COMPARISON OF RISK FACTORS FOR CORONARY HEART DISEASE IN A SAMPLE OF THE RURAL AND URBAN POPULATIONS OF TANZANIA WITH SPECIAL REFERENCE TO THE LEVEL OF PHYSICAL ACTIVITY

BY

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A thesis submitted in partial fulfillment of the requirements for the degree of PhD at the University of Dar Es Salaam and the Norwegian University of Sport and Physical Education, Oslo 2003.

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I hereby declare that this is my own original work and has not been submitted for a similar degree in any another University

Signed Julia Anetth Mbahibaki

Date 31.01.05, Oslo

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ACKNOWLEDGEMENTS

Many people have contributed greatly to the completion of this doctoral work. I wish to thank all who tirelessly assisted and supported me. Mentioning them all would take a decade.

My heartfelt thanks go to Professor Dr. med. Arne T. Høstmark, for his kind and effective supervision, enthusiasm, wisdom, and sound criticism. I really appreciate all the scientific advice, motivating discussions and arguments as well as his comments, patience and encouragement, throughout the study. My great gratitude also goes to Professor. PhD. Sigmund B. Strømme for his fine supervision, understanding, never-ending support and practical assistance, which helped me to complete my study. I give my sincere thanks to both of you for leading me into this scientific world. Furthermore, I am very thankful to Dr. Zablon Masesa, my co-supervisor, for his supervision, and interest in conducting the study.

My warmest thanks and compliments go to Eva Kristensen, laboratory technician, for all the hours we spent together in the laboratory and during the data collection in Tanzania especially in the villages. I genuinely value her professional work, great support and wonderful friendship. I am also greatly indebted to Eva and her husband Terje, for making my life in Oslo comfortable by providing me with shelter. I also want to thank Benjamin Lujani, and Rachel Missingo for their kind assistance and co-operation during the data collection.

I am very thankful to Ine Wigernæs and Sissel Tomten for the help I received on statistic.

Thanks also go to Anne Sofie Røysland. Without her never-ending friendship, courage, support and laughter, I could never have reached this stage. Furthermore, thanks go to Henny and Tor Volla, Robert Stallmann, Frank Evertsen, Merete Lund Fasting, Linda Thorsen, Prisca Massao, Vivi Klette, Vivi-Ann Garden, Ola Normann Klafstad, Christina Majumbu, Joyce Nyambelwa, Dorothy Kashebo and the Traaen family for their endless friendship and support mentally and morally.

My warm-hearted thoughts go to my brothers and sisters, Vickie Kokushubira, Phoebe Milembe, Nelia-Peace Twinaombezi, Merabo Kekisha, Frida Kuumula, Barnabas Muanguzi, Mercy Atugonza, Apollos Mulisa, Karen-Hope Sima and Justace Mbonimpaye for their love and support. Especially thanks go to Vickie for giving me the opportunity of coming to Norway and Mercy because you have been always there for me.

DEDICATION

This work is dedicated to my parents for their support, courage, tolerance and unrestricted love.

***Dear Daddy**, your gifted ability of fairness, giving and receiving love, has made me to be the way I am. You were a man with a heart of gold to me. Your place in my heart is still there, but I really miss your presence. Rest in peace.*

***Dear Adam Martin Luther**, my beloved brother, it was too early to leave the rest of the family and I. I was not ready for it, nor would I have ever been. I love you so much and I terribly miss you. May our Lord God rest your soul in eternal life.*

ABSTRACT

Objective

To estimate and compare the level of some risk factors for coronary heart disease (CHD) in a sample of the rural and urban populations of Tanzania, with particular reference to the level of physical activity, and the relationships between physical activity level and other coronary risk factors.

Design

A cross-sectional study to estimate levels of selected coronary risk factors in females and males aged 30 – 60, such as blood pressure, body mass index, obesity, serum lipids, physical activity and percentage of alcohol and tobacco users, and users of several types of diets.

Setting

The indigenous inhabitants of Temeke - Kigamboni, Tanga - Handeni and Arusha - Monduli districts (rural population), and residents of the city of Dar-Es-Salaam and Morogoro town (urban population).

Participants

A sample of 985 subjects was surveyed. From the rural area 501 subjects (females: 256, and males: 245), and from the urban area 484 subjects (females: 255, and males: 229) participated in the study.

Main outcomes

Several rural-urban differences in the observed variables were found in this study. A higher prevalence of a cluster of major CHD risk factors was noted in the urban than

in the rural population. The rural population had a significantly higher physical activity level (PAL) than the urban population, i.e. 29.8±15.8 against 16.5± 8.6 kcal/kg/d (mean±SD) ($p < 0.001$). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly lower in the rural than in the urban population, i.e. 129.8±23.8 against 133.5±24.6 mm Hg ($p < 0.02$), and 77.5±12.7 against 82.1±14.3 mm Hg (mean±SD) ($p < 0.001$). Prevalence of systolic hypertension, (defined as ≥ 140 mm Hg), was found in 31% - females, and 29% - males of the rural subjects and in 28% - females, and 36% - males of the urban subjects. Prevalence of diastolic hypertension, (defined as ≥ 90 mm Hg), was found in 20% - females, and 12% - males of the rural population, and 23% - females, and 29% - males of the urban population. The body mass index (BMI) was significantly lower in the rural population than in the urban population, 22.5±5.0 vs. 27.4±5.6 kg/m^2 (mean±SD) ($p < 0.001$). Prevalence of overweight (defined as BMI ≥ 25 $kg/m^{2)}$ was found in 22% - females, and 13% - males of the rural population, and 37% - females, and 45% - males of the urban population. Prevalence of obesity (defined as BMI ≥ 30 kg/m^2) was found in 13% - females, and 7% - males of the rural and 45% - females, and 25% - males of the urban population. Waist and hip circumferences, and waist-to-hip ratio were significantly lower in the rural population, i.e. 73.5 ±19.2, 83.9±22.0 cm, and 0.88±0.1 (mean±SD) ($p < 0.001$) compared with corresponding values 90.9±12.8, 98.0±11.8 cm, and 0.93±0.1 (mean±SD) ($p < 0.001$) in the urban population. The rural population had slightly lower serum values of all selected lipids than the urban population. Values in the rural group were: total cholesterol (TC) 3.7±1.1 mmol/L, triglycerides (TG) 1.4±0.7 mmol/L, high-density lipoprotein cholesterol (HDL-c) 1.0±0.3 mmol/L, low-density

lipoprotein cholesterol (LDL-c) 2.1±0.9 mmol/L, total cholesterol to high-density lipoprotein cholesterol ratio (TC/HDL-c ratio) 4.2 ±1.8, and free fatty acids (FFA) 0.2±0.2 mmol/L, (mean±SD). Corresponding values in the urban group were: TC 4.5±1.1 mmol/L, TG 1.6±1.1 mmol/L, HDL-c 1.1±0.3 mmol/L, LDL-c 2.7±1.0 mmol/L, TC/HDL-c ratio 4.5±1.6 mmol/L, and FFA 0.3±0.2 mmol/L, (mean±SD). Prevalence of hypercholesterolemia (defined as TC ≥ 5.2 mmol/L) was found in 9 % - females, and 7% - males of the rural, and 22% - females, and 26% - males of the urban population. The PAL was inversely related to most of the selected risk factors of CHD P<*0.001*). The strongest inverse relationship was between PAL and BMI. In univariate scatter plots, for groups, SBP and DBP blood pressure decreased with increasing PAL, and increased with increasing BMI. For both groups, SBP and DBP blood pressure increased with increasing age, but the increase was steeper for the urban than for the rural group. In multivariate analysis, PAL was a significant negative predictor of several other coronary risk factors, but the apparent influence was low compared to other predictors ($p < 0.001$). Age, BMI and TG were positive predictors of both SBP and DBP. Overall, cigarette smoking was relatively common in the rural population, i.e. 20% (6% of females, and 31% of males) against 9%, in the urban population (2% of females, and 14% of males). The prevalence of cigarette smoking was higher among males than females ($p < 0.001$). Smokeless tobacco use was also prevalent in the rural population: 12% (14% of females, and 11% of males), but not observed in the urban population. The number of subjects reporting alcohol consumption was lower in the rural population, i.e. 20% (13% of females, and 27% of males) compared to the urban population 27% (17% of females, and 36 % of

males) ($p < 0.01$). The major proportion of rural subjects reported either high fat/low carbohydrate intake or low fat/high carbohydrate intake, while high fat/high carbohydrate seemed to be the main diet pattern of the urban group.

Conclusion

The findings from this population-based survey in Tanzania suggest that urbanization is accompanied by an unfavourable alteration of several coronary risk factors. The urban group had a lower level of physical activity than the rural group, higher blood pressure, body mass index, blood lipids, prevalence of obesity and a higher percentage of subjects reporting high fat/high carbohydrate diet. Although the levels of some selected coronary risk factors in the sample of the Tanzanian population were low compared to those reported from studies conducted in western communities, the observed urban-rural differences might be indicative of a progress towards an increase in coronary heart disease, as the population becomes more urbanized.

Key words: Coronary, risk factors, physical activity, diet, blood pressure, serum lipids, rural, urban, population, Tanzania, Africa.

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ABBREVIATIONS AND DEFINITIONS

The following abbreviations are used in this report:

ADP:	adenosine diphosphate
Apo A-1:	apolipoprotein A-1
Apo B:	apolipoprotein B
Apo C-1:	apolipoprotein C-1
BMI:	body ma
CAD:	
CHD:	

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PAI-1:	plasminogen activator inhibitor-1
PAL:	physical activity level
SBP:	systolic blood pressure
SNS:	sympathetic nervous system
TC:	total cholesterol
TG:	triglycerides
t-PA:	tissue-type plasminogen activator
VLDL-c:	very low-density lipoprotein cholesterol
WHR:	waist-to-hip ratio

Hypercholestrolemia	total cholesterol $\geq$ 5.2 mmol/L
Hyperglycemia	fasting blood glucose $\geq$ 6.1 mmol/L
Hypertension	blood pressure (systolic/diastolic) $\geq$ 140/90 mm Hg
INTERSALT	International Cooperative Study on the Relation of Blood Pressure to Electrolyte Excretion in Population
Obesity	body mass index $\geq$ 30 kg/m^2
Overweight	body mass index of $\geq$ 25 - 29.9 kg/m^2
Alcohol user	currently alcohol user
Tobacco user	currently cigarette smoker, or user of other tobacco products

PREFACE

This doctoral work was conducted at NUSPE (The Norwegian University of Sport and Physical Education) Oslo, and at the Department of Preventive Medicine and Epidemiology, University of Oslo, Norway in a NUFU programme (NUFU: "Nasjonalt utvalg for utviklingsrelatert forskning og undervisning" Centre for international university co-operation), regarded as a research project in co-operation with MUCHS (Muhimbili University College of Health Science) in Dar-Es-Salaam, Tanzania.

As, a master's degree student at NUSPE, I wanted to write about heart diseases especially in my home country, Tanzania. I thank Prof, dr.med Sverre Mæhlum and Dr. Scient Sigmund A. Anderssen, my supervisors for the master's degree dissertation, for introducing me to research-work in this area, and both inspiring and encouraging me to become a researcher. I knew that heart disease could be a major problem in the future owing to increased urbanization. Personal observation indicated that the people of Tanzania were changing their traditional lifestyles to affluent lifestyles. Chronic health problems such as diabetes mellitus, hypertension, and stroke were common topics of daily conversation in the society. I knew about the role of physical activity in the prevention of the heart diseases. The purpose of the present work was to extend my previous studies to provide some more data on physical activity and coronary risk factors in the Tanzanian population, with particular reference to differences between the urban and rural populations.

CHAPTER 1. GENERAL INTRODUCTION

Coronary heart disease (CHD) is considered to be an important public health problem in developed countries, but it is also increasing in the developing countries owing to demographic transition: reduction in mortality and fertility and an increase in life expectancy, nutrition transition: a decline in the prevalence of under-nutrition and a shift away from traditional diets towards "westernized" one: i.e. a diet high in saturated fat, sugar, and refined foods and low in fiber, and epidemiologic transition: a shift from a pattern of predominantly infectious and under nutrition-related diseases to chronic non-communicable conditions, such as CHD, cerebrovascular disease, and cancer (Kutty et al. 1993, Muna 1993, Popkin 1994, Cadha et al. 1997). Those transitions, which have already taken place in developed countries, are now affecting developing countries with limited health care resources. With the epidemiologic transition phenomenon, developing countries has to manage a "double burden" of pre-transitional such as infectious and undernutrtition-related diseases, and post-transitional diseases; non-communicable conditions, such as CHD, cerebrovascular disease, and cancer. Pre-transitional diseases not completely eradicated, and post-transitional diseases such as CHD are emerging alongside (Reddy and Yusuf 1998, Yusuf et al. 2001). Given the limited health and financial resources in many of those countries, inadequate management of either category of disease is likely to result. Additionally, some African countries, mostly notably in Sub-Saharan Africa including Tanzania, are facing the enormous burden imposed by the HIV/AIDS epidemic, and other accompanying infectious diseases that have re-emerged, for instance tuberculosis.

Furthermore, urbanization seems to be an important phenomenon with implications for the prevalence of CHD. Urbanization has been associated with deterioration in the profile of CHD risk factors, because of its adverse implication for diet, regular physical activity, and other behavioral aspects such as smoking and alcohol intake. In addition to the growth of urban areas due to natural growth and rural-urban migration, rural areas themselves are undergoing transformation (Reddy and Yusuf 1998, Yusuf et al. 2001, Walker et al. 2002). Increased mechanization of agricultural methods, availability of transport means and globalization (in the form of television images and increased availability of processed food) has brought about decreases in daily physical activity and slow abandonment of traditional dietary habits (Yusuf et al. 2001, Walker et al. 2002). Therefore, in terms of its health implications, urbanization can be seen as two-way process that includes, not only the transfer of rural dwellers into urban areas, but also the spread of urban influences into rural communities, and as such urbanization becomes an issue of how rather than where one lives.

Recently, in some African countries, changes from the traditional African way of life to an affluent lifestyle together with changes in the environment, economy, socio-cultural status and rapid urbanization appear to result in an increase in the prevalence of CHD and its risk factors (Forrest et al. 2000, van der Sander et al. 2000, Seedat 2000). Research done in Africa has shown that the prevalence of CHD is nearly absent in rural areas, and still very uncommon in urban centres, where many Africans are in an advanced stage of the epidemiologic transition. Total food consumption has increased while the intake of fibre-containing foods has decreased (INTER SALT

1988, Lang 1997, Walker and Sareli 1997a,b, Mennen et al. 2001). Mean blood cholesterol level of the urban populations is almost doubled as compared to the rural populations with a traditional life-style (Foucan et al. 2000). Obesity in females has increased extensively (Kruger et al. 2001, Walker et al. 2001, and the prevalence of hypertension has exceeded that in the developed communities (Seedat 2000). Furthermore, the prevalence of cigarette smoking has also increased in males, but not in females (WHO; Tobacco health 1996, and Seedat 2000), as has alcohol intake (Chiyadza et al. 1993, Baleta 1998, Walker et al. 2002). The level of physical activity has decreased generally, especially in urban areas (Walker et al. 2002). With these increases in risk factors, a higher CHD morbidity and mortality can be expected, especially among urban Africans, as is now experienced by Afro-Americans (Walker and Sareli 1997a,b, Walker et al. 2002).

The daily active life is the most important element of health (Bourchard et al. 1994, Pate et al. 1995, Mensik et al. 1997). Habitual physical activity promotes optimal performance of all body systems: the musculoskeletal, cardiovascular, hormonal-immunological, haematological, neuro-sensory, and gastrointestinal (Bauman and Owen 1999). The benefits of regular physical activity are certainly desired in contrast to the negative consequences associated with physically inactive living (Bourchard et al. 1994, Pate et al. 1995, U.S. Surgeon General 1996, Blair and Cooper 1997, Williams 1998). Physical inactivity denotes a level of activity less than that needed to maintain good health (NIH consensus conference 1996). A physically active life was common for almost everyone before modern technology introduced the benefits of the automobile, labour-saving devices, television and computers. These changes in

technology have made it possible to minimize one's daily energy expenditure and reduce one's daily physical activity by using labour saving devices.

The consequences of a greatly reduced level of physical activity have been well studied under controlled conditions and include major physiological changes, especially in the circulatory system, such as orthostatic hypotension, a reduction in blood volume, and a marked lowering in maximum oxygen uptake (VO_2 max). Furthermore, significant metabolic changes in the form of a negative nitrogen balance, lowered glucose tolerance, raised calcium excretion in the urine, and muscle atrophy takes place (Strømme et al. 1984a, b). Such changes may justifiably be regarded as detrimental to health because of the diminished ability of the body to carry out the functions of daily living. Evidently, daily physical activity has long been shown to play a central role in health promotion and chronic disease prevention (Powell et al. 1987, Berlin and Colditz 1990, Bouchard and Perussè 1994, Powell and Blair 1994, Rodriquez et al. 1994, Pate et al. 1995, U.S. Surgeon General 1996). On the other hand, a low level of habitual physical activity is considered as an important risk for major chronic diseases (Shinton 1993, Lord 1995, Colditz et al. 1997, Mensink et al. 1997, Farmer and Gotto 2000, Tenant and Mclean 2000) as well as cardiovascular diseases, particularly coronary heart disease (Blair et al. 1995, Hardman 1995, Mensink et al. 1996, Rosengren and Wihelmsen 1997, Leon et al. 1987 and 1997, Haapanen 1997, Fried 1998, Kujala 1998).

With the epidemiological transition phenomenon, Tanzania is now facing a growing prevalence of chronic diseases, such as CHD. Environmental and behavioural changes such as the adoption of new dietary habits, a sedentary lifestyle, and the

stress of the urbanization and working conditions, all lead to the rise in CHD risk factors. These have been observed among Tanzanians, particularly in the urban areas. Previously, CHD and its risk factors have not been considered to be a serious problem in rural and urban populations in Tanzania (Kitange et al. 1993, Swai et al. 1993). However, the incidence of CHD risk factors among rural and urban populations in Tanzania is on the increase (Edwards et al. 2000, Njelekela et al. 2001). For this reason one may deduce that with a boost in industrial output, a rise in the incidence of CHD may occur as well. Consequently, further studies are needed. This thesis is therefore designed to study and compare CHD risk factors with particular emphasis on the level of physical activity in a sample of the rural and urban population of Tanzania.

CHAPTER 2. BACKGROUND FOR THE PRESENT STUDY

2.1 CORONARY HEART DISEASE AND ITS CLINICAL DETECTION

Coronary heart disease tends to be classified as the major form of cardiovascular disease, and is a major cause of death, particularly in developed societies, but increasingly elsewhere as well (Farmer and Gotto 2000). CHD is predominantly a disease of old age (Ashwell 1997). The peak age of death from CHD is 70-74 in males and 75-79 years in females (Uemura and Pisa 1988, Cheitlin et al. 1993). However, CHD is also a major cause of premature death before 65 years in males (Ashwell 1997). It is known that incidence of CHD in males younger than 60 years is three times that of females (Virmani et al. 2000). It has been suggested that menopausal status negates the beneficial effects of oestrogen and leads to accelerate disease in older females. It takes 20 years after menopause for the incidence of CHD to parallel that of males (Ashwell 1997).

The clinical manifestation of CHD also known as (CAD) coronary artery disease varies with a spectrum ranging from angina pectoris (severe chest pain on exertion or excitement), myocardial infarction, heart attack, and sudden cardiac death (Willerson and Maseri 2000). These syndromes result from multiple interactions between the coronary circulation and the heart muscles (myocardium). It is usually coronary atherosclerosis, with thrombosis as a major factor that causes obstruction in the arteries supplying the heart thereby resulting in decreased blood flow to the myocardium (Ashwell 1997, Buja and McAllister 2000, Willerson and Maseri 2000).

Angina pectoris

Angina pectoris (*angere* means "to choke"; *pectoris* refers to the chest) is the clinical term used to express chest pain or discomfort resulting from a relative oxygen insufficiency in the heart muscles due to inadequate perfusion of blood to the endocardial, myocardial, or epicardial layers of the heart resulting in myocardial ischemia (Baroldi 1991, Fuster et al. 1992, Buja and McAllister 2000). The ischemia would impair aerobic energy production and increase lactic acid formation. The patients usually complain of a left precordial tightness or ache provoked by exercise or emotion and usually relieved by rest. It occurs when oxygen demand exceeds supply (Ashwell 1997). The usual pathologic correlate of angina pectoris is coronary atherosclerosis with luminal narrowing of one or more of the major coronary arteries (Buja and McAllister 2000). However, there is essential alteration in the anatomic extent of large vessels associated with the development of symptomatic CHD (Buja and McAllister 2000). The change of atherosclerosis is influenced by a number of inter-related factors, including the rate of progression of large vessel disease and the development of coronary collateral blood flow, coronary occlusion may lead to major myocardial infarction or to little or no myocardium damage, unstable angina pectoris and related syndromes (Fuster 1992). These are associated with a high incidence of acute alterations of plaque on top of thrombotic lesions, usually platelet aggregates or non-occlusive thrombi as well as platelet aggregates in the microcirculation of the myocardium (Fuster 1992, Buja and McAllister 2000). The accumulation of mononuclear cells at sites of unstable plaques, suggesting an inflammatory component to these vascular lesions, has also been demonstrated (Casscells et al. 1996).

