J. E. HEUSER, and S. KAUFMAN. Autoradiographic localization of new RNA synthesis in hypertrophying skeletal muscle. J. Cell Biol. 57: 743-759, 1973.

KARLSSON, J., L.-O. Nordesjö, L. JORFELDT, and B. SALTIN. Muscle lactate, ATP, and CP levels during exercise after physical training in man. J. Appl. Physiol. 33: 199-203, 1972.

KARLSSON, J., B. SJÖDIN, A. THORSTENSSON, B. HULTEN, and K. FRITH. LDH isozymes in skeletal muscles of endurance and strength trained athletes. Acta Physiol. Scand. 93: 150-156, 1975.

KASCH, F. W., and J. P. WALLACE. Physiological variables during 10 years of endurance exercise. Med. Sci. Sports 8: 5-8, 1976.

KEMP, R. G. Phosphofructokinase from rabbit skeletal muscle. In: Methods in Enzymology, Vol. XLIII. Carbohydrate Metabolism Part C, edited by W. A. Wood. New York: Academic Press, 1975, p. 71-77.

KIESSLING, K.-H., L. PILSTRÖM, A-Ch. Bylund, B. SALTIN, and K. PIEHL. Enzyme activities and morphometry in skeletal muscle of middle-aged men after training. Scand. J. Clin. Lab. Invest. 33: 63-69, 1974.

KIISKINEN, A. Adaptation of connective tissues to physical training in young mice. Studies in Sport, Physical Education and Health 9, Univ. Jyväskylä, 1976.

KIISKINEN, A., and E. HEIKKINEN. Physical training and connective tissues in young mice - biochemistry of skin. Brit. J. Dermat. 95: 525-529, 1976.

KIVIRIKKO, K. I., O. LAITINEN, and D. J. PROCKOP. Modifications of a specific assay for hydroxyproline in urine. Anal. Biochem. 19: 249-255, 1967.

KIVIRIKKO, K. I. and D. J. PROCKOP. Enzymatic hydroxylation of proline and lysine in protocollagen. Proc. Nat. Acad. Sci. (Wash.) 57: 782-789, 1967.

KLISSOURAS, V. Genetic limit of functional adaptability. Int. Z. Angew. Physiol. 30: 85-94, 1972.

KOHN, R. R. Principles of Mammalian Aging. New Jersey: Prentice-Hall, 1971.

KOMI, P., V. KLISSOURAS, and E. KARVINEN. Genetic variation in neuromuscular performance. Int. Z. Angew. Physiol. 31: 289-304, .1973.

LANGE ANDERSEN, K., R. J. SHEPHARD, H. DENOLIN, E. VARNAUSKAS, and R. MASIRONI. Fundamentals of Exercise Testing. Geneva: WHO, 1971.

LINDNER, J. Altern des Bindegewebes. In: Handbuch der allgemeinen Patologie, VI/4, Altern, edited by G. Holle. Berlin: Springer-Verlag, 1972, p. 245-368.

MARGARIA, R., P. AGHEMO, and E. ROVELLI. Measurement of muscular power (anaerobic) in man. J. Appl. Physiol. 21: 1661-1664, 1966.

MINARI, O., and D. B. ZILVERSMIT. Use of KCN for stabilization of color in direct nesslerization of Kjeldahl digests. Anal. Biocem. 6: 320-327, 1963.

MORGAN, T. E., L. A. COBB, F. A. SHORT, R. ROSS, and D. R. GUNN. Effects of long-term exercise on human muscle mitochondria. In: Muscle Metabolism During Exercise. Advances in Experimental Medicine and Biology, Vol. 11, edited by B. Pernow and B. Saltin. New York: Plenum Press, 1971, p. 87-95.

ÖRLANDER, J., K.-H. KIESSLING, J. KARLSSON, and B. EKBLOM. Low intensity training, inactivity and resumed training in sedentary men. Acta Physiol. Scand. 101: 351-362, 1977.

PADYKULA, H. A., and E. HERMAN. The specifity of the histochemical method of adenosine triphosphatase. J. Histochem. Cytochem. 3: 170-195, 1955.

PEARSON, S., S. STERN, and T. H. McGavack. Rapid, accurate method for the determination of total cholesterol in serum. Anal. Chem. 25: 813-814, 1953.

PLAUT, G. W. E. Isocitrate dehydrogenase (DPN-specific) from bovine heart. In: Methods in Enzymology, Vol. XIII. Citric Acid Cycle, edited by J. M. Lowenstein. New York: Academic Press, 1969, p. 34-42.

POLLOCK, M. L., H. S. MILLER, Jr., and J. H. WILMORE. Physiological characteristics of champion American track athletes 40 to 75 years of age. J. Geront. 29: 645-649, 1974.

RIES, W., I. SAUER, B. JUNKER, D. PÖTHIG, and U. SCHWERDTNER. Methodische Probleme bei der Ermittlung des biologischen Alterns. Z. Inn. Med. 31: 109-113, 1976.

ROBINSON, S., D. B. DILL, S. P. TZANKOFF, J. A. WAGNER, and R. D. ROBINSON. Longitudinal studies of aging in 37 men. J. Appl. Physiol. 38: 263-267, 1975.

RUSKO, H. Physical performance characteristics in Finnish athletes. Studies in Sport, Physical Education and Health 8, Univ. Jyväskylä, 1976.

SALTIN, B. Metabolic fundamentals in exercise. Med. Sci. Sports 5: 137-146, 1973.

SALTIN, B., G. BLOMQVIST, J. H. MITCHELL, R. L. JOHNSON, Jr., K. WILDENTHAL, and C. B. CHAPMAN. Response to exercise after bedrest and after training. Circulation Suppl. 5, 1968.

SALTIN, B., L. H. HARTLEY, Å. KILBOM, and I. ÅSTRAND. Physical training in sedentary middle-aged and older men. II. Oxygen uptake, heart rate, and blood lactate concentration at submaximal and maximal exercise. Scand. J. Clin. Lab. Invest. 24: 323-334, 1969.

SALTIN, B., and J. KARLSSON. Muscle glycogen utilization during work of different intensities. In: Muscle Metabolism During Exercise. Advances in Experimental Medicine and Biology, Vol. 11, edited by B. Pernow and B. Saltin. New York: Plenum Press, 1971, p. 87-95.

SALTIN, B., K. NAZAR, D. L. COSTILL, E. STEIN, E. JANSSON, B. ESSEN, and P. D. GOLLNICK. The nature of the training response; peripheral and central adaptations to one-legged exercise. Acta Physiol. Scand. 96: 289-305, 1976.

SALTIN, B., J. WAHREN, and B. PERNOW. Phosphagen and Carbohydrate metabolism during exercise in trained middle-aged men. Scand. J. Clin. Lab. Invest. 33: 71-77, 1974.

SELYE, H. A. Stress and aging. J. Am. Geriat. Soc. 18: 669-690, 1970.

SHEPHARD, R. J. World standards of cardiorespiratory performance. Arch. Environ. Health 13: 664-672, 1966.

SHOCK, N. W. Physiological aspects of aging. Ann. Rev. Physiol. 23: 97-122, 1962.

SHOCK, N. W. Physiological theories of aging. In: Theoretical Aspects of Aging, edited by M Rockstein, M. L. Sussmann, and J. Chesky. New York: Academic Press, 1974, p. 119-136.

SILBERBERG, R., W. G. STAMP, P. A. LESKER, and M. HASLER. Aging changes in ultrastructure and enzymatic activity of articular cartilage of guinea pigs. J. Geront. 25: 184-198, 1970.

SKINNER, J. S. The cardiovascular system with aging and exercise. In: Physical Activity and Aging. Medicine and Sport, Vol. 4, edited by D. Brunner and E. Jokl. Basel: Karger, 1970, p. 100-108.

SKINNER, J. S. Age and performance. In: Limiting Factors of Physical Performance, edited by J. Keul. Stuttgart: Georg Thieme, 1973, p. 271-282.

STREHLER, B. L. Time, Cells, and Aging. New York: Academic Press, 1962.

SUOMINEN, H., and E. HEIKKINEN. Effect of physical training on collagen. Ital. J. Biochem. 24: 64-65, 1975.

TURTO, H., S. LINDY, and J. HALME. Protocollagen proline hydroxylase activity in work-induced hypertrophy of rat muscle. Am. J. Physiol. 226: 63-65, 1974.

VANFRAECHEM, J., and R. VANFRAECHEM. Studies on the effect of a short training period on aged subjects. J. Sports Med. 17: 373-380, 1977.

VARNAUSKAS, E., P. BJÖRNTORP, M. FAHLÉN, I. PŘEROVSKÝ, and J. STENBERG. Effects of physical training on exercise blood flow and enzymatic activity in skeletal muscle. Cardiovasc. Res. 4: 418-422, 1970.

VIHKO, V., P. J. SARVIHARJU, M. HAVU, Y. HIRSIMÄKI, A. SALMINEN, P. RAHKILA, and A. U. ARSTILA. Selected skeletal muscle variables and aerobic power in trained and untrained men. J. Sports Med. 15: 296-304, 1975.

von DÖBELN, W. Anthropometric determination of fat-free body weight. Acta Med. Scand. 165: 37-41, 1959.

von DÖBELN, W. Kroppstorlek, energiomsättning och kondition. In: Handbok i Ergonomi, edited by G. Luthman, U. Åberg, and N. Lundgren. Stockholm: Almquist & Wiksell, 1966, p. 245-253.

WEBSTER, I. W., and A. R. LOGIE. A relationship between functional age and health status in female subjects. J. Geront. 31: 546-550, 1976.

WEG, R. B. Changing physiology of aging: normal and pathological. In: Aging. Scientific Perspectives and Social Issues, edited by D. S. Woodruff and J. E. Birren. New York: van Nostrand Company, 1975, p. 229-256.

WEISS, A. K. The physiology of aging. Major Probl. Clin. Surg. 17: 1-13, 1975.

WILMORE, J. H., H. L. MILLER, Jr., and M. L. POLLOCK. Body composition and physiological characteristics of active endurance athletes in their eighth decade of life. Med. Sci. Sports 6: 44-48, 1974.

WOESSNER, J. F., Jr. The determination of hydroxyproline in tissue and protein samples containing small proportions of this imino acid. Arch. Biochem. 93: 440-447, 1961.