Myocardial infarction

Myocardial infarction is defined as death of heart muscles from severe prolonged ischemia (reduced blood supply). Myocardial infarction often involves the left ventricle (Olsen 1991). It is not unusual to have right ventricular infarcts occur in association with left ventricular infarcts (Buja 2000). Most often myocardial infarction occurs in a single coronary artery that has been narrowed from changes associated to atherosclerosis, but multi-regional myocardial infarction may also occur (Olsen 1991). The overall incidence of occlusive coronary thrombosis and associated plaque fissure or rupture has been observed to be high in acute myocardial infarction (Davis 1985). Thrombus typically involves the major coronary artery in the distribution of the infarcted myocardium. However, there is a significant difference in the incidence of thrombosis according to the type of infarction (Buja 2000). The major complication of acute myocardial infarction are infarct expansion (shape change leading to stretching and thinning of the ventricular wall), infarct extension (necrosis), ventricular aneurysm, cardiogenic shock, papillary muscle dysfunction and rupture, external cardiac rupture, pericarditis and systemic embolisation from embolism (Olsen 1991, Buja 2000).

2.2 PREVALENCE OF CHD WORLDWIDE

CHD have traditionally been considered as diseases of developed societies, namely Western Europe, North America, New Zealand, and Australia (Gintner et al. 1995, Pearson 1999, Farmer and Gotto 2000, Seedat 2000). The burden of CHD differs characteristically between regions of the world, with declines in USA, Australia, Israel, Canada, Japan and New Zealand (Kaplan 1993, Kunst et al. 1996, Ashwell

1997, Pearson 1999). Countries such as Finland, Norway, Italy and UK have also had reductions of CHD incidence and mortality in the last century (Ashwell 1997, Pearson 1999). However, the incidence of such diseases have increased in some parts of the world, for example in eastern Europe such as the former Czechoslovakia, Yugoslavia, Bulgaria, Romania, Hungary, and some countries in developing societies, in both females and males (Gintner et al. 1995, Ashwell 1997, Pearson 1999). These European Eastern block countries had the highest CHD rates in the world in 1990s (Marmot et al. 1991, Bobadilla et al. 1997, Notzon et al. 1998).

The reason for a prediction of a global CHD epidemic lies in the "epidemiological transition" in which control of infectious and nutritional disease allows most of the society particularly in developing communities to reach the ages in which CHD manifests itself (Pearson 1999). In reality, CHD is considered as the leading cause of death, not only in developed societies, but also as of the mid-1990s, in developing societies as well as in India especially in the urban population (Krishnamoothy 1999). It has been predicted that CHD will be the most common cause of disability by the year 2020 in all parts of the world (Pearson 1999). However, increases to that year, predict an expansion of CHD exceeding other disease in all regions except sub Saharan Africa and the Middle East. Concerns about the growing problem of CHD in developing countries started to be an issue between the late 1980s and 1990s (Pearson et al. 1993, Pearson 1999). At that time, increasing magnitudes of hospital beds started to be occupied by CHD cases (Dodu 1988). A variety of increases and trends made it clear that a CHD epidemic was almost inevitable in developing societies (Pearson et al. 1993, Whelton et al. 1995, Reddy and Yusuf 1998). A study

conducted by Murray and Loped (1996) also documented an increase of CHD and the author suggested that CHD and the communicable diseases had the same burdens of death for developing countries in 1990s.

In Asian populations the rate of CHD mortality was lower as compared with northern European populations, but in south Asia, and especially in India the prevalence of CHD was increasing as reported by Reddy (1993). Even Indian immigrants to the Western Europe and North America and South Africa have higher CHD mortality rate compared to those of their adopted countries (Enas et al. 1996, Krishnamoorty 1999, Pearson 1999). In USA and UK, Asian Indians are found to have higher CHD rates than any ethnic minority (Enas et al. 1992 and 1996, Ashwell 1997, Pearson 1999). In the CHD (CADI) study among Asian Indians, the prevalence of CHD was found to be 10.2% compared within 2.5% in whites in the same age groups (Enas et al. 1996).

Epidemiological studies of black populations in developed and developing countries have confirmed that CHD is rare in black populations in Africa (Betrand 1995). These studies also suggest that CHD was a much less significant cause of morbidity and mortality in black populations in the Caribbean than in US blacks (Watkins 1984, Betrand 1995). The prevalence of CHD and its related complications have been noted to be low in most countries in Africa especially Sub Saharan Africa, but the situation has changed in some countries (Hutt 1991, Muna 1993, Walker and Sareli 1997a,b, Okesina 1999). Several studies of city dwellers in Africa, for example in South Africa, have confirmed that this population approaches the CHD morbidity and mortality rates of Afro-American, whose mortality rate has now

reached that of white Americans (Keil et al. 1993, South African Health Review 1995, Walker and Sareli 1997a,b, Yonga 1998).

In East and West Africa the prevalence of CHD morbidity and mortality have been reported to be low in urban as well as rural dwellers (Watkins 1984, Olubuyide and Solanke 1990, Muna 1993, Oludunni et al. 1996). Betrand (1995), also found the lower level of CHD and its risk factors, but it has increased at the end of the last decade as reported by Walker and Sareli (1997a), and Pearson et al. (1999). In the 1990s, hospital-based reports in Kenya have also documented an increase of CHD particularly among urban dwellers (Yonga et al. 1993, Gikonyo 1997, Okanga and Thuo 1998, Yoga 1998). Furthermore, CHD appeared to be more common in the urban and rural North Africans as reported by Muna (1993). These trends towards urbanisation, with accompanying lifestyle changes, are thought to be responsible for the rise of CHD prevalence in those North African communities (Ghannem and Fredj 1997). Abraham (1982) also reported that the CHD rate in hospitals in Ethiopia was accounted for only 5-6%. Later however, (1996), in two studies conducted by Bayourova and Estrine (1996), and Gizaw (1996), it was observed a marked increase in the extent of CHD in Ethiopia.

2.3 PATHOLOGICAL PROCESS LEADING TO CHD

The heart muscle receives blood via the coronary arteries (Ashwell 1997, Buja and McAllister 2000). If these arteries become blocked, blood supply to the heart muscle is impaired and the tissue suffers from a lack of oxygen and nutrients. The coronary arteries may either become blocked by a blood clot in conjunction with atherosclerosis, or deposition of various materials forming a fibrous plaque on the

inner arterial walls: (Buja and McAllister 2000). The events leading to arterial blockage can be explained in different stages or processes as described below.

Atherosclerosis

The term "*atherosclerosis*" (arteriosclerosis) is derived from the Greek "athero" (porridge) and "sclerosis" (hardening). There are three major forms of atherosclerotic disease. Coronary atherosclerosis in one or both coronary arteries, may be accompanied by aortic atherosclerosis, and is often found in other major arteries (Badimon et al. 1993, Ross 1997). Atherosclerotic narrowing of the carotid or basilar arterial system may lead to stroke and other forms of cerebral vascular disease. In a femoral artery it can result in intermittent claudication. In addition, other arteries can be affected, such as renal arteries (Badimon et al. 1993, Ross 1997). It is a progressive disease process that generally begins in childhood and has clinical manifestations in middle to late adulthood (Ross 1997). Although prevalent, and with its pathologic characteristics having been confirmed for more than a century, the mechanism behind the development of atherosclerosis is still not well understood (Cheitlin et al. 1993, Ross 1997).

Fatty streaks

The fatty streaks and the fibrous plaque reduce the diameter of the arteries (Ross 1995 and 1997, Buja 2000). Fatty streaks are the earliest representation of visible lesions of atherosclerosis. The first lesion is situated mainly in the aortic branches or bifurcation (Buja and McAlliester 2000). They do not protrude into the arterial lumen, and do not disturb blood flow arteries (Cheitlin et al. 1993, Ross 1995 and 1997). Fatty streaks are characterised by the sub-endothelial accumulation of large

"foam cells", and consist of an intracellular accumulation of lipids derived from low density lipoprotein cholesterol (LDL-c) within the intima (Ross 1997). There is a slight focal thickening of the intima, an increased number of fibroblasts and possible precursors of smooth muscle cells. The end result is a small round plaque that can be visible by the naked eye. In CHD, fatty streaks may be discovered in the aorta at the age of 20 (Cheitlin et al. 1993, Ross 1997). Between adolescence and early adulthood the fatty streaks may be found in the coronary arteries. They do not cause symptoms, and in some locations in the vasculature, they may decline over time (Cheitlin et al. 1993). Although these are considered to be precursors of the atherosclerotic lesion, they certainly are reversible at this stage.

Fibrous plaque

Usually fatty streaks do proceed to become fibrous plaque, which is regarded as irreversible and leads to complicated lesion particularly in the coronary arteries (Cheitlin et al. 1993, Ross 1995 and 1997, Buja and McAllister 2000). This process develops as a response of the vessel wall to chronic, multi-factorial injury and leads to the formation of atherosclerotic plaque: fibrous plaque atheroma (Buja et al. 1990, Ashwell 1997). The plaques are regions of thickened intima that are composed of a changing mixture of fibrous tissue, cells, and lipids (Buja et al. 1990, Ashwell 1997). To begin with, atherosclerosis is a focal disease. There is predilection for formation of atherosclerosis plaques adjacent to branch points in areas of low velocity flow (Buja and McAllister 2000). It is postulated that the flow patterns in such regions promote endothelium with monocytes and platelets. Areas of predilection for severe coronary atherosclerosis include either one or both coronary arteries, especially the proximal left anterior descending coronary artery or the proximal and distal right

coronary arteries (Badimon et al. 1993, Ross 1997). Established atherosclerosis involves all three layers of the arterial wall, such as that in addition to intimal thickening, diseased areas exhibit medial degeneration and weakening and intimal fibrous, with lymphocytic inflammatory infiltrates (Buja 2000).

Atherosclerotic disease leads to broad alteration of the vessel walls. Dilation of the vessels occurs in such a way that the lumen is maintained despite the presence of intimal plaque (Glagov et al. 1987 and 1988). Luminal narrowing occurs only when atherosclerotic disease is advanced. Approximately 50% narrowing of luminal diameter occurs before blood flow is affected (Buja 2000). Areas of severe narrowing often develop in the setting of multifocal disease.

Thrombosis

Thrombosis is the condition, which occurs when a blood clot blocks an artery and slows or stops the blood flow through it. This situation often occurs in acute CHD and is initiated by acute changes on top of atherosclerotic plaque (Buja et al. 1981 and 1987, Fuster et al. 1992). The endothelium may be lost when ulceration occurs at the surface and the fatty contents may be exposed to the blood circulation system (Burk et al. 1999). The range of thrombotic lesions includes platelet aggregates, non-occlusive and occlusive thrombi (Cassells et al. 1996, Burke et al. 1999). Major thrombi are frequently associated with significant disruptions in plaque surface, which may appear as cracks erosion, ulceration, or rupture (Fuster 1992, Ashwell 1997). Such thrombosis can block the vessel and result in, for example, myocardial infarction or stroke. Organization of the thrombus is followed by its incorporation into the plaque, enlarging its size, and it may eventually become covered by

endothelium (Ross 1997). Coronary lesions that are mainly susceptible to such changes are atheromatous plaques with thin fibrous capsules and large cores of lipid-rich debris. Factors that probably contribute to endothelial injury and disruption of the plaque surface include hemodynamic trauma, local attachment and activation of platelets and blood cells, inflammatory process in the plaque, and cytotoxic effects of plaque contents that are present at the sites of plaque rupture (Fuster 1992, Casscell et al. 1996, Burke et al. 1999).

The likely pathogenic sequence of plaque is endothelium injury, flux of blood component, increase in intra-plaque pressure, and outward rupture of the fibrous capsule (Falk 1983, Fuster et al. 1992, Buja and McAllister 2000). Plaque breaking seems to be more distinct process (Falk 1983, Davie and Thomas 1985). A higher incidence of plaque rupture has been found in patients, especially males dying suddenly during exertion than in patients dying suddenly at rest (Burke et al. 1999). Disturbance of the plaque surface via any mechanism predisposes the formation of intra-plaque thrombi. Plaque haemorrhage may also occur with or without thrombus and comes either from the rupture of the fibrous cap or from the tiny capillaries or small deep vessels or from the lumen of the artery through a surface fissure that vascularises the plaque (Ross 1997). The resulting hematoma may further occlude and narrow the vessel lumen (Buja 2000).

The final period is referred to as the clinical period, in which disease manifestation become apparent. Weakening of the coronary artery wall, as the fibrous plaque subjects the neighbour medial layer to increased pressure, may provoke atrophy and loss of elastic tissue. Finally, the coronary artery fails to supply sufficient oxygen to

the myocardium, resulting to clinical complications such as, angina pectoris, acute myocardial infarction, cardiac failure and sudden death (Cheitlin et al. 1993, Ross 1997).

Relationship between atherosclerosis and thrombosis

In atherosclerosis, increased tendency for coagulation has been recognised as a major modifiable risk factor. It has been associated with and interrelated with endothelial dysfunction, hyperlipidaemia and hypercoagulability (Farmer and Gotto 2000). Acute ischemic syndromes have been related to the formation of occlusive intravascular thrombi, secondary to breaking of an unprotected plaque. The local balance of procoagulant and fibrinolytic activity is a major cause due to interaction between levels of coagulation factors, platelet activation, tissue factors and dyslipidemia (Farmer and Gotto 2000). Dyslipidaemia has been correlated with procoagulant factors such as increased levels of fibrinogen, plasminogen activator inhibitor-1, and abnormal platelet binding and aggregation (Farmer and Gotto 2000). Endothelial damage has been correlated with increased levels of von Willebrand factor (the plasma factor VIII related protein), which has been correlated with both increased platelet aggregation and the binding to the dysfunctional endothelium. The severity of atherosclerosis has been correlated with endothelial damage, implying a relation between the progression of vascular injury and a hypercoagulable state. The von Willebrand factor has also been correlated with elevated levels of LDL-c, and decreased after treatment (Montalescot et al. 1998).

Cellular elements derived from the macrophage line are a source of platelet activating factor, which is generated at sites of inflammation within the intimal

surface of the arterial beds (Farmer and Gotto 2000). Activation of platelets results in the up-regulation of thrombi receptors, which are localised on vascular smooth muscle and thus enhance the vasoconstriction activity of thrombin. Dyslipidaemia has been associated with increased platelet aggregation in addition to increased levels of beta-thromboglobilin and thromboxane A_2 and B_2. Therefore, dyslipidaemia has been related to both lipid peroxidation and resultant platelet activation (Di Minno et al. 1986).

Tissue factor is known as a lipoprotein co-factor that increases the activity of factor VII-A by acting on factor XI and factor X (Broze 1994). Tissue factor activity has also been associated with endothelial injury. It is elevated in inflammation or smooth muscle cell migration and it is increased in atherosclerotic lesions (Sato et al. 1996). Additionally, hyperlipidemia has been associated with increased tissue factor activity (Lesnik et al. 1992).

Elevated levels of fibrinogen have been associated with enhanced risk for atherosclerosis, due to its increasing influence on both coagulation and blood viscosity (Danesh et al. 1998). It is well known to be a co-factor for platelet aggregation and is included in growth factor activity that may play a role in the early stage of atherosclerosis (Ernst 1994). Furthermore, elevated fibrinogen levels have also been correlated with other coronary atherosclerosis risk factor, as well as dyslipidemia.

Plasminogen activator inhibitor type1 has been associated with increased coronary atherosclerosis risk, including elevated levels of triglycerides, insulin resistance, and

elevated blood pressure (Holvoet and Collen 1997). The endothelial-mediated balance between procoagulatant and fibrinolytic activity is disrupted when the endothelium is dysfunctional and is associated with an elevated production of plasminogen inhibitor type-I coupled with a reduced in plasminogen activator. Plasminogen activator inhibitor type-I interfere with the formation of plasmin from its precursors and therefore give to a potential hypercoagulable state (Buja 2000).

High levels of total homocysteine (Hcy) are also correlated with increased risk for elevated levels of coagulant factors, myocardial infarction and vascular disease (Kuller and Evans 1998). However, the mechanism behind increased levels of Hcy related with coagulants and development of CHD is not yet clears (Mayer et al. 1996).

2.4 RISK FACTORS FOR CORONARY HEART DISEASE

The definition of a risk factor

The unfolding of the idea of "*risk factor*" and its associations to the occurrence of CHD evolved from prospective epidemiological studies in developed communities (Chetlin et al. 1993). These studies interpreted a consistent association among characteristics noticed at one point in time in evidently healthy individuals with the subsequent incidence of CHD in those individuals (Wilhelmsen and Marmot 1996).

It is should be noted, however, that the presence of a risk factor does not necessarily show a direct causal relationship to the disease (Wilhelmsen and Marmot 1996). In most instances, a risk factor is the feature that predicts the risk of development of clinically significant disease within a society. In some instances, it may be involved

in the causation of the disease; however, to validate the latter requires a proven epidemiological association that is statistically valid. The risk factor concept is very useful because it permits one to assess the importance not only of the mentioned risk factors but also of genetic traits in given individuals, such as a family history of premature CHD. Using such information, one may ask whether modification of a given risk factor will result in modification of the risk of a particular disease (Chetlin et al. 1993, Wilhelmsen and Marmot 1996).

The term "risk factor" can be defined in different ways, but the simplest and most commonly used definition by epidemiologists is a factor that is related to the increased risk of suffering from the disease in the future without necessarily implying a direct causal relationship between the factor and the disease. A risk factor may be a causative agent but it is not necessary one, and risk can be either an inborn attribute or an acquired one. The risk factor should be present before the disease (Chetlin et al. 1993, Wilhelmsen and Marmot 1996).

Different personal characteristics and environmental factors have been revealed that appear to play causative roles in making individuals more susceptible to CHD. These factors are categorised in three different groups: *physiological;* factors influenced by lifestyle and inheritance, *modifiable;* factors related with lifestyle, and *non-modifiable;* background factors. Non-modifiable factors are age, heredity, sex, and race or ethnicity. The modifiable factors include: physical inactivity, diet, alcohol use, smoking and psychological stress. Physiological factors are plasma lipids: total cholesterol, total triglycerides, low density lipoproteins, high density lipoproteins, apolipoprotein A and B, plasma homocysteine, plasma antioxidants, blood pressure,

obesity, diabetes mellitus and metabolic syndrome (Wilhelmsen and Marmot 1996, Farmer and Gotto 1998 and 2000).

Interaction of risk factors

It is not easy to determine the importance of any single CHD risk factor in comparison to any other due to their being interrelated (Wilhelmsen and Marmot 1996, Farmer and Gotto 1998). Consequently, the risk of CHD cannot be predicted from a single factor. CHD is a multi-factorial disease that occurs out of different combinations of risk factors. The combinations of risk factors in CHD can be especially atherogenic and these interactions may explain some of the observed anomalies in cross-cultural comparisons (Ashwell 1997).

Epidemiological studies have provided evidence that there is a synergism between the CHD risk factors. For example, blood lipid abnormalities, diabetes, heredity, and obesity often go hand in hand. Studies reveal for example males living in Ireland eat more saturated fat than their cousins do in USA, yet the former had a much lower incidence of CHD risk factors (Rivere 1989). This is due to being more physically active. The same findings have been revealed in the Masai Tribe in East Africa (Mann et al. 1965). These people have a diet with high saturated fat from cow and goat products but they also have a high degree of physical activity and physical fitness. This is also the case with labourers in the state of Georgia, USA. Each of these groups had a low incidence of CHD (McDonough et al. 1965). Their higher level of physical activity protects them from acquiring CHD. Another example is insulin resistance syndrome, the condition that has been described as span "Syndrome X". Hypertension, non-insulin-dependent diabetes and obesity occur

together with greater than chance frequency. Insulin resistance has been found in all three conditions and is related with an adverse lipid profile (low high-density lipoprotein (HDL) cholesterol and high triglycerides) and increased risk of CHD. The obesity in this syndrome is characterised by a central fat distribution with an increased waist-hip ratio. Insulin resistance denotes an elevated requirement of insulin to maintain normoglycaemia. The impact is relative hyperinsulinaemia. This hyperinsulinaemia may be an etiological factor in hypertension or a marker consequent to a linked cellular abnormality. A high insulin level in the blood circulation is atherogenic and may act as an independent risk factor for CHD (Chetlin et al. 1993). Thus, the presence of simultaneous risk factors increases the onset of disease more than would be expected from the sum of the risk factors. The more the exposure to risk factors the higher the chance of CHD development. However, the mechanism by which these risk factors operate to enhance the development is not precisely known (Chetlin et al. 1993, Wilhelmsen and Marmot 1996).

2.5 DIFFERENT CATEGORIES OF CHD RISK FACTORS

In this chapter, the traditional CHD risk factors and their relationship to physical activity will be reviewed as follows: (1) Non-modifiable risk factors: *age, female-male differences, inherited factors, and ethnic differences,* (2) Modifiable risk factors (predominantly lifestyle-related risk factors): *diet factors, alcohol consumption, coffee, cigarette smoking, psychosocial and behavioural factors*, and (3) Risk factors influenced both by lifestyle and inheritance: *obesity, blood pressure, serum lipids, clotting factors, homocysteine, albumin, diabetes mellitus and metabolic syndrome* will be described and discussed

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Non-modifiable risk factors

Age

Coronary atherosclerosis, CHD incidence and mortality are more common with advanced age. Investigators have found that the incidence and prevalence of CHD increase with age, consequently age may be mentioned as one of the strongest CHD risk factors (Lakkatta 1993 and 1993, Wilhelmsen and Marmot 1996). Although, it is more difficult to determine whether ageing itself acts as a pathogenic mechanism, as seems likely, age increases the impact of other risk factors because the pathogenic effect on CHD takes longer to operate (Wilhelmsen and Marmot 1996). In addition, it has also been found to be more difficult to separate ageing influences from some lifestyle behaviours such as physical activity, smoking, and personal characteristics related with CHD (Gerstenblit and Lakatta 2000). The interaction among these may have anatomical and physiological major consequences on the cardiovascular system and may alter the manifestation of pure ageing effects on that system (Gerstenblit and Lakatta 2000).

It has been shown that, from the ages of 34-44 to 55-64 there is about a 15-fold increase in CHD mortality among males and about a 30-fold increase in females, and consequently the ratio between females and males decreases with advancing age (Wilhelmsen and Marmot 1996). CHD is the leading cause of death among males by their 4th decade of life and among females by their 6th and 7th decades (Wilhelmsen and Marmot 1996, Farmer and Gotto 1998 and 2000). Since this proportion increases from 64 to 85 years of age CHD mortality and morbidity will continue to increase in older males and females (Farmer and Gotto 1998). The Framingham Study has also shown that many of the major CHD risk factors such as low levels of high-density

lipoprotein cholesterol (HDL-c) and high levels of low-density lipoprotein cholesterol (LDL-c) and triglycerides, obesity, high blood pressure, diabetes mellitus, and left ventricular hypertrophy, are operative in the old aged groups, but not smoking (Wilhelmsen and Marmot 1996).

Genetic Factors

It is well known that CHD tends to run in families. It has been reported that, the close relatives of patients with CHD have a 5 to 7 fold risk of eventually dying from heart disease. They are also more likely than relatives of healthy people to show signs of arterial disease even before they develop symptoms (Wilhelmsen 1990, Superko 1997). In addition, different studies, both case-control and prospective studies, have pointed to familial inheritance of CHD risk factors, including cholesterol, lipoproteins, blood pressure, diabetes mellitus, and obesity (Wilhelmsen and Marmot 1996).

The relationships and interaction of genetic and environmental causes of CHD risk are very complicated to distinguish (Fleinleib 1983). A population predisposition to hypertension or hypercholesterolemia may be determined by its intake of salt and saturated fat (Wilhelmsen and Marmot 1996). The family at high risk of developing CHD often has at least one member who has hyperlipidemia, low HDL-c, hypertension, a positive family history of CHD, or a positive family history of premature CHD (Wilhelmsen 1990). Familial-aggregation studies, and genetic studies, have provided evidence that children born to families with a high prevalence of these risk factors also are at high risk of developing CHD (Wilhelmsen 1990, Wilhelmsen and Marmot 1996, Farmer and Gotto 1998 and 2000). Becker et al.

(1988), in a study of siblings, also found that 48% of the brothers and 41% of the sisters were hypertensive, and 45% of the brothers and 22% of the sisters had lipid abnormalities. There were also high percentages of cigarette smoking and diabetes mellitus. Therefore, gathering of risk factors frequently co-existed in the siblings, and seemed to be a high degree of modifiable risk factors in the families of a member affected by premature atherosclerosis (Farmer and Gotto 1998).

Inheritance of the atherogenic lipoprotein pattern associated with LDL has been established (Superko 1997). Family-inherited hypercholesterolemia is well known to have a strong association with premature atherosclerosis (Superko 1997, Farmer and Gotto 1998). In familial hypercholesterolemia clinical evidence of atherosclerosis includes myocardial infarction and severe coronary atherosclerosis, and aortic stenosis may occur in the first decade of life (Farmer and Gotto 1998 and 2000). The primary genetic defect in familial hypercholesterolemia has shown to be an autosomal dominant disorder caused by a mutant in the LDL receptor gene (Superko 1997). LDL production is increased whereas the cells ability to recognise and take up LDL from the blood is decreased. Also, the production of LDL may be increased due to a decrease in IDL removal by the liver and enhanced conversion to LDL. The resulting high levels of blood cholesterol predispose an individual to develop atherosclerosis prematurely and most die of heart attacks at an early age resulting from CHD (Farmer and Gotto 1998 and 2000). Another inheritance for the atherogenic hypercholesterolemia is familial combined hyperlipidemia. It is also associated with an increased risk of premature atherosclerosis and CHD.

Ethnic Differences

Limited data exist regarding risk factors for CHD as well as incidence rates and mortality in various races. Even though the genetic background regarding major risk factors such as lipid abnormalities, coagulation abnormalities and blood pressure have not yet been fully investigated, and the evidence suggests that no racial group is immune to CHD (Farmer and Gotto 1998). Some genetic hyperlipidaemia does occur with greater frequency in certain racial groups, but these abnormalities generally make a very small contribution to the overall risk of CHD in any community (Wilhelmsen and Marmot 1996). Migration studies and time trends, as previously reported, have made it clear that environmental factors such as diet and cigarette smoking are all closely associated with changes in the incidence of CHD. Studies of Japanese subjects in Japan, Hawaii and the USA are good examples of such environmental effects (Marmot et al. 1975).

It has been documented that Asian immigrants to the UK appear to have a higher incidence of CHD than British-born people (McKeigue et al. 1989 and 1991). Up to now, available evidence on risk factors status suggests that the established risk factors do not adequately explain this excess rate. Cigarette smoking rates are lower in Asian males and very low in Asian females. Blood pressure is not higher and their diet is not especially high in saturated fats. However, non-insulin-dependent diabetes mellitus (NIDDM) plays a greater role than in many other populations. The prevalence of this type of diabetes mellitus in some Asian communities in London has been shown to be four times the national average (Woods et al. 1989, McKeigue et al. 1991). Furthermore, another feature, which was present among Asian immigrants in the UK was central obesity and metabolic syndrome characteristically

thought to be associated with insulin resistance. Psychosocial factors relating to the stress and adaptation to a westernized lifestyle may also play a major role (McKeigue et al. 1991).

Gender and Sex Differences

The incidence of CHD has been shown to be higher among males than females for most age groups, and in the age group 50-59 it is about five times as common among males as to females (Wilhelmsen and Marmot 1996, Ashwell 1997). However, while the relative difference declines, the absolute difference in CHD rates between females and males increases with increasing age (Wilhelmsen and Marmot 1996, Khaw 1997). Although CHD levels are lower in post-menopausal females than in age-matched males, angina pectoris seems to be more common in females (Khaw 1997). The claimed protection of females from CHD becomes less evident in their post-menopausal years, when the CHD rates for males and females equalize (Wilhelmsen and Marmot 1996, Khaw 1997). The process of atherosclerosis does not appear to differ between females and males and the risk factors correlated with the development of CHD seems to affect both sexes equally (Farmer and Gotto 1998).

The difference in prevalence rates of coronary CHD between females and males seems to be related to the hormonal functions of oestrogen and androgenic hormones (Khaw 1997). Oestrogen has an anti-proliferative effect on smooth muscle cells, protective to the endothelium, and capable of modulating acetylcholine-mediated dilation of atherosclerotic coronary arteries (Williams et al. 1994, Ross 1997).

The pre-menopausal females have low levels of triglycerides, cholesterol, LDL-c and high levels of HDL-c (Farmer and Gotto 1998). In fact, HDL-c levels are almost the

same in males and females until puberty, when they drop in the males as a result of the androgenic effect of testosterone (Khaw 1997). In females who undergo natural menopause, serum levels of HDL gradually decline and the total serum cholesterol, triglycerides and LDL levels gradually also rise as a predisposition to coronary atherosclerosis (Farmer and Gotto 1998).

The effects of oral contraceptives have been known to increase risk of venous thrombosis and cerebral vascular disease as well as CHD (Khaw 1997). Longitudinal studies and case-control have also demonstrated that the use of oral contraceptives increases the risk of CHD, especially myocardial infarction (Wilhelmsen and Marmot 1996). However, the impact on risk from the use of oral contraceptives seems to be low, but increases by the accompanying use of tobacco products (Wilhelmsen and Marmot 1996).

Modifiable risk factors (Predominantly lifestyle-related risk factors)

Eating Behaviour

In western societies, the relationship between daily diets, particularly high-unsaturated fat intake and CHD has been confirmed by several epidemiological investigations (Bouchard et al. 1990). Likewise, diet plays an important role in modifying the risk factors for CHD (Krisnamoorthy 1999). With continuing industrialization daily diet changes occurred, concomitant with increasing morbidity and mortality in western as well as developing populations (Ashwell 1997, Walker et al. 2002). The effect of increased industrialization is the globalization of food production and marketing of energy dense food. One particular feature is the

production of refined food, poor in dietary fibre and several micronutrients. Daily over-consumption of diets high in saturated fat, and refined food low in fiber such as sugar and white bread, which would lead to obesity, glucose intolerance, hypertension, and hyperlipidaemia and CVD, especial CHD, in later life.

Furthermore, the habitual diet patterns are different from culture to culture depending on differences in agricultural and in food production. When people migrate from one place to another they soon adopt the diet of the new place and change their traditional eating behaviour (Bouchard et al. 1990).

Fat intake

Dietary fat has been documented to play a major role in the atherosclerosis process (Yu-Poth et al. 1999). It seems to facilitate the development of CHD by influencing cholesterol synthesis (Drevon 1999). Independently, the percentage of daily energy intake coming from saturated fat, and amounts of cholesterol in the diet have been associated with CHD occurrence in different populations (Hegsted et al. 1993, Ashwell 1997).

Saturated fat diet has been associated with blood total cholesterol (TC), but the influence on TC concentration in human is different. Some people appear to respond to dietary cholesterol with a significant increase (Hegsted et al. 1993), while others respond weakly, or not at all (Ashwell 1997). Also, it has been detected that countries with a high average of saturated fat intake tend to have high rate of CHD (Ashwell 1997). People who migrate from countries where saturated fat intake and serum LDL-c are low to countries where saturated fat intake is high also show an increase in LDL-c. This was confirmed in a study of Japanese immigrants to USA,

which, showed that they changed their customary diet to that of high fat and as a result increased their serum TC concentration levels (Davidson et al. 1975).

The difference in the incidence of CHD and serum TC concentration levels between populations have been shown to be associated with differences in lifestyles, including fat diet intake, and with genetic factors (WHO`s Study Group 1990, Ashwell 1997). Thus the distribution of these factors in different populations is likely to be of importance for CHD (Wilhelmsen and Marmot 1996). In addition, serum TC, LDL-c, and HDL-c concentration levels can be manipulated by changes in the type and amount of fat in the diet. A diet high in saturated fats has a tendency of raising TC, and polyunsaturated fats have a tendency to lower the serum TC concentration levels (Wilhelmsen and Marmot 1996, Ashwell 1997). Several studies have focused on the effects of different diets on CHD risk and LDL-c concentration levels. In a study comprising five countries, it was shown that high concentration of serum TC and LDL-c levels were due to increased production of LDL-c combined with slow catabolism contributing to their maintenance (ICSG 1986). Low serum TC and LDL-c levels were due to decreased production of LDL-c and more rapid catabolism.

Carbohydrate intake

A diet high in carbohydrate intake has been recognised to elevate plasma TG concentration (Liu et al. 1984, McLaughlin et al. 2000). It has been suggested that high carbohydrate intake may provoke insulin resistance in diabetes mellitus type II (NIDDM) and CHD (Ashwell 1997). This is due to that, when carbohydrates represent a very large proportion of energy intake and intake exceeds overall energy

expenditure, an increase in body lipid is bound to occur. Daily carbohydrate intake must be adequate to maintain the body`s relatively limited store. Once the capacity of the cell for glycogen storage is reached, excess sugar is coverted to and stored as lipid. Resistance to the action of circulating insulin may play a role in the dyslipidaemia of diabetes. Insulin normally suppresses plasma concentration of free fatty acid, and in insulin-resistance syndrome, the decreased suppression results in an increase in circulating levels of freee fatty acids, which in turn stimulates triglyceride synthesis as a result of increased small, dense LDL particles which occurs in conjuction with decreased HDL-c (Farmer and Gott 2000). In contrast, as reported by Bjørneboe and Aarsland (1999), and many epidemiological studies have suggested that people who consume high carbohydrate diet have a low occurrence of diabetes mellitus type II and CHD, compared with people who consume diets low in carbohydrates and high in saturated fat. That type of diet reduces the blood concentration of small, dense LDL particles, and does not provoke insulin resistance.

Salt intake

Salt intake has been recognized to influence blood pressure. Sodium is essential for the maintenance of normal blood volume and blood pressure. Sodium in the diet tends to come less from sodium naturally present in foods, and more from salt added to food during processing or the addition of salt to foods (Ashwell 1997, Waeber et al. 2000).

High dietary sodium intake has been associated with increased incidence of CHD risk factors especially in blood pressure, but the association is somehow controversial (Muntzel and Drucke 1992). The effect of dietary sodium chloride on

high blood pressure is usually assumed by looking at average salt intakes in different countries (BNF 1994, Waeber et al. 2000). This has shown a strong association between high blood pressure and high sodium intake, and low blood pressure and low salt intake (Ashwell 1997). However, assessing high blood pressure and the sodium dietary intake of individuals within populations does not show a significant association (BNF 1994). Migration has also been associated with dietary sodium intake and to increase in blood pressure (Waeber et al. 2000). This could explain why people migrating from a low sodium intake country where blood pressure is low to a high sodium intake country adopt the diet behaviour of the new place and show an increase in blood pressure (Waeber et al. 2000). In contrast, many studies have not found any close relationship between dietary sodium intake and blood pressure (The INTERSALT study 1988, Law et al. 1991). The INTERSALT study (1988) showed that the average systolic blood pressure would rise by 2-3 mmHg for every 100mmol increase in daily sodium intake. Likewise, in a meta-analysis study it was estimated that the average systolic blood pressure would rise by 5-10 mmHg, for every 100-mmol sodium intake, though it is dependant on age (Law et al. 1991).

Furthermore, the ratio of sodium to potassium in the diet has been shown to be more important than either sodium or potassium only in determining blood pressure. Thus, an increase of 50% in potassium consumption could lead to a decrease of about 1.6 mmHg of systolic blood pressure (INTERSALT study 1988). In USA, high blood pressure is more prevalent among the black than white populations. This could be explained, in part, by black people lower intake of potassium than whites (Waeber et al. 2000).

Fruits and vegetables

Fruits and vegetables are main sources of antioxidants, which include vitamins E and C, carotenoids and flavonoids (Ashwell 1997). Individuals who consume higher amounts of fruits and vegetables have lower rate of CHD risk (Gaziano 1999). The mechanism behind antioxidants in protecting CHD risk is probably by increasing peroxidation and susceptibility of LDL-c to oxidation modification (Ashwell 1997, Delport et al. 1998).

An inverse relation between vitamin E intake and CHD events has been suggested (Rimm et al. 1993, Stampfer et al. 1993). For example, a cross-sectional study done by Gey et al. (1991), in different towns in Europe, showed that high concentration of vitamin E in the blood was associated with decrease of CHD death rate in the different populations. The population with the lowest rate of CHD attained the highest levels of plasma vitamin E.

Vitamin C, carotenoids and flavonoids supplements have not been found to provide any protective effect on CHD (Rimm et al. 1993, Stampfer et al. 1993, Delport et al. 1998). However, the study of Delport et al. (1998) showed that vitamin A, C and E were decreased in CHD patients. After other CHD risk factors were adjusted, for β carotene and vitamin D concentrations were associated independently with increased CHD risk. The uses of antioxidant vitamin supplements to reduce CHD risk are still not recommended to because of insufficient data supporting their cardiovascular benefits (Ashwell 1997).

Alcohol Consumption

Many of studies examined the association of alcohol use with CHD have suggested either a negative or a J-U-shape relationship (Marmot et al. 1981, Shaper et al. 1988, Wannamethee and Shaper 1997, and 1999, Shaper and Wannamethee 2000). Despite the facts that chronic alcoholics tend to die suddenly, alcohol is known to have beneficial effects on lipoprotein metabolism when consumed in moderate doses. Epidemiologic studies convincingly demonstrate a reduction in the risk of CHD especially myocardial infarction among moderate drinkers compared with nondrinkers, even when other risk factors are adjusted. This protective effect of alcohol applies only to moderate consumption, as heavy drinkers have an increased riks of CHD, laeding to a so-called J-shaped mortality curve (Eichhorn and Graybun 2000). The mechanism by which modearate alcohol consumption (1-2 drinks per ay) protects against CHD is not fully understood. However, alcohol in moderate doses, the majority red wine has been associated with decrease of CHD risk by increasing HDL-c and apoliprotein A-1 (Ashwell 1997). It might have phenolic substances with antioxidative properties inhibitive of LDL oxidation (Frankel et al. 1993). (The antagonism mechanism between HDL-c and LDL-c is further discussed on page 56-58). All these mechanisms may help to explain the "French paradox" with reference to lower than expected incidence of CHD in the French population, in relation to their intake of high saturated fat (Frankel et al. 1993, Ashwell 1997). Despite that the mean plasma HDL-c level in the France is similar to that in other countries having a diet fairly high on saturated fat (Renaud and de Lorgeril 1992). The positive mechanisms of alcohol intake, especially red wine, in the French population are also believed to include the inhibitory effect of platelet aggregation and the antioxidant

effects of red wine (Renaud and de Lorgeril 1992, Frank et al. 1993, Belleville 2002).

Alcohol abuse and its toxic effects are major problems all over the world (Roberts 1995, Regan 1998). The damage to health caused by chronic alcohol consumption is evident, and has major consequences both for the individuals and society (Eichhorn and Grayburn 2000). Abuse and prolonged use of alcohol affects many vital organs and may causes various chronic diseases such as liver diseases, cancer, osteoporosis and cardiovascular disease such as CHD, haemorrhagic stroke, congestive cardiomyopathy, systemic hypertension and neuromyopathy (Marmot and Brunner 1991, Williams et al. 1994, Nachahal et al. 2000). In contrast to the negative effects of excessive alcohol use, regular moderate use of alcohol has been suggested to have various health benefits (Eichhorn and Grayburn 2000). Large clinical studies, have found that habitual moderate consumption of alcohol has a positive influence on overall mortality and can significantly reduce both primary and secondary incidence and mortality of CHD (Williams et al. 1994, Gronbæk et al. 2000). The habitual consumption of small amounts of alcohol may be healthy but occasional large amounts or binge consumption of alcohol is negative (Ajani et al. 2000, Meister et al. 2000, Solomon et al. 2000).

Alcohol consumption and blood lipids

Moderate alcohol consumption (e.g. 1 to 2 glasses of red wine) has been related to a reduced risk of CHD, through its effects on the metabolism of plasma lipoprotein (Eichhorn and Grayburn 2000). It serves as a substrate for lipoprotein triglyceride synthesis, changes synthesis of apoproteins, and affects the activity of the key

enzymes of lipoprotein metabolism, specifically lipoprotein lipase and hepatic lipase, and cholesterol ester transfer protein (Fuhrman et al. 1995, Froehlich 1996). In addition, moderate alcohol intake has been shown to increase levels of high HDL-c and apoprotein A-1 (Eichhorn and Grayburn 2000). These two types of lipids tend to reverse cholesterol transport from tissue to the liver for metabolism. This could be the mechanism behind alcohol in moderate doses protecting against CHD (Hojnacki et al., 1991).

On other hand, both high and low doses of alcohol have been shown to increase LDL-c. Veenstra et al. (1990) and Steinberg et al. (1991) reported that regular heavy alcohol use was associated with high levels of LDL-c and liver damage, resulting in low levels of HDL-c. In contrast Williams (1994), and Bönaa and Thele (1991) found that, low to moderate alcohol consumption increases HDL-c. Alcohol intake may also reduce hepatic endothelial lipase (HL), which is inversely related to HDL-c (Hartung et al. 1983). Additionally, Hartung and coworkers also found an increase in the adipose tissue lipoprotein lipase (LPL-A) along with increased alcohol intake, which has been controversial.

Alcohol consumption and blood coagulation

Several epidemiological studies have indicated that moderate alcohol consumption reduces the risk of CHD by inhibiting thrombosis (Eichhorn and Grayburn 2000, Mukamal et al. 2001). This may be mediated by increasing fibrinolysis of endothelial cells (ECs) synthesis of plasminogen activators, tissue-type plasminogen activator (t-PA), increasing fibrinolytic activity, and inhibiting platelet aggregation (Renaud and

de Lorgeril 1992, Hendriks and van der Gaag 1998, Tabengwa et al. 2000, van de Wiel et a. 2001).

Alcohol consumption and blood pressure

Heavy alcohol consumption increases blood pressure and death from stroke (Horan and Lenfant 1990, Thu et al. 1997, Ashwell 1997, Waeber et al. 2000). It has been reported that excessive alcohol consumption was responsible for 5 to 10 % of the hypertensive males in the US (Kaplan 2000). According to the review by McMahon (1987), the negative effects of alcohol seem to be evident when average daily consumption is greater than 2 drinks (equivalent of 1 ounce of ethanol). Furthermore, decrease of blood pressure has been shown when consuming not more than 2 drinks per day when compared with those who drank more (Rimm et al. 1993). Alcohol changes cell membranes, by allowing more calcium to enter, perhaps by inhibition of sodium transport (Hammet et al. 1991).

Alcohol intake and diabetes mellitus

Habitual excessive alcohol consumption has been recognised to be one cause of diabetes mellitus type II among males (Holbrook 1990, Williams 1994). A study done by Wei et al. (2000) showed an increased risk of developing type II diabetes mellitus in male high alcohol consumers, when compared with those who reported moderate alcohol intake. Moderate alcohol consumption has also been recognised as being associated with an increase of insulin resistance (Kornhuber et al. 1990). On another hand, moderate alcohol consumption is associated with reduced CHD risk in diabetic patients (Solomon et al. 2000).

Alcohol consumption and blood homocysteine

Moderate alcohol consumption is related to lower homocysteine (Hcy) values (Ueland et al. 2001). It has showed that chronic high alcohol consumption increased the level of Hcy (Hurtberg et al. 1993a, Cravo et al. 1996), and decreased vitamin B_6, and folate concentrations (Cravol et al. 1996 and 1997). This was associated with gastrointestinal disturbances that may result in decreased absorption of vitamins, which would contribute to high levels of total homocysteine.

Coffee Intake

Coffee consumption has been associated with CHD events (Rosmarin 1989, Thelle 1991 and 1995, Wilhelmsen and Marmot 1996). Both prospective and case-control studies have reported different outcomes. In a study conducted in Norway, a strong relationship was found between coffee intake and increase in CHD death (Tverdal et al. 1990). In contrast other studies have revealed modest (Klatsky et al., 1990 and 1993, Stensvold and Tverdal 1996), or no effect of coffee consumption on increased risk of CHD or death (Grobbee et al. 1990, Rosengren and Wilhelmsen 1991, Kawachi et al. 1994, Kleemola et al. 2000). The methods used for preparing coffee seem to be of importance for the relation between coffee consumption and CHD. By comparing studies done in Finland, Norway and Sweden (Tverdal et al. 1990, Rosengren and Wilhelmsen 1991), it was discovered that filtered coffee commonly used in Swedish did not affect the serum TC concentration levels. In contrast the boiled coffee consumed in Norway, appeared to affect serum TC concentration levels.

Coffee intake and blood homocysteine

High coffee consumption has been related to increased levels of homocysteine (Hcy). Thus, a study conducted among Norwegians, demonstrated that high or moderate consumption of coffee elevated Hcy levels (Nygård et al. 1995). Correspondingly, coffee drinking was related to smoking and low intake of fruit and vegetables (Jacobsen and Thele 1987). However, the correlation between coffee consumption and Hcy was still highly significant after adjustment for these confounding variables.

Tobacco Use

Cigarette smoking is the leading preventable cause of CHD death in developed countries (WHO, Tobacco or Health 1996). It has been observed that, rates of hospital admission are twice as high among smokers as among non-smokers in developed societies (Vaillant et al. 1991, Blomhoff and Ekblad 1995). While cigarette smoking shows a declining trend in western countries, it is increasing in developing countries (Muna 1993, Walker and Sareli 1997a,b, Walker et al. 2001). Overall, however, world tobacco consumption is increasing (Chollat-Traquet et al. 1993). Cigarette smoking is addictive. Nicotine elicits a psychological state of alertness and relaxation. These facts are the basic reasons why individuals keep on smoking (Williams 1994). Smoking causes a remarkable disability burden on many populations in developed societies (Vaillant et al. 1991, Blomhoff and Ekblad 1995). In terms of health status, the more an individual smokes the less healthy he or she is likely to be in the future (Novello 1990, Williams 1994).

Cigarette smoking and atherosclerosis

Tobacco products accelerate the process of atherosclerosis in CHD by different mechanisms (Lloyd-Jones and Kannel 2000). Inhalation of cigarette smoke has been

suggested to result in the exposure of arterial cells to free radicals and result in the stimulation of their proliferation (Oates et al. 2000). It has been shown that cessation of cigarette smoking decreases the risk for development of the clinical sequelae of arteriosclerosis, and possibly a sign of regression of lesions (Tsevat et al. 1991). Identified agents derived from cigarette smoke have been found to be injurious to the arterial wall (Lloyd-Jones and Kannel 2000, Oates et al. 2000). Cigarette smoking provides presumably the strongest and most consistent correlation with the increased incidence of atherosclerotic disease and appears to be a major contributor to increased risk of disease, in association with other CHD risk factors (Maron et al. 1998).

Cigarette smoking and lipid profiles

Cigarette smoking has been related with lipid abnormalities that may contribute to the development of arteriosclerosis in CHD (Duthie et al. 1993). It has been found that smokers have increased levels of oxidation products, including oxidised LDL-c (Morrow et al. 1995). Compared with non-smokers, especially heavy smokers have lower levels of HDL-c and high levels of LDL-c and triglycerides (Brockie et al. 1990, Handa et al. 1990, Farmer and Gotto 1998). Cigarette smoking has been found to affect HDL-c metabolism and structure, by modifying the activity of LCAT (Williams 1994). Furthermore, cigarette smoking has been found to affect plasma apo A-I and apo A-II, which are believed to change the function of HDL-c (Oates et al. 2000). By considering the cardioprotective effect of HDL-c, these changes may provide a mechanism by which cigarette smoke increases the risk for CHD. These effects, along with direct effects of carbon monoxide and nicotine, possibly produce endothelial function damage, and vascular reactivity. However, the real mechanism

by which smoking alters the lipid profile is still unclear (Pittilo et al. 1990, Celermajer et al. 1996).

Cigarette smoking and blood pressure

Cigarette smoking and also use of other tobacco productions have been suggested to have a detrimental effect on coronary flow by increasing vasospasm and vasoconstriction (Zeiher et al. 1991, Campisi et al. 1998, Oates et al. 2000). In particular, the acute inhalation of tobacco smoke is associated with a rise in blood pressure (Trap-Jensen 1988). However, several epidemiological studies have shown that chronic smokers tend to have lower blood pressure than non-smokers, an effect possibly due to lower body weight (Green et al. 1986).

Cigarette smoking and blood homeostasis

The inhalation of cigarette smoke exerts many effects on blood clotting factors, platelet function, and other homeostasis parameters as a result of a hyper-coagulable state (Folsom et al. 1991, de Maat et al. 1996, Oates et al. 2000). These homeostatic changes involve an increase in fibrinogen, red blood cells mass, and platelet activation with thromboxane A, and impaired tissue plasminogen activator release from endothelia cells (Benowitz et al. 1993, Newby et al. 1999). This may play a major role in the etherosclerotic process by injuring the endothelium (Oates et al. 2000).

Cigarette smoking and blood homocysteine

A number of studies among adults in Norway conducted by Nygård et al. (1995) have shown elevated levels of Hcy values due to cigarette smoking. The number of cigarettes smoked per day was the major cause of Hcy levels. In both sexes the Hcy

increased according to the number of cigarette smoked per day. The mechanism behind cigarette smoking in increasing levels of Hcy has been suggested to be methylation reactions influenced by nicotine (Godin and Crook 1986), or could be an enzyme activity in the liver by polycyclic aromatic hydrocarbons, and increased catabolism of folate (Bolander-Gouaille 1999). In several studies, decreased levels plasma folate and vitamin B-12 concentrations have also been observed in cigarette smokers (Vermaark et al. 1990, Piyathilake et al. 1994, Mansoor et al. 1997). In addition, it has been found an interaction between nitrous compounds from the smoke and methionine synthase (Bolander-Gouaille 1999).

Cigarette smoking related to CHD

Cigarette smoking remains a major independent risk factor for the development of CHD, which may be magnified by the presence of other risk factors (Farmer et al. 1992, Chetlin et al. 1993, Wilhelmsen and Marmot 1996, Lloyd-Jones and Kannel 2000, Oates et al. 2000). For example in Japan, where there is a very high rate of cigarette smoking, there is a low rate of CHD, which is most likely due to low serum cholesterol levels (Wilhelmsen and Marmot 1996). It has been suggested that regular smoking of only 1-4 cigarettes per day confer a substantial increase in risk of CHD in middle-aged males (Rosengren et al. 1992). Studies world-wide have shown that males have a higher smoking rate than females, and from 1 to 2.5 times the mortality rate from CHD of non-smokers (Davidson et al. 1975, Muna 1993, Wilhelmsen and Marmort 1996).

The nicotine is absorbed through the lung alveoli, and is rapidly transported to the brain where it acts on neurotransmitters (Oates et al. 2000). Nicotine acts as an

agonist for the adrenergic nervous system and causes increased plasma norepinephrine release (McGill 1990). Thus, it increases of coronary tone and enhances vasoconstriction (Davidson et al. 1975, McGill 1990). The enhanced vasoconstriction may result in an imbalance between oxygen supply and demand. This may increase the risk of myocardial infarction (Deanfield et al. 1986). Several studies have shown that smokers have higher risk of CHD than non-smokers (Lam et al. 1997, Oates et al. 2000). In the Framingham Study, those who stopped smoking had a reduction of myocardial infarction risk after 2 years (Kannel 1978). However, another study has shown that males who have given up smoking for over 20 years still had e an increased risk for CHD (Cook et al. 1986). Even light or non-smokers may be exposed to increased risk by passive smoking (Glantz and Parmley 1991). Passive cigarette smoking has also been demonstrated to increase the risk of CHD (Glantz and Parmley 1995, Steenland et al. 1996, Kawachi et al. 1997). The mechanism behind passive cigarette smoking and increase in the risk for CHD is probably the same as for active smokers (Celemajer et al. 1996, Roberts et al. 1996, Neufeld et al. 1997, Hausberg et al. 1997, Valkonen and Kuusi 1998).

The risks for developing CHD from smoking pipes and cigars are substantially lower than those from smoking cigarettes, probably because of the fact that most pipe and cigar smokers do not inhale (Dep. Health Hum Service publication 1983). The use of smokeless tobacco, whether chewing or snuffing, seems to have equal and comparable adverse effects on lipid profiles, thereby increasing CHD risk. Additionally, chronic elevation of blood pressure due to smokeless tobacco has been found (Maron et al. 1998).

Psycho-Social Factors

Psychological stress, emotional distress and strain are more frequent in developed countries (Chetlin et al. 1993). Evidence has documented many of the profound interrelationships of the brain and stress and confirmed the association between emotions and some illnesses, including CHD, particularly sudden death (Jiang et al. 1996, Eliot et al. 1998). However, the role of psychological stress as a risk factor for CHD remains unclear (Farmer and Gotto 2000). The type A behaviour, as explained later, has been proposed to be one of the psycho-social risk factors for CHD, including, reduced social support and isolation, lower socio-economic status and depression (Jonston 1993, Wilhelmsen and Marmot 1996, Eliot et al. 1998).

Effects of psychosocial factors and CHD

The sympathetic nervous system (SNS) function has been found to be the major mechanism associated with psychosocial factors, which may increase the risk of CHD (Wilhelmsen and Marmot 1996, Eliot et al. 1998, Farmer and Gotto 1998). An imbalance between SNS mediated release of catecholamine and an acute increase in blood pressure has been detected to play a major role in CHD occurrence (Eliot et al. 1998). For example, Veith et al. (19942) demonstrated an increase of SNS outflow in patients with serious depression compared to non-depressed controls. (Fleming 1982) also discovered increased urinary catecholamine excretion among individuals with lower levels of social support than among others with higher levels of support. Suarez and Williams (1989) found an increase of SNS outflow accompanied by increased catecholamine excretion among individuals with high hostility scores (Eliot et al. 1998). In addition, it has been postulated that long term increased SNS tone may increase myocardial electrical instability, platelet activation, and

myocardial workload, possibly precipitating coronary atherosclerosis and acute CHD occurrence (Eliot et al. 1998). Individuals with either serious depression or high hostility behaviour, associated with CHD, have often been recognized to have an inclination for cigarette smoking, coffee and alcohol consumption (Eliot et al. 1998).

Personality variations influence on CHD

Personality traits are relatively stable personal characteristics that predispose a person to think and behave in certain ways in given situations (Eliot et al. 1998). The type A, known also as CHD-prone behaviour has been clinically diagnosed in individuals with a strong sense of time urgency, hostility, competitiveness, ambitiousness, and constant struggle with their environment, as well as chronic impatience (Farmer and Gotto 1998). In contrast Type B behaviour is described as having greater passivity and fewer disturbances from environmental stress (Farmer and Gotto 1998). Type A behaviour was first recognized to be a psychosocial predictor of CHD in the studies by Friedman and Rosenman in 1959. Rosenmann et al. (1975) found that males with extreme type A behaviour that expressed anger and hostility had two to four times higher risk of developing CHD than males with type B characteristics. The association between anger and hostility and the incidence of CHD has also been documented in younger males (Rosenmann et al. 1975, Dembroski and McDougall 1985). Unlike behaviour, individuals of type B with high hostility were more likely to have significant coronary occlusion than low-hostility type A individuals. Likewise, hostility indices were positively related with the 20-year risk of death from CHD in both type A and type B, as reported by Eliot et al. (1998).

Social isolation has also been predicted to increase CHD risk (Williams et al. 1992, and Berkman et al. 1992), and more severely when other clustering of CHD risk factors are present, particularly in type A males (Orth-Gomer and Unden 1990). Case et al. (1992) found a doubled rate of myocardial infarction (MI) among patients who lived when compared with those who lived with another person.

Work stress effect on CHD

Occupational stress and shifting-job have been related to CHD especially myocardial infarction (Knutsson et al. 1986, Wilhelmsen and Marmot 1996, Eliot et al. 1998). Job-factors that appear to influence the induction of CHD include irregular working hours, overtime and long working days, perceived job stress, role ambiguity, working speed and monotony, insufficient chances to control's one's own working situation and lack of personal progress (Karasek et al. 1990). For example a job characterised with the variable *«high demand low decision latitude»* was found to be associated with CHD among Finnish blue-collar workers (Wilhelmsen and Marmot 1996). Additionally, stresses such as time pressures on assembly-line workers and those who are responsible for others safety, as in the case of air-traffic controllers, myocardial infarction, and other health illnesses have been noted to be related to an increased incidence of high blood pressure (Eliot 1992, Eliot et al. 1998). Non-supportive bosses at wok have similar effects (Eliot 1992).

The human socio-cultural environment in many countries has been characterized by increasingly hectic psychological situations (Eliot et al. 1998). It increases the action of the sympathetic nervous system (Wilhelmsen and Marmot 1996, Eliot et al. 1998). This can be related to social status, interactions with other people and changes in

social elements with negative health impacts (Eliot et al. 1998). It has also been recognized that when people change environments (jobs, move from their place of residence, or other major life changes) the risk of CHD may increase two to three times, independent of CHD risk factors.

Risk factors influenced by both lifestyle and inheritance

Obesity

Obesity is defined as an excess of adipose tissue resulting from a systematic imbalance between caloric intake and energy expenditure (Atkinson and Walberg-Rankin 1994, Hill et al. 1994, Alexander 2000). Obesity occurs when energy balance is consistently positive (Hill et al. 1994). It is widely accepted that obesity is harmful to both health and longevity (Bjørntorp 1990a). Likewise, obesity is an independent risk factor for atherosclerosis (Després and Lamarche 1993). Obesity has therefore taken on the role as a marker of chronic disease, such as: cardiovascular diseases including coronary heart diseases (myocardial infarction, and cerebrovascular accidents), peripheral heart disease, diabetes mellitus, dyslipidaemia, hypertension and cancer (Atkinson and Walberg-Rankin 1994). All are the major contributors to morbidity and mortality (Gotto and Farmer 2000). Beside the pathophysiology, genetic predisposition is the most crucial factor on the disease related to obesity (Bjørntorp 1990a and 1992, Bouchard et al. 1993a).

Obesity and body mass index

The body mass index (BMI) has been developed as one of indices used to assess the relationship between body weight, height and body fatness (Alexander 2000). A link between the population mean body mass index (BMI) and the prevalence of obesity

clearly has been established (Després and Lamarche 1993). Within population, BMI has been acceptable as an indicator for the degree of fatness (Alexander 1998 and 2000). In developed countries, the recommended BMI is less than 25 kg/m^2; anything above this is considered overweight, and above 27 kg/m^2 indicates obesity (WHO study group 1990), and the population should have an average BMI of about 22 kg/m^2 (Després and Lamarche 1993). In addition, wide variations in BMI have also been shown in populations from different societies (Wilhelmsen and Marmot 1996). In general, the BMI in poorer communities, e.g. Africa, has shown to be lower than in more affluent communities (Bjørntorp 1990c). High BMI has been shown to be an important variable for the prevalence of obesity associated with CHD (Farmer and Gotto 1998 and 2000, Alexander 2000). Even individuals with a high-normal BMI appear to be at increased risk for CHD (Farmer and Gotto 1998).

Obesity and waist-to-hip ratio

Abdominal distribution of fat is a much greater risk factor for CHD than similar amounts of fat distributed on the hips (Bjørntorp 1990 and 1992, Folsom et al. 1993, Després and Lamarche 1993). This is widely accepted with the suggestion that there is an interaction between the BMI and waist-to-hip ratio (WHR), in terms of risk for CHD (Bjørntorp 1990c, Folsom et al. 1993). A high WHR (>1.0 in males and >0.85 in females) seems to be risky even in modestly overweight adults. However, it has been suggested that by simply using the waist measurement one achieves nearly as good (Lapidius et al. 1984) an estimation of the risk level as by including the hip measurement to produce a ratio (Bjørntorp 1990c, Després and Lamarche 1993). Thus, a simple waist-measurement-taken at the mid-point between the lower border of the rib cage and the iliac crest-may not only be a simple guide for individuals to

assess their risk, but also a valuable additional tool for combining with a BMI measurement in epidemiological analyses. Measures of abdominal obesity are probably more effective discriminators of risk than measurements of truncal subcutaneous skinfold thickness, that correlate with but are not direct measures of intra-abdominal fat (Bouchard et al. 1993a, Després and Lamarche 1993).

Gender fat distribution and development of coronary heart disease

Several studies carried out in many countries have shown the importance of the fat distribution as a CHD risk factor (Alexander 2000). The difference in fat patterns between males and females implicates a hormonal basis for the variable degree of fat deposition in different anatomical areas (Després 1991, Virmani 2000). The waist-to-hip ratio (in females) has been positively correlated with the level of androgens (Farmer and Gotto 1998). Upper values of body mass index and increased central obesity, as estimated by abdominal girth or waist-hip ratio, have been associated with increased risks of CHD in both males and females (Lapidius et al. 1984). Fat deposition in the abdomen has been associated with both hypertension and other risks for developing CHD complications (Larson et al. 1984). In both males and females, CHD was found to correlate with the abdominal distribution of adiposity, which appeared to be independent of total body obesity (Després 1991). In addition, among females, the deposition of intra-abdominal fat constitutes greater risk for the development of CHD than obesity alone (Bjørntorp 1990c, Després and Lamarche 1993). Therefore, a masculine distribution of adipose tissue has been confirmed to increase CHD risk in both females and males (Farmer and Gotto 1998).

The mechanisms behind the relationship between upper body fat accompanied by the accumulation of visceral abdominal fat and the development of CHD risk factors remain to be established. However, it has been proposed that elevated levels of visceral abdominal adipose tissue causes the high lipolytic activity of omental and mesenteric adipocytes and contributes to a greater, flux of free fatty acid (FFA) into the liver through portal circulation (Kissebah et al. 1989, Bjørntorp 1990c). High levels of FFA reduce the hepatic extraction of insulin, contributing to systemic hyperinsulinemia. Increased FFA levels also stimulate hepatic glucose production and triglyceride synthesis (Bjørntorp 1988). Furthermore, it has been suggested that the increase of glycerol as a substrate for hepatic gluconeogenesis may contribute to the elevated hepatic glucose production present in visceral obesity.

Obesity and high blood pressure

Obesity is associated with hypertension (Godring et al. 1977, Shamarin et al. 1980, Alexander 2000). The prevalence of hypertension is greater in people with central, abdominal obesity, as reflected by a high waist-to-hip ratio, than in those with peripheral, gluteal fat and a low waist-to-hip ratio (Alexander 2000). Also, hypertension in the upper body obesity is often associated with insulin resistance and high blood lipids (Alexander 2000). Longitudinal studies have shown that obesity, which is related to hypertension, is apparent among individuals who gain weight most rapidly as they become older (Alexander 2000), but the correlation of obesity with hypertension appeared to be low (MacMahon et al. 1990). However, a better correlation between central obesity and hypertension has been documented, as indicted by the waist-to-hip measurement ratio (Stamler 1991, Bjørntorp 1990a,b). The mechanism underlying the development obesity-related hypertension has been

connected to increase insulin levels that link the occurrence of insulin resistance and increased level of sympathetic nervous system activity (Alexander 2000). It has been noticed that chronically increased level of sympathetic activity, increased cardiac output and peripheral vasoconstriction with insulin-mediated enhancement of renal sodium reabsorption produce hypertension (Krieger and Landsberg 1988, Landsberg 1991, Mikhail et al. 1999, Sharma et al. 2001). However, the impact of increased insulin by itself appears to be less associated with hypertension, because it has been shown that many patients with high levels of insulin were not hypertensive (Bjørntorp 1990). Genetic factors have been suggested to play a major role in insulin resistance and obesity-related hypertension, but studies have failed to show a consistent association (Landsberg 1995, Mark and Anderson 1995).

Obesity related to blood lipids

Obesity is associated with hyperlipidemia (Wilhelmsen and Marmot 1996, Ashwell 1997, Alexander 2000). Increase BMI tends to increase the atherogenic lipid levels such as blood VLDL-c, LDL-c, and triglyceride levels, while HDL-c levels decrease (Reeder 1992, Superko 1995, Alexander 2000). Blood TC has also been found to increase with increased BMI until about 28 but afterwards it shows no further increase (Young 1995). However, central obesity in terms of waist-hip-ratio has shown to be consistent and highly correlated with the serum VLDL-c, LDL-c, and triglycerides (Després et al. 1989). The development of obesity-related hyperlipemia has been connected to changes in the activity of enzymes involved in lipoprotein metabolism such as lipoprotein lipase: LPL and hepatic lipase: HL (Després 1989, Bjørntorp 1990, Després 1991).

Obesity associated to diabetes type II

The relationship between obesity and diabetes type II has been well documented (NIHCDP 1985, Alexander 2000). Particularly, individuals with a major increase in BMI, accompanied by elevated levels of insulin, and insulin resistance (Pi-Sunyer 1991, Young and Gelskey 1995). Mechanisms behind increased insulin or insulin resistance as a CHD risk factor is still not well described (Alexander 2000). Although, insulin resistance has been suggested mainly as an independent CHD risk factor (Després et al. 1996, Farmer and Gotto 2000), a metabolic linkage with increased atherogenic lipids, for instance elevated triglycerides and reduced HDL-c level have been recognized (Law and Raven 1992). Therefore, insulin resistance per se is not enough in the absence of other CHD risk factors (Stern 1996). It has been suggested to be an indicator of other hormonal or metabolic defects not sufficiently assessed by an association to traditional risk factors (Després et al. 1996). These insulin abnormalities and glucose intolerance and decreased HDL-c have shown to correlate with upper body fatness, but not with total body obesity (Ostlund et al. 1990). Additionally, diabetes type II has been associated with fibrinogen and increased blood viscosity (Alexander 2000).

In developing countries, such as Africa and Asia, obesity is common and strongly linked to diabetes type II, but in such population CHD prevalence is lower compared to westernised countries (Després et al. 1996). This suggests that insulin resistance and glucose intolerance are not necessary for the development of atherosclerosis and CHD (Stern 1994).

Obesity related to cigarette smoking

Obesity has also been associated with all the CHD risk factors except smoking (Kannel and Gordon 1979). Cigarette smokers have a lower average body weight than nonsmokers (Froom et al. 1998). The number of cigarettes smoked per day shows an inverse trend when compared with body weight. This may be due to appetite suppression by cigarette smoking and possibly increased metabolic rate (Higgins et al. 1988). However, the cessation of smoking is associated with weight gain, and this weight gain does not counteract the health benefits of smoking cessation (Froom et al. 1998). Cigarette smoking cessation is also associated with increased adipose tissue metabolism, in particular increase in adipose tissue lipoprotein lipase activity. This increase in lipoprotein lipase may contribute to the increase in body weight associated with cigarette smoking cessation (Ferrara et al. 2001, Alexander 2000). There is a strong inverse association between BMI and cigarette smoking, which makes a major contribution to the increased mortality in lean males (<20 BMI). In males who have never smoked, lean males have the lowest mortality and in the remaining males, there is a significant tendency for mortality to increase with increasing BMI, suggesting that when smoking does not confirm the issue, increasing BMI is associated with increasing mortality (Wannamethee and Shaper 1990).

Obesity and CHD

Extreme obesity increases the risk of CHD mortality, although it is still controversial as to the exact level of obesity that should be marked as hazardous (Sjostrum 1992, Eckel 1997, Farmer and Gotto 1998). Generally, most of the risk factors for CHD rise progressively from low body weight to high body weight (Wilhelmsen and

Marmot 1996, Farmer and Gotto 1998). In most developed communities obesity carries a twofold risk of CHD, in both males and females (Alexander 2000). Obesity per se appears not to be a necessary cause of CHD, but some pathways to obesity and some patterns of obesity are more positively more atherogenic than others (Bjørntorp 1990c, Casassus et al. 1992, Bourchard et al. 1993a). Obesity is closely associated with hypertension, dyslipidaemia, diabetes mellitus, and hyperuricemia (Alexander 2000). Although once these have been adjusted, obesity no longer has an independent effect in predicting CHD (Després and Lamarche 1993, Farmer and Gotto 1998). Therefore, studies have failed to establish a clear mechanism related to obesity associated with CHD (Sjostrum 1992, Manson et al. 1995). Rather it seems that in the presence of obesity, the predisposition to CHD is mediated by the development of a variety of factors subject to hereditary predisposition and environmental circumstances, as reported by Després and Lamarche (1993), Farmer and Gotto (1998), and Alexander (2000).

Hypertension

High blood pressure as a risk factor of vascular complications rises with increasing levels of systolic and diastolic blood pressures without a clear threshold (MacMahon et al. 1990). The definition of hypertension is based upon an arbitrary level at which people are labelled as hypertensive and treatment is initiated (Rose 1992, WHO: 1994, Wilhelmsen and Marmot 1996). Therefore, from the epidemiological point of view there is no natural level at which an individual can be defined as "hypertensive" (Rose 1992). However, normal blood pressure is assumed to be 120/80mmHg or $\leq$ 140/90 mmHg (JNC VI 1996, Fagard and Tipton 1994, Wilhelmsen and Marmot 1996). It has been reported that there is usually a gradual rise in blood pressure, as

one grows older (Bittner and Oparil 1997). Also, in all ethnic groups, males tend to have higher blood pressure than females, and through middle age, the prevalence of high blood pressure has shown to be generally higher in males than in females (Yong et al. 1993, Himmelmann et al. 1994, Burt et al. 1995). However, it has been found that at advanced ages, high blood pressure prevalence is higher in females than in males. At around 65 years of age, blood pressure is assumed to be 160/90mmHg (Wilhelmsen and Marmot 1996, Bittner and Oparil 1997, Kaplan 2000). In the USA, age-related to blood pressure increases were observed to increase more rapidly in blacks than whites. Thus, Cornoni-Huntley et al. (1989) found that over nearly 10 years of follow-up, high blood pressure rates increased with age in both races and sexes, but were higher in blacks than whites in each age group; but significant gender differences were not apparent. However, there are in fact communities in which blood pressure does not increase with age, among people living a traditional rural life for example Masai in the rural East Africa, when they maintain their traditional life style (Muna 1993, Wilhelmsen and Marmot 1996). Moreover, hypertension has been appreciably related to environmental factors, which are obesity, psychological stress, high salt intake, saturated fats intake, high alcohol intake, and serum TC (Kaplan 2000).

Hypertension and coronary heart disease

Through several observational epidemiological studies in geographically and ethnically diverse populations there has been established a direct relationship between elevated blood pressure and incidence of CHD (Kaplan 1989, MacMahon et al. 1990, Kannel and Hings et al. 1990, Keil et al. 1991, Reavan 1991, Stamler et al. 1993, Wilhelmsen and Marmot 1996, Bittner and Oparil 1997). Hypertension is as a

major modifiable risk factor for the development of coronary atherosclerosis across racial, gender, and age categories (Fagard and Tipton 1994, Kaplan 2000, Lloyd-Jones and Kannel 2000). A 6-year follow-up study, conducted by Fiebach et al. (1989), gave strong evidence that hypertension is a strong and independent predictor of CHD. Hypertension often exists together with other risk factors, and the impact may be synergistic with those risk factors. Such factors are obesity (Stamler 1991), physical inactivity (Fletcher et al. 1995, Blair et al. 1995), intake of salt (Law et al. 1991), alcohol (McMahon et al. 1986), polyunsaturated to saturated fat ratio (Bönaa et al. 1992) hyperlipidemia (Farmer and Gotto 1998) and psychological stress (Wilhelmsen and Marmot 1996).

Hypertension has been found to be an aggravating factor that makes CHD more serious, especially in the presence of other CHD risk factors (Kapla 2000). It appeared to be less important for CHD risk in countries where blood TC concentration is low e.g. Japan and rural communities in Africa (Nissinen et al. 1988). Nevertheless, in communities with relatively high levels of blood TC, the risk increases at similar rate for blood pressure as for blood TC concentration associated with CHD when fifths of the population are considered (Wilhelmsen and Marmot 1996).

Investigators have found that the mechanism behind hypertension and a CHD event might be the result of the changed arterial structure and function accompanied by abnormal flow (Heistad et al. 1991). This includes impaired endothelial function, increased endothethelial permeability to lipoproteins; increased adherence of leukocytes, increased oxidative stress may trigger acute plaque rupture (Panza et al.

1990, Brush et al. 1992, Taddei et al. 1993, Crockcroft et al. 1994, Antony et al. 1995, Kaplan 2000). Hypertension alone is not sufficient to cause atherosclerosis in CHD. However, in the present of other risk factors, particularly hypercholesterolemia, atherosclerosis in coronary vessels the progression of the CHD accelerates (Heistad et al. 1991, Bittner and Oparil 1997). Furthermore, high blood pressure may increase the filtration of lipid from plasma to the intimae in the presence of elevated plasma lipids (Heistad et al. 1991). This may result from injury of the intima, leading to platelet aggregation and proliferation of smooth muscle cells in the media (Ross 1998). It may also cause hypertrophy of the myocardium of the left ventricle and congestion of the pulmonary or systemic veins (Cheitlin et al. 1993).

Blood Lipids

Lipids play a major role in the development of atherosclerosis, which sooner or later affects most medium-sized and large arteries (Thompson 1998, Grundy 2000). The main blood lipids are cholesterol, triglycerides and phospholipids. Cholesterol and phospholipids are important constituents of cell membranes and help to regulate their permeability to ions. These three lipids are transported in blood plasma within lipoprotein particles. Lipoproteins are water-soluble molecules formed in the liver in the union of protein with triglycerides or phospholipids, free cholesterol and apolipoproteins (Wilhelmsen and Marmot 1996). There are basically four major types of lipoproteins: chylomicron, VLDL-c, LDL-c, and HDL-c. They are categorized according to their gravitational density (Superko 1997). Chylomicrons are formed after emulsified lipid droplets (including triglycerides, phospholipids, and free fatty acids) leave the intestine and enter the lymphatic duct. Very low-density

lipoprotein (VLDL) contains the greatest percentage of lipid (95%) of which about 60% are in the form of triglycerides (Grundy 2000). This lipoprotein is transported to muscle and adipose tissue; the triglycerides are formed in the liver from lipids, carbohydrates, and cholesterol. Once VLDL-c is acted upon by the enzyme lipoprotein lipase, it becomes a denser LDL-c molecule because it contains fewer lipids.

Low-density lipoprotein cholesterol (LDL-c) known as "dangerous cholesterol" carries between 60% and 80% of the total blood cholesterol. Most LDL-c exists in the liver after binding to LDL-c receptors; only small amounts of LDL-c go to other tissues. Most of the blood cholesterol comes from newly secreted VLDL-c. Normally, the blood concentration of cholesterol consists mainly of LDL-c and is influenced by the expression of liver of LDL-c receptors. In addition, the LDL-c receptor synthesis is controlled by the concentration of cholesterol in liver cells. When hepatic cholesterol rises, synthesis of hepatic LDL-c receptors is suppressed, and when hepatic cholesterol falls, synthesis of receptors rises (Grundy 2000).

High-density lipoprotein (HDL), "good cholesterol", removes cholesterol from the arterial wall and transports it to the liver, where it is incorporated into bile and excreted via the intestinal tract (Grundy 2000). The liver and intestine, as well as apoproteins and phospholipids excrete HDL-c (Bruce et al. 1998, Farmer and Gotto 2000). Lecithin cholesterol acyltransferase (LCAT) activity is associated with HDL particles. Nascent of HDL particles initially forms HDL_3 in plasma but are converted to large HDL_2 particles by the action of LCAT, which is activated by Apo A-I; synthesized both in the liver and small intestine (Thompson 1998). Apo A-I, A-III,

along with Apo C-I, are activators of LCAT. Plasma A-I and A-II are located on DHL-c particles, and Apo B serves as an identification protein of specific receptors located on hepatic and peripheral cells involved with lipoprotein metabolism particularly, chylomicrons, LDL-c, and VLDL-c (Superko 1997, Thompson 1998).

High levels of blood lipids

An elevated level of plasma lipids, which is known as hyperlipidaemia, or dyslipademia may be defined in relation to levels of lipids associated with a low risk of CHD disease in a specific community (NCEP 1993, NCEP II 1993, Wilhelmsen and Marmot 1996, Thompson 1998). The relation between lipids and CHD has focused more on the blood TC and triglycerides, than the lipoproteins LDL-c and HDL-c (Lloyd-Jones and Kannel 2000). There is a positive correlation between total cholesterol, LDL-c, triglycerides, and CHD, but a negative correlation between HDL-c and CHD (Wilhelmsen and Marmot 1996, Farmer and Gotto 2000). The levels of LDL-c and HDL-c have shown to be important in the development of CHD among people aged 45 to 84 (Wilson 1990). TC and triglyceride values are also considered to be positively associated with CHD (Hulley et al. 1986), although, TC-related risk differs widely depending on age, gender, and the burden of other risk factors CHD (Lloyd-Jones and Kannel 2000). TC levels increase with age, so does the risk of CHD (Farmer and Gotto 2000). The atherogenic effects of the blood TC depends on the comparative levels of its LDL-c and HDL-c constituents (Kawakami et al. 2000, Lloyd-Jones and Kannel 2000). Consequently, measurements of these two lipoprotein fragments is necessary after 55 years of age, when the blood TC shows to be less identified with victims of CHD. Furthermore, males have been noticed to be at higher risk in acquiring hyperlipidaemia than females (Wilhelmsen

and Marmot 1996, Farmer and Gotto 2000). Several studies have demonstrated that the population level of blood TC roughly predicts the level of CHD in that population. Populations with high levels of other risk factors such as hypertension (West Africa), hypertension and smoking (Japan) but low blood cholesterol values in the range of 160 to 190 mg/dl still have a low incidence of CHD (Farmer and Gotto 1998, Lloyd-Jones and Kannel 2000).

Low-density lipoprotein cholesterol

Both lesion initiation and lesion progression in CHD atherosclerosis seem to be associated with increased levels of blood TC, especially the fraction of LDL-c (LaRosa et al. 1990, Navab 1996, Ross 1998). LDL-c is the source of most of the cholesterol in atherosclerotic plaque (Glagov et al. 1995, Kawakami et al. 2000). LDL-c also seems to be an inflammatory cause (Navab et al. 1996). It may cause the disruption of endothelial cells functioning by the oxidized LDL-c (Flavahan 1992), with the subsequent loss of production of endothelial derived relaxing factors (Maron et al. 1998). The active region of atherosclerotic plaque contains mainly macrophages (Ross 1995); influx of LDL-c into the arterial wall apparently attracts circulating monocytes and transforms them into active macrophages (Glagov et al. 1995, Wissler 1995, Grundy 2000). According to existing concepts, LDL must undergo modification before it can attract and activate macrophages (Grundy 2000). Likewise, the modifications of LDL-c within the intima include oxidation (Heinecke 1997), glycation (Millican et al. 1998), and enzymatic degradation (Bhakbi et al. 1998). Consequently, LDL-c plays multiple roles in the initiation and maintenance of CHD atherosclerosis (Slyper 1994, Maron et al. 1998, Grundy 2000). Increased LDL-c has been considered as a major cause of CHD (Goldbourt et al. 1985, Stamler

et al. 1986, Law et al. 1994, Austin 1994, Austin et al. 1994). This relationship has been confirmed in different countries in both young and middle-aged adults as well as in the elderly (Law et al. 1994). Also it has been shown that increased blood TC levels due to increased LDL-c developed in young adulthood predict CHD later in life (Klang et al. 1993, Austin et al. 2000). The level of TC and LDL-c interacts with other risk factors to multiply the risks of CHD (Pekkanen et al. 1992, Wilson et al. 1994).

Total triglycerides

Triglycerides, VLDL-c and chylomicrons have been positively related to CHD risk (Lloyd-Jones and Kannel 2000, Krauss 1998, Grundy 2000). Many studies have indicated that the excess risk observed in case of elevated levels of blood triglycerides are primarily dependent on co-existing low blood HDL-c values, obesity, impaired glucose tolerance, and metabolic syndrome (Criqui et al. 1993, Wilhemsen and Marmot 1996, Farmer and Gotto 1998, Grundy 1998, Lloyd-Jones and Kannel 2000). Actually, since the metabolisms of triglycerides and HDL-c are closely linked, and there is a strong inverse correlation between their levels, it has not been easy to separate the possible independent effects of triglycerides (Jeppesen et al. 1998). However, elevated levels of triglycerides have been found to be an independent risk factor in both sexes even after adjustment for HDL-c and other risk factors (Hokanson and Austin 1996). For example in the study reported by Wilhemsen and Marmot (1996), the triglyceride values were found to be an independent risk factor for CHD in the Swedish population. Furthermore, elevated levels of triglycerides seem to be more important and common in females than males, and they may be more important in older than in younger men (Wilhemsen

and Marmot 1996, Lloyd-Jones and Kannel 2000). The additional value of measuring triglycerides has been controversial, but the present attitudes seem to favour measurement of both blood TC and triglycerides and subfractions of TC particularly at elevated levels of the total (Wilhemsen and Marmot 1996).

High-density lipoprotein cholesterol

Studies from different parts of the world have established a negative relationship between high HDL-c level and CHD risk (Wilhelmsen and Marmot 1996, Vega and Grundy 1996, Farmer and Gotto 1998, Wilson et al. 1998, Lloyd-Jones and Kannel 2000). Two important mechanisms by which HDL-c is thought to play a protective role against atherosclerosis are reverse cholesterol transport and inhibition of LDL-c oxidation. It means that, HDL-c is directly antiatherogenic, or a reduction of HDL-c usually reflects the presence of other atherogenic lipoproteins such as increased triglycerides, small dense LDL-c, elevated VLDL-c, and chylomicrons, and is always accompanied by other non-lipids factors of the metabolic syndrome (Vega and Grundy 1996, Austin et al. 2000). However, a decrease of HDL-c has been found to be more of a risk than an increase in LDL-c or TC levels in CHD (Kannel 1985). The ratio of LDL/HDL-c or TC/HDL-c (desirable cut-off, < 5.0, borderline;5.0 – 6.0, abnormal; > 6.0) is a better predictor of CHD than either level alone, or levels of apoprotein apo A-B (Lloyd-Jones and Kannel 2000). This pointed to the benefits of decreasing LDL-c and increasing HDL-c, that LDL-c leads to increased uptake of lipid in cells, whereas HDL-c plays a role in removing lipid from cells and is thus protective (refer page 56-58). Furthermore, the TC/HDL-c ratio has been found to be more effective in recognizing the increase of CHD risk than on the LDL-c alone (Wilhelmsen and Marmot 1996, Vega and Grundy 1996, Farmer and Gotto 1998).

The reduction of HDL-c levels has been associated with the occurrence of myocardial infarction in both sexes (Lloyd-Jones and Kannel 2000). Studies done by Wilson (1990) and Manson et al. (1992) highlighted the consequences of decreased HDL-c levels on CHD with emphasises on myocardial infarction. In addition, HDL-c has been noted to be a central factor in the genetic dyslipademia and it is termed as a hypoalphalipoprotein because the alpha band is the location of HDL particles. Abnormally low HDL-c can occur as a result of several environmental factors that often are related to elevated triglycerides (Superko 1997). The hypoalphalipoprotein has been retained for very low HDL, less than 25mg/dl (25mmol/litre), and is felt to have a genetic aetiology transmitted in an autosomal dominant manner, potentially connected to early CHD. It can also be defined as an HDL-c < 10%, which is less than approximately 0.83 mmol/L for middle-aged males and less than 1 mmol/L for middle-aged females (Vergani 1981).

Diabetes Mellitus

Diabetes mellitus is not a single disease, but rather an accumulation of metabolic and pathologic abnormalities, with a variety of causes, which are accompanied by hyperglycaemia (Leahy 1990, Lavis and Willerson 2000). Diabetes mellitus has also been associated with an excess secretion of hormones that antagonize the action of insulin, cortisol, epinephrine, growth hormone, and glucagon from the alpha islet cells of the pancreas (Atkinson and Maclaren 1994, Lavis and Willerson 2000). Diabetes mellitus is a complex condition, involving different subgroups of disorders with different pathophysiology, and is commonly classified into two major types; Type I (idiopathic-insulin-dependent-diabetes; IDDM), also known as juvenile-onset diabetes mellitus (Nerup et al 1987, Atkinson and Maclaren 1994), and Type II (non-

insulin-dependent-diabetes; NIDDM), also referred to as adult or maturity-onset diabetes mellitus (Polonsyk et al. 1996, Gerich 1998, Ferrannin 1998, Lavis and Willerson 2000).

Insulin-Dependent Diabetes Mellitus (Type I)

IDDM is mainly due to a physical destruction of pancreatic beta cells by an autoimmune process in antibodies to islets of Langerhans cells causing to their destruction (Nerup et al. 1987, Atkinson and Maclaren 1994). It is believed that environment triggers such as toxic, chemical or viral infection are involved (Atkinson and Maclaren 1994). It damages beta cells and causes antigen release, which initiates the progressive autoimmune destructive process, especially in genetically susceptible people (Atkinson and Maclaren 1994). Although hyperglycaemia in IDDM is due to insulin deficiency, it is also contributed by a defect in insulin-stimulated glucose uptake, which may be caused by hyperglycaemia (Lavis and Willerson 2000). Usually, IDDM becomes clinically evident with an abrupt onset of classical symptoms and signs before the age of 30 and especially during childhood or adolescence (Atkinson and Maclaren 1994, Lavis and Willerson 2000). However, it may occur at any age. Individuals with IDDM are usually of normal weight or underweight and they often have a family history of type I diabetes mellitus, so genetic predisposition is likely (Lavis and Willerson 2000).

Non-Insulin-Dependent Diabetes Mellitus (Type II)

NIDD has been noticed to be the most common form of diabetes all over the world, particularly in adulthood after the ages of 40 (Farmer and Gotto 2000). It has been recognized to have less severe symptoms than Type I diabetes mellitus, and is more common in males than females (Lavis and Willerson 2000). It is also detected in

asymptomatic individuals by the finding of an increased blood glucose level or glycosuria. Furthermore, it has been related with other CHD risk factors such as obesity, hypertension, dyslipidaemia, and thrombotic tendency by elevated levels of circulating PAI-1 (Juhan-Vague et al. 1989, Stern 1996), and physical inactivity as well as with a strong family history of type II diabetes mellitus (Wilhelmsen and Marmot 1996). In difference to IDDM, the pathophysiology of NIDDM includes impaired action of insulin (insulin resistance) and abnormal secretion of insulin, particularly in response to hyperglycaemia has been observed (Polonsky et al. 1996, Leahy 1990, Ferrannini 1998, Gerich 1998, Lavis and Willerson 2000). However, reduced beta cell mass and function seemed to be contributing factors, and beta cell failure may develop later, particularly in overweight people (Stern 1995 and 1996). Consequently, circulating insulin always is detectable for example plasma insulin levels often are higher than in non-diabetic individuals, and hyperinsulinemia may be present at least in the early stages of the disease (Bierman 1992, Farmer and Gotto 1998). Therefore, the primary deficiency exists in the ability of insulin to maintain glucose homeostasis, in which the liver and peripheral tissues are insensitive or resistant to insulin (Lavis and Willerson 2000). Although a great deal of experimental evidence supports this conclusion, the cellular mechanisms responsible for the insulin resistance are not well known (Lavis and Willerson 2000). It appears that deficiencies may exist in both cell insulin receptor binding and post-receptor effectors activity in liver, muscle, and other insulin-sensitive tissues (Reaven 1988, Farmer and Gotto 1998).

Diabetes Mellitus as related to coronary heart disease

Coronary heart disease is a major complication and common cause of death of both IDDM and NIDDM (Moss et al. 1994, Després et al. 1996, Farmer and Gotto 1998 and 2000, Lloyd-Jones and Kannel 2000). Diabetic females are more at risk to develop CHD than males (Barret-Connor et al. 1991, Gotto and Farmer 1998 and 2000). Females with diabetes mellitus do not share the relative gender-mediated pre-menopause protection against CHD of females without diabetes (ADA 1993). Diabetes mellitus has also been recognized as an independent risk factor for CHD, and at any level with other major risk factors the presence of diabetes doubles the risk for CHD (Wilhelmsen and Marmot 1996). It is commonly linked to an abnormal blood lipid profile, elevated blood pressure, and/or cigarette smoking (Farmer and Gotto 1998). On the other hand, in Africa society and any society where atherosclerosis is uncommon, diabetes mellitus has not been associated with increased CHD risk (Wilhelmsen and Marmot 1996). Thus it depends on the prevalence of diabetes in the population and the population's characteristic risks of diabetic changes. For example two studies conducted in two different populations, Swedish and Indian, could document that in the Swedish population CHD, especially myocardial infarction, was found in about 3% of the study population, while in the Indian population CHD was found in about 20 %. The latter may be due to their high level of diabetes mellitus prevalence (Rosegren et al. 1989, Wood et al. 1989).

According to observational epidemiological studies, CHD atherosclerotic events appear to occur at earlier ages, and are more severe and frequent in individuals with diabetes type II as compared to non-diabetic individuals (Williams and Braunwald 1992, Lavis and Willerson 2000). Furthermore, it has been found that painless

myocardial infarction and ischaemia are more common and likely to appear among diabetic individuals and those who are under 35 years of age (Nesto et al. 1988, Roy et al. 1989, Farmer and Gotto 1998, Lavis and Willerson 2000). This is the consequence of damaged cardiac nerves resulting to autonomic neuropathy (Ambepityia et al. 1990). In addition, diabetic individuals who have sustained myocardial infarction have a poorer prognosis and survival rate compared to non-diabetic individuals as a consequence of a higher incidence of congestive heart failure, myocardial rupture and heart attacks (Farmer and Gotto 1998).

The physiologic changes following diabetes mellitus and an increase of the risk of CHD atherosclerotic manifestations is still controversial, but there are many possible mechanisms. Diabetes mellitus is commonly linked to an abnormal blood lipid profile such as decreased HDL-c levels, elevated blood levels of LDL-c, VLDL-c, Lp (a), triglycerides, elevated blood pressure, platelet aggregation levels, and/or cigarette smoking (Austin 1995, Stern 1995 and 1996, Wilhelmsen and Marmot 1996, Farmer and Gotto 1998). Increased insulin and insulin resistance have been focused on as the factors, which may play a major role in the elevated levels of lipid profiles of diabetes mellitus (Reaven et al. 1988, Gotto and Farmer 1998, Lavis and Willerson 2000). One well recognized action of insulin is the suppression of free fatty acids, though in diabetes mellitus the suppression is decreased. This results in an elevation in circulating levels of free fatty acid, which again stimulates triglyceride synthesis and decreased HDL-c (Dzau 1990, Stern 1995 and 1996, Farmer and Gotto 1998).

It has been assumed that lipoproteins, LDL-c and HDL-c may be changed in diabetes mellitus by glycation, which influences their recognition and coupling, by receptors (Farmer and Gotto 1998). Glycation of LDL-c causes its accumulation in macrophages (Lopes-Virella et al. 1988). Glycation of HDL-c may also promote cholesteryl ester accumulation in the arterial wall (Duel et al. 1991). Furthermore, through glycation, oxidation of LDL-c may be increased in individual, although extensive studies have not been performed (Morel and Chisolm 1989, Farmer and Gotto 1998).

Regarding CHD, diabetes mellitus has been associated with a pro-coagulant state caused by elevated platelet aggregabilty (Farmer and Gotto 1998), and elevated PAI-1 (Juan-Vague 1989, Stern 1995 and 1996). Insulin may contribute to atherogenesis by promoting smooth muscle cell proliferation and cholesteryl ester accumulation in the arterial wall (Bierman 1992).

Blood Homocysteine

Homocysteine (Hcy) is a sulphur containing amino acid produced from methionine during the processing of dietary protein (Moustapha et al. 2000). It has gained considerable attention since the end of the last century, because elevated concentrations of Hcy are believed to be associated with an increased risk of cardiovascular, cerebrovascular and peripheral vascular disease (Boushey et al. 1995, Graham et al. 1997, Nygård et al. 1997, Moustapha et al. 2000). Wilcken and Wilcken (1976) were the first to show an association between CHD and increase in homocysteine levels, in a case-control study. Genetic defects, diseases, age, vitamins deficiency and one or more modifiable life-style factors have been related to the

increased levels of Hcy (Selhub et al. 1993, Chauveau et al. 1993, Boushey et al. 1995, Nygård et al. 1995, Robinson et al. 1996, Refsum et al. 1998, Bolander-Gouaille 1999, Moustapha et al. 2000). The most important lifestyle factors are cigarette smoking, a low nutritional intake of vitamins, high coffee consumption, and too little physical activity (Nygård et al. 1995 and 997, Bolander-Gouaille 1999).

Homocysteine age and gender

Hcy levels increases with age and become common at the highest ages and in both females and males (Brattström et al. 1992 and 1994, Selhub et al. 1993, Robinson et al 1995, Nygård et al. 1995, Moustapha et al. 2000). It begins to increase earlier in males than females regardless of race or ethnicity (Jacques et al. 1994, Mayer et al. 1996, Refsum et al. 1998). Homocysteine levels in males have shown to be about 10 % higher than females. However, homocysteine levels in females increase after menopause (Dudman et al. 1993, Nygård et al. 1995, Wouters et al. 1995). The lower levels of homocysteine in pre-menopausal females are perhaps due to higher levels of estrogens (Wouters 1995). Increased age parallel with a deficiency of vitamins B_6 and B_{12} and folic acid has also been suggested to cause elevation of plasma Hcy levels (Selbub et al. 1993, Brattström et al. 1994). BMI value increases also with age and relates significantly with high Hcy levels along with plasma albumin (Brattström et al. 1994, Koehler et al. 1996, Bolander-Gouaille 1999).

Homocysteine as related to CHD

High level of homocysteine (hyperhomocystenemia) defined as fasting blood Hcy levels above 15 μmol/l, has been shown to be an independent risk factor for CHD (Stampfer et al. 1992, Alfthan et al. 1994, Arnesen et al. 1995, Nygård et al. 1995,

Robinson et al. 1995, Graham et al. 1997, Wald et al. 1998, Bollander-Gouaille 1999, Gheye et al. 1999, Moustapha et al. 1998 and 2000, Ford et al. 2002). Studies conducted by the European Concerted Action Project among CHD patients and a control group of individuals aged less than 60 years, documented that an increased level of blood Hcy was associated with an increased risk of CHD (Graham et al. 1997). In Graham and coworkers study also found that an elevated fasting blood Hcy level is a risk factor for CHD disease similar to that of high blood pressure, cigarette smoking, and elevated cholesterol levels. An elevated fasting Hcy level showed a more than multiplicative effect on risk in individuals who smoked or had high blood pressure.

The result from these studies indicates that control of hypertension and cigarette smoking may particularly be important in individuals with elevated blood Hcy levels, and determination of Hcy should be included when studying CHD. In addition, there is also evidence that Hcy is a strong predictor of mortality in patients previously diagnosed with CHD, as reported by Nygård et al. (1997). The precise mechanism by which elevated blood Hcy increases risk for CHD has not been well established (Bolander-Gouaille 1999). It may be that elevated Hcy levels alter the activities of cells in the vascular endothelium and smooth muscle in ways that either cause disease or promote its progression (Bolander-Gouaille 1999). Elevated blood Hcy appear also to transform the vascular endothelium from an anti-coagulant to a pro-coagulant phenotype (D`Angelo and Selhub 1997). Hcy is capable of inhibiting endogenous anti-coagulant activity by blocking the activation for protein C, as well as the indication of thrombomodulin from the endothelial cell surface (Rodgers and

Conn 1990, Lentz and Sadler 1991). The Hcy has also been specifically associated with a selective reduction in binding sites for tissue plasminogen activator (t-PA) with a resultant decrease in t-PA activity (Hajjar 1993). In addition, other data show that Hcy reduces the anti-thrombi III binding capacity of heparin sulfate (Nishinaga et al. 1993). Furthermore, to inhibit endogenous anti-coagulating activity, Hcy can enhance endogenous pro-coagulant activity. In cell culture, Hcy also increases he activation of pro-coagulant cofactor V and induces the activity of the procoagulant (TF) tissue factor (Rodgers and Kane 1986, Fryer et al. 1993). High homocysteine levels have also been shown to increase the affinity of the atherogenic lipoprotein (a), (Lp [a]) to bind to plasmin-modified fibrin (Harpel et al. 1992).

Elevated levels of Hcy have also lead to loss of endothelial function. A comparative study by Tawakol et al. in 1997 among individuals with elevated or normal levels of Hcy showed that hyperhomocystenemia is an independent risk factor for arterial dysfunction. Individuals with elevated levels of Hcy had endothelial–dependent vasodilatation impairment in the brachial arteries. Furthermore, a high level of Hcy is believed to interfere with the cell cycle of vascular endothelial and smooth muscle cells both directly and indirectly. Tsai et al. in 1994 reported that in vitro Hcy could directly induce the expression of cyclin A, a cell cycle protein, to stimulate proliferation of vascular smooth muscle cells.

Blood Coagulation Factors

Thrombogenic factors such as platelet aggregation, blood coagulation factors and fibrinolysis have been demonstrated to predict CHD events, and have been documented as major elements in pathogenesis of the atherosclerotic and thrombotic

formation (Meade et al. 1986, Rauramaa and Salonen 1994, El-Sayed 2000, Salomaa 2002). Several studies have also shown a strong correlation between fibrinogen concentration and CHD risk, especially myocardial infarction. Indeed, this correlation appeared to be independent of other risk factors (Meade et al. 1993, Green et al. 1994).

Fibrinogen

Fibrinogen has been shown to be a major independent CHD risk factor (Defronzo and Ferrannini 1991, Rauramaa and Salonen 1994), even though its increase occurs in combination with other risk factors such as age, cigarette smoking, high blood pressure, and obesity (Ernst 1990, Heinrich et al.1994, Farmer and Gotto 1998, and Lloyd-Jones and Kannel 2000). An elevated level of fibrinogen has also been noted to enhance risk, especially in hypertensive individuals' and cigarette smokers (Rosengren et al. 1990, Möller and Kristensen 1991, Rauramaa and Salonen 1994). Elevated fibrinogen has been related to HDL-c, LDL-c, TG, obesity and physical inactivity (Connelly et al. 1992, Eliason 1995). It has been observed that high-normal and increased fibrinogen levels may cause a prothrombotic environment through increased blood viscosity, increased platelets aggregability, increased fibrin formation, and perhaps, through direct infiltration of the vascular wall by fibrinogen. However, the mechanism behind fibrinogen and CHD is still controversial (Lloyd-Jones and Kannel 2000).

Fibrinolytic activity

A low level of fibrinolytic activity, which means decreased ability to release a clot and clear fibrin debris, may play a role in CHD (Rauramaa and Salonen 1994). Thus, it has been found that, fibrinolytic activity was decreased in atherosclerotic vessels in

CHD patients, while vessels without atherosclerosis had normal fibrinolytic activity (Rauramaa and Salonen 1994). Meade et al. (1993) documented a significant association between decreased fibrinolytic activity and CHD events in middle-aged males.

Coagulation factor VII

Coagulation factor VII increases the risk of CHD, especially in myocardial infarction (Miller 1992a, Moons et al. 2002). Furthermore, a directly association between factors VII and total blood TC has been established (Miller 1992b, Kelleher 1992). The mechanism behind increased levels of factor VII and CHD risk may perhaps be an augmented thrombin production, leading to a hypercoagulant condition (Rauramaa and Salonen 1994). Elevated coagulation factor VII has also been related to HDL-c, LDL-c, TG, obesity and physical inactivity (Connell et al. 1992, Eliason 1995).

Plasminogen Activator Inhibitor –1

Elevated levels of plasminogen Activator Inhibitor –1 (PAI-1) have been reported to be associated with CHD. It has also been observed that decreased fibrinolytic activity may result from increased levels of PAI-1 (Farmer and Gotto 1998). In several cross-sectional and case control studies it has been found an increase of PAI-1 in CHD patients (Juhan-Vague and Allesi 1993). Elevated levels of PAI-1 are directly associated with triglycerides and insulin levels, confirming its` major role in the insulin resistance syndrome (Juhan-Vague et al. 1993). Increased PAI-1 has also been shown to play a role especially in first myocardial infarction occurrence in males before the age of 45 (Hamsten et al. 1987). In addition, elevated PAI-1 has

been related to HDL-c, LDL-c, TG, obesity and physical inactivity (Connell et al. 1992, and Eliason 1995).

Platelet aggregation

Increased platelet aggregability is a major risk factor for thrombosis (Rauramaa and Salonen 1994, Miyamoto et al. 2001). It has been strongly associated with acute cardiac events particularly in patients with previous myocardial infarction who were not at high risk (Trip et al. 1990, Elwood et al. 1991). Increased platelet aggregability due to adenosine diphosphate (ADP) has also been associated with increased CHD mortality in healthy, middle–aged males independent of other risk factors (Thaulow et al. 1991). Platelet aggregability seems to increase with age, and is higher in females than in males (Meade et al. 1985, Rauramaa and Salonen 1994). It has been found to be lower in alcohol consumers compared to alcohol abstainers (Meade et al. 1985).

Metabolic Syndrome

Metabolic syndrome is a multifactorial syndrome, which often appears in the population of developed countries (Lloyd-Jones and Kannel 2000, Roberts 2000, Timar et al. 2000). It has also been termed: syndrome X, insulin resistance syndrome IRS (Reavan 1988), deadly quartet (Kaplan 1989), secret killer (Foster 1989), and atherothrombogen syndrome (Hjermann 1992). The syndrome occurs in early middle age, and is twice as common in males as in females (Barnad and Wen 1994). It has been related to genetic, hormonal, and lifestyle factors such as obesity, sedentary living, and over-consumption of a diet rich in fat and refined sugar (Barnad and Wen 1994, Timar et al. 2000). However, the exact mechanisms behind the development of metabolic syndrome are still unclear.

Metabolic syndrome and risk factor interaction

Metabolic syndrome is a clustering of risk factors (Barnad and Wen 1994, Poulter 1999), e.g. insulin resistance and high levels of plasma insulin (Kaplan 1989, DeFronzo and Ferrannin 1991), increased levels triglycerides (Landin et al. 1990), low levels of HDL-c (Eliason (1995), and high levels of small, dense LDL-c (Krauss 1994 and 1995). The presence of small, dense LDL-c in this syndrome has been strongly related to myocardial infarction (MI) risk (Krauss 1994 and 1995, Austin et al. 1994, 1995 and 2000). Furthermore, elevated blood pressure, obesity with central fat distribution and increased waist-hip-ratio, glucose intolerance or NIDDM, has been strongly associated with the increased risk of atherosclerosis in this syndrome (Bjørntorp 1992c, McKeigue 1996, Garvey and Hermayer 1998, Timar et al. 2000).

In some individuals with insulin-resistance, insulin secretion has been found to start to deteriorate under chronic stress and overt diabetes mellitus will occur. If not, individuals may remain hyperinsulinemic, with some degree of glucose intolerance accompanied with other risks of metabolic syndrome. In the presence of metabolic syndrome insulin resistance has also been considered to be a powerful independent risk for developing both diabetes mellitus and CHD (McKeigue 1996, Garvey and Hermayer 1998, Frayn 2000).

Also, blood coagulation abnormalities such as elevated levels of plasminogen activator inhibitor type 1 (PAI-1) and fibrinogen (Landin et al. 1990, Juhan–Vague and Allessi 1993 and 1997, Juhan-Vague et al. 1993), hyperuricemia (DeFronzo and Ferrannini 1991, Timar et al. 2000), and microalbuminuria (Timar et al. 2000) have been demonstrated in metabolic syndrome. Cigolini et al. (1995) reported that

elevated levels of PAI-1 were found to be relating to the syndrome in which a significant correlation was found between plasma PAI-1 levels and body mass index, triglycerides levels, insulin levels, and systolic blood pressure. Likewise, obese people, especially those with android obesity also have been reported to have high PAI-1 levels. Furthermore, in comparing the lowest and the highest levels of insulin, body mass index and triglycerides in almost 1500 patients, Juhan-Vague et al. (1993) observed a 2 to 3-fold differences in PAI-1 levels.

2.6 PHYSICAL ACTIVITY AS RELATED TO CHD RISK FACTORS

Physical inactivity is considered to be an independent and modifiable factor and risk factor for the development of CHD (Powell et al. 1987, Ekelund et al. 1988, Blair et al. 1989, Berlin and Colditz 1990, Morris et al. 1990, Blair 1994, Lee et al. 1995, Fletcher et al. 1996). In the last century the daily level of physical activity has decreased in many parts of the world, especially in developed societies, due to mechanisation and automation both at work and the domestic envorinment (Powell and Blair 1994, NIH Consensus 1996, Hardmann 1996, Bauman and Owen 1999). Physical inactivity has been related to other CHD risk factors such as obesity, decreased HDL-c, elevated blood pressure and some thrombogenic factors, tobacco smoking, and psychological factors (Powell and Blair 1994, US Surgeon General 1996, Wilhemsen and Marmot 1996, Kohl 2001).

In line with this, the prevalence of CHD in physically inactive individuals has been reported to be higher than in active ones (Powell et al. 1987, Berlin and Colditz 1990, Blair 1994). An inverse association between physical activity levels and CHD

risk has been demonstrated in many studies. For both females and males who are more active at work and during leisure time have a lower occurrence of CHD (Morris et al. 1958, Berlin and Colditz 1990, NIH Consensus 1996, and Kennon 1998). In addition, several population and cohort studies have also confirmed a significant reduction in ischemic events among individuals who perform regular physical activity either at work or during leisure time, e.g. in London transportation workers and civil servants (Morris et al. 1966), San Francisco longshoremen (Paffenbarger and Hale 1975), railroad workers (Slattery et al. 1989), white-collar civil service workers (Lie et al. 1985), participants in the Framingham study (Leon et al. 1987), and lipid research Clinic studies (Ekelund et al. 1988).

Physical activity per se may prevent the risk of developing CHD through different favourable physiological mechanisms, including the following:

- Increases heart muscles oxygen supply, and improves heart muscles contraction and its electrical impulse stability (Ekelund et al. 1988, Hambrecht et al. 2000).

- Decreases the systolic and diastolic blood pressure (Fagard and Tipton 1994), heart rate at rest, and reduces the sympathetic tone (Kujala et al. 1998).

- Increases the diameter and dilatory capacity of coronary arteries, increases collateral artery formation, and reduces the rate of progression of coronary artery atherosclerosis (Leon et al. 1987).

- Prevents blood clotting and other irregularities in the blood flow that may decrease plasminogen activator inhibitor-1 (Rauramaa and Salonen 1994). There is a reduction of blood lipids profiles (Leon and Sanches 2001).

- Increases insulin sensitivity and glucose tolerance (Kriska 2000), and decreases levels of homocysteine (Nygård et al. 1995).

- Contributes to a favourable body composition and to better fat distribution (Ross et al. 2000).

- It also reduces psychological stress and tension (Haskell et al. 1994).

It is, however, not clear what level of physical activity is needed to convey the benefit. Moderate activity levels done at least 30 minutes, repeated over several times a week seem to be protective (Pate et al. 1995, Fletcher et al. 1996, NIH consensus 1996, Blair and Cooper 1997).

People who are engaged in moderate-intensity activities are more likely to continue than those who are engaging in high-intensity activities (Pate et al. 1995, NIH consensus 1996). Activities such as walking, gardening, fishing, bicycling, house work, farm work, running/jogging, hiking, stair-climbing, rowing, swimming, soccer, basketball, yard work, dancing and home exercise have been found to be beneficial when performed regularly (Pate et al. 1995, NIH consensus 1996). The greatest benefit may be obtained when changing physical activity from a sedentary lifestyle to moderately active one and the degree of improvement may increase at higher physical activity (Pate et al. 1995).

Age and Gender Differences

Regular physical activity produces physiological improvement regardless of age and sex (Paffenbearger et al. 1986, Fletcher 1991, Fletcher et al. 1992, Pate et al. 1995, U.S. Surgeon General 1996, NIH 1996, Shephard 1997, Blair and Wei 2000), although the magnitude of the changes depends on the initial fitness status, age and type of physical activity. It has also documented that physical activity especially moderate intensity exercise extends the period of active life expectancy by reducing the time period of functional impairments in both older males and females (DiPietro 1996, Davis et al 1998, Pascatello 1999). Ability to improve the physical fitness levels in both males and females may be aged-related. Older individuals have often shown less improvement when they begin with physical activity later in life than younger counterparts who start with physical activity at the same initial level of fitness (Wannamethee et al. 1998, Pescotello 1999). However, older people generally elicit the same beneficial adaptations in response to physical activity. Endurance physical training has been suggested to have several physiological benefits for younger and older people (Hagber 1994). The benefits include improvement of many risk factors for CHD such as blood pressure, HDL-c, diabetes mellitus, obesity, blood coagulation, and heart function (Hagber 1994).

Obesity

Generally, a negative association has been observed between the level of physical activity and the level of body fat (Dauncey 1990, Bourchard et al. 1993b). However, many studies of physical activity and its effects on body fatness have shown that the net energy deficit that can be produced by physical activity is small and not likely to

induce major changes in body weight and adipose tissue (Hill et al. 1994). Thus, a physical activity programme designed for weight loss should aim at a considerable increase in the habitual energy expenditure rate (Bourchard et al. 1993b, Dèspre 1994). The reduction of body fat has shown to be more easily achieved and maintained when physical activity is combined with a low energy diet as a part of the weight-loss programs (Bouchard et al. 1990, Kayman 1990, Després and Lamarche 1993).

Physical activity has also been associated with lower levels of adipose tissue. A study conducted among young and middle-aged males showed that physical activity decreased adipose tissue, independent of energy intake (Ballor and Keesey 1991, Duncan et al. 1991, Seidell et al. 1999). Regular physical activity facilitates protein retention in skeletal muscle, while at the same time retarding its rate of breakdown, leading to an increase in fat free body mass (Després and Lamarche 1993).

It has been shown that individuals with modest obesity (BMI; 27-30) respond more favourably to physical activities than those with accumulated fat, especially around the lower body and hips (Goldstein 1992). The possible sex difference in the responsiveness of weight loss to physical activity may relate to differences in fat deposits in the upper body and the abdominal regions; male-pattern obesity is highly responsive to neurohumoral stimulation (Després and Lamarche 1993). This deposit of body fat is especially mobilised during physical activity compared to fat deposited in the gluteal and femoral regions female-pattern obesity (Després and Lamarche 1993). Furthermore, maintenance of even modest weight loss is sufficient enough to

improve glycemic control, reduce blood pressure, and normalise lipid profiles (Blair et al. 1995b).

Blood Pressure

Physical activity lowers blood pressure. Several well-controlled studies have shown an inverse relationship between regular physical activity and blood pressure (Blair et al. 1983, Hartung et al. 1990, Fagard and Tipton 1994, Kokkinos et al. 1995, Fagard 1999 and 2000). Numerous surveys show a lesser incidence of hypertension in those who are physically active and fit (Blair et al. 1984, Fagard and Tipton 1994, Kokkinos et al. 1995). Most studies have recommended an endurance type of physical activity to be beneficial to individuals with hypertension and have been shown to decrease both systolic and diastolic blood pressure (Am. Col. Sport Med. 1993). The most commonly cited mechanism to explain the effect of physical activity in lowering blood pressure is associated with decrease in the sympathetic nervous system activity, resulting in decreasing peripheral resistance (Amery et al. 1985, Hagberg 1989, Am. Col. Sport Med. 1993, Berg et al. 1994, Blair et al. 1995b). The sympathetic nervous system has been proposed as a mediating factor through a reduction of the catecholamine, especially noradrenalin concentration, increased baro-receptors sensitivity (Convertino et al. 1990, Tipton 1991), and decreased blood renin activity, or insulin concentration (Tanji 1992).

Another mechanism behind the blood pressure reduction associated with physical activity is the increase of cardiac output and the decrease in systemic vascular resistance (Folkow 1982). It may also alter the renin-angiotensin system, with

subsequent decreases in circulating renin levels, although the changes in renin have not been documented uniformly (Tanji 1992).

Furthermore, there is strong evidence that endurance training when combined with a low fat and salt diet, which results in weight loss, effectively reduces blood pressure, (Tanji 1992). However, the decrease in blood pressure associated with physical activity and diet is not dependent on an absolute loss in weight, and is not necessarily related to a loss in percentage of body fat. It was found in an 18-month diet and walking program that those who lost weight also had decreased blood pressure but not all those who had demonstrated a drop in blood pressure, had lost weight (Tanji 1992).

Blood Lipids

Regular physical activity particularly endurance has been related to favourable blood lipid profiles (Williams et al. 1990, Berg et al. 1994, Kokkinos and Fernhall 1999, Wannamethee and Shaper et al. 2001). In both cross-sectional and longitudinal studies in both males and females have found that physical activity, particularly endurance training induces changes in lipoprotein patterns, which leads to the reduction of coronary atherosclerosis risk and its manifestations. Physical activity induces changes in lipoprotein patters, including reduction of triglycerides, VLDL-c and LDL-c, and increase of HDL-c levels (Wood et al. 1984, Williams et al. 1990, Wood and Stefanick 1990, Crouse et al. 1997). Physical activity may influence the activity of key enzymes in lipoprotein metabolism, thus improving lipid profile, and may also have selective effects on total body fat distribution (Duncan et al. 1991, Cox 1994, Hardman 1995, Wannamethee and Shaper 2001).

The protective role of increased physical activity against CHD may partly be explained by the increase in HDL-c levels as observed in both females and males (Stefanick and Wood 1994, Pate et al. 1995, Kokkinos and Fernhall 1999, Wannamethee and Shaper 2001). The increase in HDL-c is mainly due to increased levels of the cholesterol-rich HDL-2 subfraction and is accompanied by decreases in triglycerides levels (Thompson et al. 1991). This may be mediated by increased activity of lipoprotein lipase (LPL) and cholesterol acyltransferase (LCAT) and reduced hepatic lipase activity (Wood and Stefanick 1990).

Most studies of physical activity and lipoprotein metabolism on CHD have been concentrated on HDL-c. Few studies deal with the influence of physical activity on the metabolism of LDL-c. The below mentioned studies have shown lower levels of LDL-c in physically active individuals than in inactive people, but they were not able to show a significant decrease in LDL-c (Lakka and Salonen 1992, Stefanick and Wood 1994, Berg et al. 1994, Leon and Sanches 2001). The exact mechanisms by which LDL-c levels are reduced, has not yet been established. An enhanced catabolism of VLDL-c and IDL-c (Thompson et al. 1991) due to increased LPL (lipoprotein lipase) activity, as well as an increased activity of LDL receptors (Williams et al. 1992) may be involved. The physical activity induced reduction in LDL-c levels has been shown to be greater when accompanied by weight loss (Tran and Weltman 1985)

It has also been shown that regular physically active individuals have lower triglycerides and VLDL-c levels than their physically inactive counterparts (Wood and Stefanick 1990). This effect is probably mediated through an increase of LPL

activity resulting in the clearance of circulating triglycerides, and conversion of VLDL-c into HDL-c (Cox 1994).

Diabetes Mellitus

Physical activity, especially endurance training, is important in managing both diabetes types: type I and type II (Wang et al. 1989, Helmrich et al. 1991, Law and Reaven 1991, Manson et al. 1991, Giacca et al. 1994). Regular physical activity improves insulin sensitivity and glucose tolerance (Law and Reaven 1991, Landry and Allen 1992, Giacca et al. 1994, Lynch et al. 1996). This increased insulin action is associated with an increase in the insulin-regulating glucose transporters, GLUT 4, and enzymes responsible for the phosphorylation, storage, and oxidation of glucose (Giacca et al. 1994). Regular physical activity may also improve hepatic glucose production by increasing the control of insulin over blood free fatty acid (FFA) levels. An elevation in FFA levels, which is associated with obesity and non-insulin-diabetes mellitus, stimulates hepatic gluconeogenesis, which in turn stimulates hepatic glucose production. An increase in blood FFA levels also inhibits skeletal muscle glucose uptake and storage. Therefore, an improved control over blood FFA level would serve to increase peripheral glucose clearance as well as to reduce hepatic production (Landry and Allen 1992, Després and Lamarche 1993, Giacca et al. 1994).

Regular physical activity decreases glucose concentration levels in both insulin dependent and non-insulin dependent diabetic patients (Law and Reaven 1991). Differences in physical activity levels are associated with differences in the prevalence of diabetes, independent of age, diet and body weight (Taylor et al. 1984).

Thus, increased physical activity may prevent the development of diabetes type II (Helmrich et al. 1991, Manson et al. 1991 and 1992a,b).

Blood Coagulation Factors

Regular physical activity, especially endurance training, provides favourable effects on thrombotic function (Rauramaa and Salonen 1994, Blair et al. 1995, Pate et al. 1995, Fletcher et al. 1996, El-Sayed et al. 2000). Physical activity influences platelet function (Rauramaa and Salonen 1994). It has been observed that physical activity may provide an increase in mean platelet volume, platelet number, and decrease platelet activation (Rauramaa and Salonen 1994). Regular physical activity of low to moderate intensity has also an inhibitory effect on platelet adhesion and aggregation at rest or during physical activity (Szymanski and Pate 1994, Rauramaa et al. 2001).

Regular physical activity also increases factor VII activity (Davis et al. 1976, Rauramaa et al. 2000). The effect of physical activity on factor VII is probably mediated through beta-adrenergic stimulation (Cohen et al. 1968). An inverse relationship between fibrinogen and physical activity and fitness has been found (Väisänen et al. 1997). This may be due to increased endogenous tissue plasminogen activation, which may be caused by the circulation of adrenaline (Rauramaa and Salonen 1994). Physical activity also causes a favourable effect on PAI-1 levels (Gris et al. 1990), by stimulating fibronolytic activity, together with the increase in blood coagulation.

Blood Homocysteine

There exist relatively few studies of effects of physical activity on blood homocysteine (Hcy) Nygård et al. (1995), compared blood Hcy level to self-reported (questionnaire-based) physical activity in males aged 40-56 years of age, and found an inverse association between blood Hcy and physical activity level. The significant differences were observed in older participants with high level of physical activity. On the other hand, studies by Wright et al. (1998), De Crèe Cole et al. (1999 and 2000), de Bree et al. (2001) observed that blood Hcy levels are not affected by physical activity. Therefore, the physical activity level and its effects on high blood levels of Hcy, is still inconclusive

Metabolic Syndrome

Studies have shown an inverse relationship between physical activity and metabolic syndromes characteristics including, insulin sensitivity, triglycerides, HDL-c levels, hypertension, and fibrinolytic capacity (Barnard and Wen 1994). Physical activity has equally been shown to lower blood pressure, reduce serum triglyceride levels, improve insulin sensitivity, and increase HDL-c levels and the fibrinolytic capacity. Therefore, metabolic syndrome characteristics seem to respond positively to physical activity (Barnard and Youngren 1992, Barnard and Wen 1994).

Since diet and physical inactivity appear to be crucial in the pathophysiology of the syndrome, it is not surprising to find that physical activity, especially endurance type of physical training, when combined with a low-fat, high-complex-carbohydrate diet, may reverse the syndrome. Physical activity combined with dieting may play important roles in controlling or preventing insulin resistance (Barnard and Wen

1994), if one assumes that insulin resistance with elevated levels of insulin are the major cause of the syndrome. A single bout of physical exercise has shown to increase the insulin-like effect, by increasing skeletal muscle glucose transport (Barnard and Youngren 1992). This effect is observed at a time when serum insulin has decreased as a result of the physical activity-induced activation of the sympathetic nervous system (Barnard and Wen 1994).

Alcohol Consumption

There is no evidence to show an effect of physical activity levels in reducing or stopping alcohol use. Many studies have been conducted but have failed to show a significant association between alcohol consumption and physical activity levels (Wood and Stefanick 1990, Wankel and Sefton 1994). Furthermore, Murphy et al. (1986) who studied the role of physical activity as a supplemental factor in treatment programs for alcohol misuse did not find any clear relationship.

Cigarette Smoking

People who are physically active smoke less compared to the physically inactive (Wood and Stefanick 1990, Wankel and Sefton 1994). Marti et al. (1989) showed that cigarette smoking appeared to decrease as physical activity levels increase and that, adoption of a physical training program helped people to stop smoking. Previously, Davidson et al. (1975) had reported that individuals who adopt an active lifestyle soon find that cigarette smoking is not compatible with their new goals and priorities. Thus, it seems that many may be able to withdraw from their dependency on cigarette smoking behaviour by becoming more physically active.

In rehabilitation programs, endurance types of activities such as jogging are used to help gradual reduction of cigarette smoking. The more physical training, the less cigarette smoking and the more increase in HDL-c levels with an accompanying decline in blood pressure (Tuomilehto et al. 1986).

Psychosocial Stress and Behavioural Factors

Although, regular physical activity may improve various indices of psychological functioning (Folkins and Sime 1981, Bourchard et al. 1990b, McAuley 1994, Paffernbarger et al. 1994), the effects of physical activity on psychological health and well being associated with CHD are still controversial. However, Tomas et al. (1981) Landers and Petruzzello (1994), and Morgan (1994) reported that physical activity had beneficial psychological effects, such as increasing the capacity to cope with stress, anxiety, depression and tension and heightened in the sense of well-being. It was suggested that low-intensity physical activity, e.g. walking might be performed for relaxation rather than for a training effect (Sextion et al. 1989, Mobily et al. 1996). Therefore, from their point of view, relaxation physical activity may be of benefit in combating anxiety and depression.

In addition, several investigators have found positive effects from physical activity on self-esteem and psychological well-being, but these are not associated directly with CHD events (McAuley 1994).

CHAPTER 3. AIM OF THE STUDY

General objectives

The aim of the study was to estimate and compare risk factors for CHD in a random sample of middle-aged males and females in rural and urban population of Tanzania, with special reference to the relationship between physical inactivity and other coronary risk factors.

Specific objectives

To estimate and compare the PAL at work, home and during leisure time, and to relate PAL to the following factors, which are central for the incidence of CHD:

Anthropometrical measures

Body weight, height, body mass index, waist and hip circumferences, and waist-to-hip ratio.

Blood pressure

Systolic and diastolic blood pressure

Blood lipids

Total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides and free fatty acids.

Significance of the study

Data on risk factors for coronary heart disease (CHD) are still scarce in developing countries including many African countries such as Tanzania. It is assumed that the burden of CHD on the health system will be increasing in the future (Walker et al.

2001, and 2002). As a result of urbanization, more people are becoming physically inactive (Walker 2001). Due to the many beneficial effects of physical activity in combating CHD, it seemed of particular interest to assess the level of physical activity in rural and urban population groups of Tanzania, and study the relationship between physical inactivity and other CHD risk factors.

To my knowledge, the only study of the association between level of physical activity and coronary risk factors has been conducted among male black middle-aged, urban dwellers of metropolitan Cape Town (Sparling et al. 1994). It was found that all participants who engaged in regular physical activity had lower level of many CHD risk factors.

Mbalilaki conducted a preliminary study of the relationship between level of physical activity and CHD risk factors, among the indigenous urban and rural adult populations of Tanzania in one village in Bukoba district, and in the city of Dar-Es-Salaam in 1995. The CHD risk profile of the urban dwellers in that study was unfavourable compared to the rural population, particularly as regards the level of physical activity. Few of the urban dwellers participated in regular physical activity, and few of them were cigarette smokers and alcohol consumers compared with the rural population. In the rural population the prevalence of cigarette smokers and alcohol users were considered high, still their CHD risk profiles were favourable compared with urban subjects. The present work was carried out to estimate and compare the physical activity level (PAL), at work, home and during leisure time, and to relate PAL to selected risk factors, which are central for the incidence of

CHD. Results from the study will provide new information as regards to the risk of CHD in the rural and urban populations of Tanzania.

CHAPTER 4. MATERIAL AND METHODS

4.1 STUDY POPULATION

This cross-sectional study is a continuation of a smaller preliminary study used for my master's degree, conducted in 1997, which investigated the level of habitual physical activity and its relationship to some CHD risk factors including blood pressure, obesity, cigarette smoking, and alcohol consumption. The study population included one rural and one urban group. Permanent residents of Kabale village in Bukoba district was chosen as the rural population, whilst the urban population was chosen from academics and administrators permanently employed by the Muhimbili University College of Health Sciences. The CHD risk profile of the urban dwellers in that study was unfavourable compared to the rural population, particularly with regards to the level of physical activity.

The current study population included several rural and urban samples. The rural sample was drawn from nearby villages in the Dar-Es-Salaam particularly Temeke district - Kigamboni division villages: Kimbiji, Kizito-Huonjwa, and Mikenge. Other rural samples were drawn from remote villages in Handeni Tanga and Monduli Arusha, involving mainly farmers depending on an agricultural cash economy. The urban samples consisted of National Insurance Co-operation, Air Tanzania Co-operation employees and Temeke suburb: Wales, miburani, Changòmbe, Mtoni, Tandika and Uwanja wa ndege residents in the city of Dar-Es-Salaam. Other urban samples were drawn from Tanzania Revenue Authority, CRDB Bank Limited, and Tanzania electricity Company in Morogoro town. The participants for both studies

were selected on a random basis, from a list of all adults aged 30 to 60 years permanently resided and employed in those selected areas. The 1997 study included 200 participants. The present study included 985 participants from a sample of about 2000 people, 501 rural (256 females and 245 males), and 484 urban (255 females and 229 males) respectively. These subjects responded to invitation letters, sent to 600 rural female and male subjects, and 600 urban female and male subjects. Thus, the response rates in the rural and urban areas were 84% and 81%, respectively. All subjects were supposed to be in "good health" without any chronic disease, alcohol or drug abuse, and females were not supposed to be pregnant. The subjects were in a non-fasting condition.

4.2 DATA COLLECTION

Data were collected during two periods. The first period was done in August and September 1998 in Temeke, Handeni, and Monduli. The data collection was done at the local administration offices or the village's primary schools. The second was carried out in November and December 1999 in National Insurance Co-operation, Air Tanzania Co-operation employees in the city of Dar-Es-Salaam, Tanzania Revenue Authority, CRDB Bank Limited, and Tanzania electricity Company in Morogoro town. The data collection took place at the work places. I administered a personal interview, using a Swahili structured questionnaire. After the questionnaire was filled in, blood pressure was taken, and finally a blood sample was drawn.

Permission to undertake the investigation was obtained from the regions and districts administration offices in Dar-Es-Salaam, Arusha and Morogoro. Muhimbili

University College of Health Sciences Ethical Committee approval was obtained for the study.

4.3 QUESTIONNAIRE

A questionnaire on lifestyle such as physical activity at work, home and leisure-time was modified from the Paffenbarger et al. (1993) physical activity questionnaire, and The MONICA optimal study of physical activity (Jones 1997; MOSPA). Diet, alcohol and cigarette consumption, as well as past and present health status were developed with certain adjustments to Tanzanian conditions (see enclosed questionnaire). The questionnaire, translated into Swahili for use in the survey, especially in rural areas (see enclosed questionnaire), contained:

1) Information on past and present health status including personal health status and family health history.

2) Information on physical activity. The subjects were asked about their daily physical activity at work, during leisure, and in housework. Time spent walking or biking to work was asked too. Physical activity was calculated and classified in METs. The MET values for each activity were obtained from existing tables (Caspersen and Powell 1986, Lee et al. 1992). *A MET is defined as a multiple of the resting metabolic rate.* Therefore, 1 MET is equivalent to a resting oxygen uptake of about 250 ml/min for an average male, and 200 ml/min for an average female. Likewise energy expenditure values were calculated from METs values as follows: Kcal/kg/day = $\sum(N \times D \times MET/365)$. Where «N» is the number of occasions of activity, in the past 12 months, «D» is the average duration in hours of that activity,

and «METs» is the energy cost of the activity expressed as kilocalories expended per kilogram of body weight per hour of activity (kcal/kg/hour).

3) Dietary and social habits were recorded and included diet information as well as whether or not the subject consumed alcohol or was a current cigarette smoker. The subjects were asked to respond for each of several food and drinking items consumed during the past 24 hours. Based on the diet data, each subject was assigned to one of 4-diet groups: *low fat/low carbohydrate, low fat/high carbohydrate, high fat/low carbohydrate, and high fat/high carbohydrate.* Otherwise no attempt was made to relate specific diets to coronary risk factors in blood.

4.4 ANTHROPOMETRY

Anthropometrical measurements including body height and weight were taken using standard protocols, and were performed while wearing light clothes and without shoes. Height was measured with a metal tape fixed to a wall and a right-angle device. Weight was measured to the nearest 0.5 kg by using a scale (SECA model 708). The body mass index (BMI) was calculated by the following formula: weight (kg)/height^2 (m^2). Waist and hip circumferences were measured by using a tape measure in a standing position. Waist circumference was measured at the smallest horizontal girth between the costal margin and the iliac crests or at the umbilicus if no narrowest point existed. Hip circumference was measured at the greatest circumference at the level of greater trochanter the widest part of the buttocks. The waist-to-hip ratio (WHR) was expressed as the ratio of waist circumference to hip circumference. Expected normal reference values for WHR were 0.85 for females and 0.95 for males.

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4.5 BLOOD PRESSURE

Brachial artery blood pressure in the right arm was measured after 5-10 min of rest in a sitting position using an oscillometric minicomputer with an automatic measuring sequence (Tensoplus OSZ 2). A pull-on Velcro cuff for either thin or fat adults was wrapped around the upper arm. To reduce the possible effect of apprehension and anxiety on the blood pressure estimation (systolic and diastolic), three measurements were taken and the mean of the last two used.

4.6 BLOOD VARIABLES AND ANALYSIS

A 10-ml venous blood sample was drawn and collected into appropriate vacutainers, and blood glucose was analysed immediately at the survey site. The glucose was measured by using the Hemo-Cue blood glucometer, using an enzymatic method reported by Banauch et al. (1975). The rest of the blood sample was kept in a cold box to be later centrifuged, and the serum was kept at - 45 ^{0}C before transportation to Norway and was packed in dry ice until further analysis. Serum total cholesterol, triglycerides, HDL-c, FFA and albumin were analysed using reagents manufactured by Boehringer Mannheim (Germany), at the Department of Preventive Medicine and Epidemiology, University of Oslo, Norway. The standard serum Seronorm Lipid (Sero AS, P.O. Box 24, N-1361 Billingstad, Norway) served as control. Serum total cholesterol was determined enzymatically as described by Trinder (1969), Seidell et al. (1983). Determination of HDL-c (high-density lipoproteins) was made after precipitation of chylomicrons, VLDL-c, and LDL-c, using phosphotungstic acid and magnesium ions (Burstein et al. 1970, and Lopes-Virella et al. 1977). Centrifuging left only HDL-c in the supernatant, to be subsequently determined enzymatically.

Serum triglycerides were assessed enzymatically according to Trinder (1969) and Wahlefeld (1974). The method was based on the enzymatic hydrolysis of triglycerides with subsequent determination of liberated glycerol, by an enzymatic and colorimetric assay. FFA was measured enzymatically as explained by Jebens and Sejersted (1992). The method is based on the principle that 1 mole of FFA will produce 2 moles of NAD^+, which can be measured fluorometrically, with exitation at 361.5 nm and emission at 458 nm. The involved enzymes are acyl CoA synthetase, myokinase, pyruvate kinase and lactate dehydrogenase. Albumin was assessed by the bromcresol green (BCG) method (Doumas et al. 1971).

4.7 STATISTICAL ANALYSIS

Data was analysed using the Statistical Package for Social Sciences for windows (SPSS; release 11). The descriptive statistics (mean and standard deviation) of continuous data were computed for the two populations and sex. For nominal variables like diet etc, the percentages in each category were calculated for comparative purposes. The Chi-square test was used to investigate the statistical significance of the association between categorical variables. The non-parametric 2-sample test (Mann-Whitney) was used to assess statistically significant differences of continuous variables between populations and sex groups. The distributions of the data were checked and are presented as histograms in Appendix (1) Pearson rank order (two-tailed *t*-tests) correlations were calculated between continuous variables. Multiple regression analysis was carried out to model the predictors of major outcome variables of the study (with calculation of standardized regression coefficients, beta). A p-value of 0.05 or less was considered as indicative of

statistical significance. All p-values less than 0.0001 have been rounded off and expressed as <0.001.

CHAPTER 5. RESULTS

5.1 CHARACTERISTICS OF THE STUDY POPULATION

Characteristics of the study population are shown in **Table 1.** The rural group had significantly lower height, body weight, body mass index (BMI), waist and hip circumferences, and waist-to-hip ratio (WHR) than the urban group, although they were on average 5 years older than the urban subjects.

TABLE 1. Characteristics of the study population (mean ±SD)

	All	Rural	Urban	P value
N	985	501	484	
Age (*years*)	43.8±24.2	46.0±9.3	41.6±8.0	0.001
Height (*cm*)	162.4±9.0	161.8±8.6	163.1±9.3	0.004
Weight (*kg*)	65.8±15.6	59.2±13.5	72.7±14.6	0.001
BMI (kg/m^2)	24.9±5.9	22.5±5.0	27.4±5.6	0.001
Waist cir. (*cm*)	82.1±18.5	73.5±19.2	90.9±12.8	0.001
Hip cir. (*cm*)	90.8±19.1	83.9±22.0	98.0±11.8	0.001
WHR	0.91±0.1	0.88±0.1	0.93±0.1	0.001

BMI = body mass index, Waist cir. = waist circumference, Hip cir. = hip circumference, WHR = waist-to-hip ratio

In **Table 2** characteristics of the study population by gender are presented. Females of the rural group had significantly lower age, height, and body weight than the males, while the BMI was higher, and waist and hip circumference larger ($P < 0.001$). Compared with the urban females, the rural females had appreciably lower body weight and BMI, and smaller waist and hip circumferences ($P < 0.001$). Similar differences were observed when comparing rural and urban males ($P < 0.001$). Urban females had significantly lower height, while the BMI was higher than in the urban males ($P < 0.001$).

TABLE 2. Characteristics of the study population by gender (mean ±SD)

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
Age (*years*)	45.1±9.3	47.0±9.2 [a]	41.2±8.2 [b]	41.9±7.8 [c]
Height (*cm*)	157.1±7.0	166.7±7.2 [a]	157.9±7.4	167.6±8.4 [d]
Weight (*kg*)	57.5±15.0	60.8±11	71.4±15.5	73.8±13.7 [c]
BMI (kg/m^2)	23.2±5.7	21.8±4.0 [a]	28.6±6.0 [b]	26.3±5.1 [c, d]
Waist cir.(*cm*)	75.5±18.1	71.4±19.9 [a]	89.2±13.1 [b]	92.4±12.3 [c, d]
Hip cir. (*cm*)	88.3±20.8	79.4±22.3 [a]	100.0±13.0 [b]	96.2±10.4 [c]
WHR	0.9±0.1	0.9±0.1	0.9±0.1	1.0±0.1

a) vs. rural females, b) vs. rural females, c) vs. rural males, d) vs. urban females BMI = body mass index, Waist cir. = waist circumference, Hip cir. = hip circumference, WHR = waist-to-hip ratio.

5.2 PHYSICAL ACTIVITY LEVEL OF THE STUDY POPULATION

As depicted in **Figure 1** (*A*), the mean physical activity level (PAL) was significantly higher in the rural than in the urban group ($P < 0.001$). Indeed, PAL in the rural group was approximately twice as high as the corresponding value for the urban group ($P < 0.001$). For both groups, no significant difference in mean PAL was observed between females and males **Figure 1** (***B***).

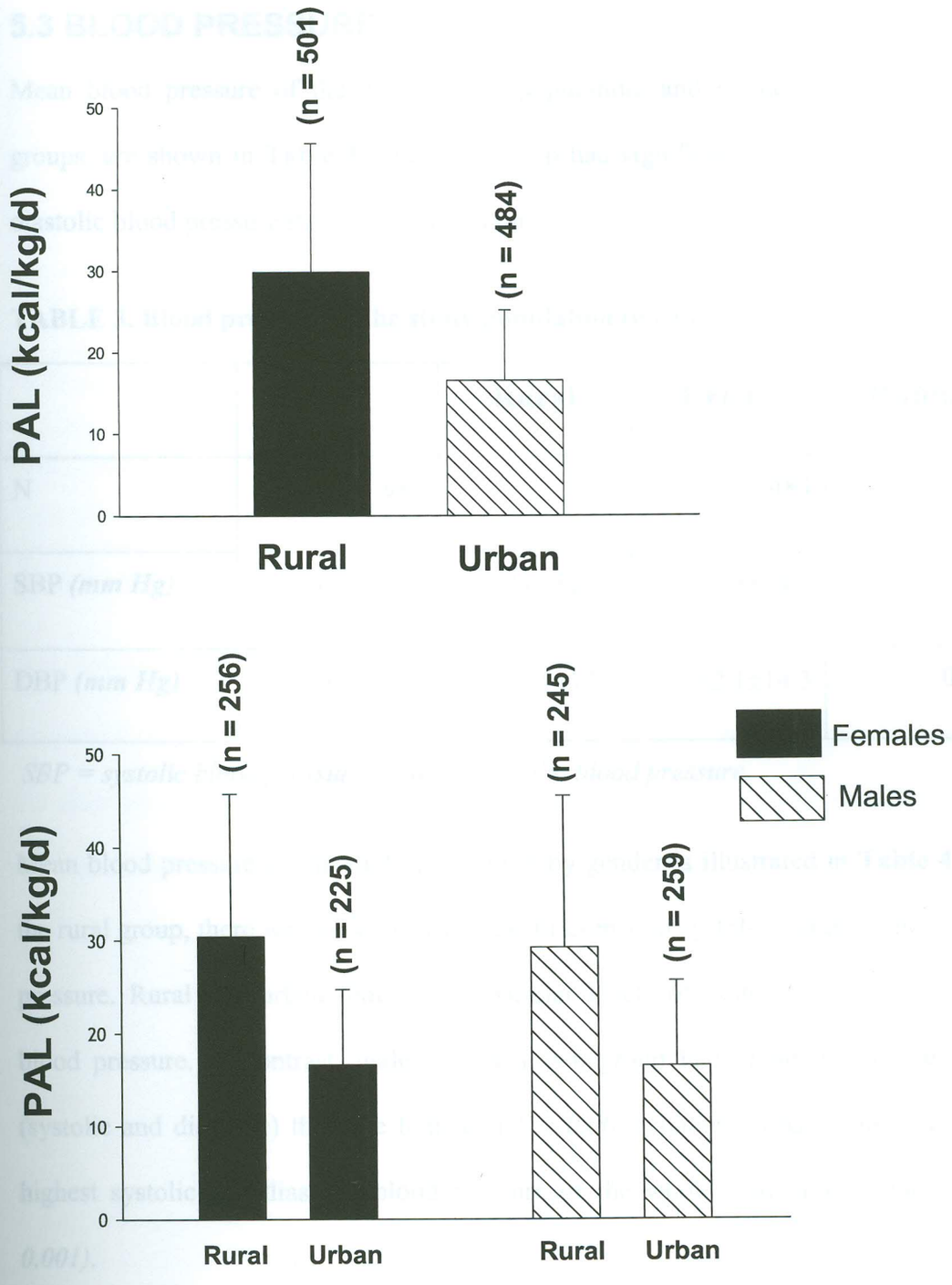


FIGURE 1. *Physical activity level (PAL) in all rural and urban subjects (A), and in each gender (B). Mean values with one SD and number of subjects are indicated on top of the bars.*

5.3 BLOOD PRESSURE

Mean blood pressure of the whole study population, and in the rural and urban groups, are shown in **Table 3.** The rural group had significantly lower systolic and diastolic blood pressure than the urban group.

TABLE 3. Blood pressure of the study population (mean ±SD)

	All	Rural	Urban	P value
N	985	501	484	
SBP ***(mm Hg)***	131.6±24.2	129.8±23.8	133.5±24.6	0.02
DBP ***(mm Hg)***	79.8 ±13.7	77.5±12.7	82.1±14.3	0.001

SBP = systolic blood pressure, DBP = diastolic blood pressure.

Mean blood pressure of the study population by gender is illustrated in **Table 4.** In the rural group, there was no significant sex difference in systolic and diastolic blood pressure. Rural and urban females had similar levels of systolic and of diastolic blood pressure. In contrast, males of the urban group had higher blood pressure (systolic and diastolic) than the females ($P < 0.001$). Indeed, urban males had the highest systolic and diastolic blood pressure of the whole study population ($P < 0.001$).

TABLE 4. Blood pressure of the study population by gender (mean ±SD)

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
SBP ***(mm Hg)***	129.4±25.2	130.1±21.7	130.2±23.9	136.4±24.8 [a, b]
DBP***(mm Hg)***	78.2±13.9	76.8±11.1	80.1±14.0	83.8±14.4 [a, b]

a) vs. rural males; b) vs. urban females. SBP = systolic blood pressure, DBP = diastolic blood pressure.

The prevalence of high systolic (≥ 140 mm Hg) and diastolic (≥ 90mm Hg) blood pressure is displayed in **Table 5.** The rural and the urban groups had approximately the same prevalence of high systolic blood pressure. By contrast, the prevalence of high diastolic blood pressure was considerably higher in the urban than in the rural groups.

TABLE 5. Prevalence (%) of high systolic and diastolic blood pressure in the study population

	All	Rural	Urban	P value
N	985	501	484	
SBP > 140 ***(mm Hg)***	31%	30%	31%	0.700
DBP > 90 ***(mm Hg)***	21%	16%	26%	0.001

SBP = systolic blood pressure, DBP = diastolic blood pressure.

The prevalence of high systolic and diastolic blood pressure of the study population by gender is exhibited in **Table 6**. In the rural group, there was no significant sex difference in the prevalence of high systolic blood pressure *($P < 0.06$)*. Females of the rural group presented a significantly higher prevalence of high diastolic blood pressure than the males *($P < 0.01$)*. In contrast, males of the urban group had a considerably higher prevalence of high systolic blood pressure than the females *($P < 0.05$) but not* diastolic blood pressure *($P < 0.1$)*. Thus, the increased prevalence of high blood pressure in the urban group is a result of the males.

TABLE 6. Prevalence (%) of high systolic and diastolic blood pressure in the study population by gender

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
SBP > 140 ***(mm Hg)***	31%	29%	28% [b]	36% [c,d]
DBP > 90 ***(mm Hg)***	20%	12% [a]	23% [b]	29% [c]

a) vs. rural females, b) vs. rural females, c) vs. rural males, d) vs. urban females. SBP= systolic blood pressure, DBP = diastolic blood pressure

5.4 BLOOD LIPIDS

Mean values of some blood lipids are demonstrated in **Table 7.** Compared with reported values in western countries, concentrations of all blood lipids were generally low in this study population. However, the urban group had slightly higher serum values of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), total cholesterol to high-density lipoprotein cholesterol ratio (TC/HDL-c ratio), and free fatty acids (FFA) than the rural group. The urban population also had higher level of triglycerides (TG), but the difference did not attain statistical difference.

TABLE 7. Blood lipid levels of the study population (mean ±SD)

	All	Rural	Urban	P value
N	985	501	484	
TC *(mmo/L)*	4.1±1.1	3.7±1.1	4.5±1.1	0.001
TG*(mmol/L)*	1.5±1.0	1.4±0.7	1.6±1.1	0.747
HDL-c *(mmol/L)*	1.0±0.3	1.0±0.3	1.1±0.3	0.001
LDL-c *(mmol/L)*	2.4±1.0	2.1±0.9	2.7±1.0	0.001
TC/HDL *ratio*	4.4±1.7	4.2±1.8	4.5±1.6	0.001
FFA *(mmol/L)*	0.3±0.2	0.2±0.2	0.3±0.2	0.001

TC = total cholesterol, TG = triglycerides, HDL-c = high-density lipoprotein cholesterol, LDL-c = low density lipoprotein cholesterol, as calculated by the Friedewald et al. (1972) formula: LDL-c = TC – HDL-c – TG/2.2, TC/HDL-c = total cholesterol to high-density lipoprotein cholesterol ratio, FFA = free fatty acids.

Table 8 illustrates mean blood lipid concentration by gender. In the rural group, there were no significant sex differences in TC, TG, LDL-c, TC/HDL-c ratio and FFA concentration, but the HDL-c level was significantly higher in the females ($P < 0.001$). The rural females and males had significantly lower level of HDL-c and LDL-c than their urban counterparts ($P < 0.001$). The urban females demonstrated significantly lower levels of serum TG, and TC/HDL-c ratio than the males, but HDL-c was significantly higher ($P < 0.001$).

TABLE 8. Blood lipid levels of the study population by gender (mean ±SD)

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
TC ***(mmol/L)***	3.8±1.1	3.6±0.1	4.5±1.0	4.5±1.1
TG ***(mmo/L)***	1.4±0.6	1.5±0.7	1.4±1.0	1.8±1.2 [c]
HDL-c ***(mmol/L)***	1.0±0.4	0.9±0.3 [a]	1.2±0.3[b]	1.0±0.3 [c]
LDL-c ***(mmol/L)***	2.1±0.9	2.0±0.8	2.7±0.9[b]	2.7±10[c]
TC/HDL-c ***ratio***	4.1±1.3	4.3±2.2	4.2±1.6	4.8±1.6 [c]
FFA ***(mmol/L)***	0.2±0.2	0.2±0.2	0.3±0.2	0.3±0.2

a) *vs. rural, females; b) vs rural males; c) vs. urban, females TC = total cholesterol, TG = triglycerides, HDL-c = high-density lipoprotein cholesterol, LDL-c = low density lipoprotein cholesterol, as calculated by the Friedewald et al. (1972) formula: LDL-c = TC – HDL-c – TG/2.2, TC/HDL-c = total cholesterol to high-density lipoprotein cholesterol ratio, FFA = free fatty acids.*

The prevalence of hypercholesterolemia (≥ 5.2 mmol/L) is displayed in **Table 9**. The prevalence of hypercholesterolemia was considerably lower in the rural group than in the urban groups.

TABLE 9. Prevalence (%) of hypercholesterolemia in the study population

	All	Rural	Urban	P value
N	985	501	484	
TC ≥ 5.2 ***(mmol/L)***	16%	8%	24%	0.001

TC = total cholesterol

The prevalence of hypercholesterolemia of the study population by gender is shown in **Table 10**. In both groups, there was no marked sex difference in hypercholesterolemia prevalence. Rural females had significantly lower prevalence of hypercholesterolemia than urban females *($p<0.001$)*. The rural males also presented lower prevalence of hypercholesterolemia than urban males.

TABLE 10. Prevalence (%) of hypercholesterolemia in the study population by gender

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
TC ≥ 5.2 *(mmol/L)*	9%	7%	22%[a]	26%[b]

a) vs. rural females, b) vs. rural males. TC = total cholester

CORRELATIONS BETWEEN VARIOUS CORONARY RISK FACTORS.

Table 11 presents the Pearson bivariate correlation coefficients for some CHD risk factors in the study population. The physical activity level (PAL) was inversely related to most of the selected risk factors of CHD, including body mass index (BMI), body weight, diastolic and systolic blood pressure, waist-to-hip ratio (WHR), waist and hip circumferences, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG), and total cholesterol to high-density lipoprotein cholesterol ratio (TC/HDL-c) ratio. The strongest inverse relationship was between PAL and BMI. Systolic blood pressure was positively correlated with diastolic blood pressure, BMI, age, body weight, waist circumferences, WHR, TG, TC, and TC/HDL-c ratio, hip circumference, LDL-c, but inversely with height. Diastolic blood pressure was positively correlated with BMI, body weight, WHR, TC, waist circumferences, age, LDL-c, TG, hip circumferences and negatively with height. BMI was positively correlated with body weight, waist and hip

circumferences, TC, LDL-c, WHR, TC/HDL-c ratio, and TG, but as expected, inversely with height. Body weight was positively correlated with TC, waist and hip circumferences, height, LDL-c, WHR, TG, and TC/HDL-c ratio. Height was positively correlated with body weight, WHR, TG, but inversely with age. Waist circumference was positively correlated with hip circumference, TC, WHR, LDL-c, TC/HDL-c ratio, and HDL-c. TC was positively related to LDL-c, TC/HDL-c ratio, hip circumference, and FFA. HDL-c was positively related to TC, and FFA, but negatively correlated with TG and TC/HDL-c ratio. LDL-c was positively correlated to TC/HDL-c ratio. TG was positively correlated with TC/HDL-c ratio, WHR, and hip circumference.

TABLE 11. Bivariate correlation coefficients between some coronary risk factors

Coronary risk factors	r	P -value
PAL *(kcal/kg/d)*		
BMI (kg/m^2)	-0. 36	0.001
Weight (cm)	-0. 32	0.001
DBP (mm Hg)	-0. 30	0.001
SBP (mm Hg)	-0. 28	0.001
WHR	-0. 23	0.001
Waist cir. (cm)	-0. 20	0.001

TC (mmol/L)	-0. 18	0.001
LDL-c (mmol/L)	-0. 16	0.001
Hip cir. (cm)	-0. 11	0.001
TG (mmol/L)	-0. 11	0.001
TC/HDL-c ratio	-0.14	0.001
SBP ***(mm Hg)***		
DBP (mm Hg)	0. 77	0. 001
BMI /kg/m^2)	0. 36	0. 001
Age (years)	0.30	0. 001
Weight (cm)	0.26	0. 001
Waist cir. (cm)	0.16	0. 001
WHR	0.15	0. 001
TG (mmol/L)	0.15	0. 001
TC (mmol/L)	0.13	0. 001
TC/HDL-c ratio	0.10	0. 001
Hip cir. (cm)	0.09	0. 001
LDL-c (mmol/L)	0.08	0. 001
Height (cm)	-0.08	0. 001
DBP ***(mm Hg)***		

BMI /kg/m^2)	0.37	0. 001
Weight (cm)	0.34	0. 001
WHR	0.22	0. 001
TC (mmol/L)	0.21	0. 001
Waist cir. (cm)	0.18	0. 001
Age (years)	0.17	0. 001
LDL-c (mmol/L)	0.16	0. 001
TG (mmol/L)	0.11	0. 001
Hip cir. (cm)	0.10	0. 001
Height (cm)	-0.06	0. 001
BMI ***(kg/m^2)***		
Weight (cm)	0.87	0. 001
Waist cir. (cm)	0.60	0. 001
Hip cir. (cm)	0.56	0. 001
TC (mmol/L)	0.32	0. 001
LDL-c (mmol/L)	0.29	0. 001
WHR	0.18	0.001
TC/HDL-c ratio	0.15	0. 001
TG (mmol/L)	0.14	0. 001

Height (cm)	-0.14	0. 001
Weight ***(cm)***		
Waist cir. (cm)	0.60	0. 001
Hip cir. (cm)	0.56	0. 001
TC (mmol/L)	0.33	0. 001
Height (cm)	0.32	0. 001
LDL-c (mmol/L)	0.29	0. 001
WHR	0.28	0. 001
TG (mmol/L)	0.20	0. 001
TC/HDL-c ratio	0.19	0. 001
Height ***(cm)***		
Weight (cm)	0.32	0.001
WHR	0.17	0. 001
TG (mmol/L)	0.11	0. 001
Age (years)	-0.12	
Waist cir. ***(cm)***		
Hip cir. (cm)	0.89	0. 001
TC (mmol/L)	0.31	0. 001

WHR	0.28	0. 001
LDL-c (mmol/L)	0.25	0. 001
TC/HDL-c ratio	0.13	0. 001
HDL-c (mmol/L)	0.09	0. 001
TC ***(mmol/L)***		
LDL-c (mmol/L)	0.91	0. 001
TC/HDL-c ratio	0.31	0. 001
Hip cir. (cm)	0.27	0. 001
FFA (mmol/L)	0.12	0. 001
HDL-c ***(mmol/L)***		
TC (mmol/L)	0.41	0. 001
LDL-c (mmol/L)	0.24	0. 001
FFA (mmol/L)	0.12	0. 001
TC/HDL-c ratio	-0.56	0. 001

TG (mmol/L)	-0.25	0. 001
LDL-c ***(mmol/L)***		
TC/HDL-c ratio	0.31	0. 001
TG ***(mmol/L)***		
TC/HDL-c ratio	0.50	0. 001
WHR	0.17	0. 001
Hip cir. (cm)	0.10	0. 001

Pearson correlation coefficient. SBP = systolic blood pressure, DBP = diastolic blood pressure, BMI = body mass index, Waist cir. = waist circumference, Hip cir. = hip circumference, WHR = waist- to hip-ratio, LDL-c = low-density lipoprotein cholesterol, HDL-c = high-density lipoprotein cholesterol, FFA = free fatty acids, TG = triglycerides, TC = total cholesterol, TC/HDL-c ratio = total cholesterol to high-density lipoprotein cholesterol ratio.

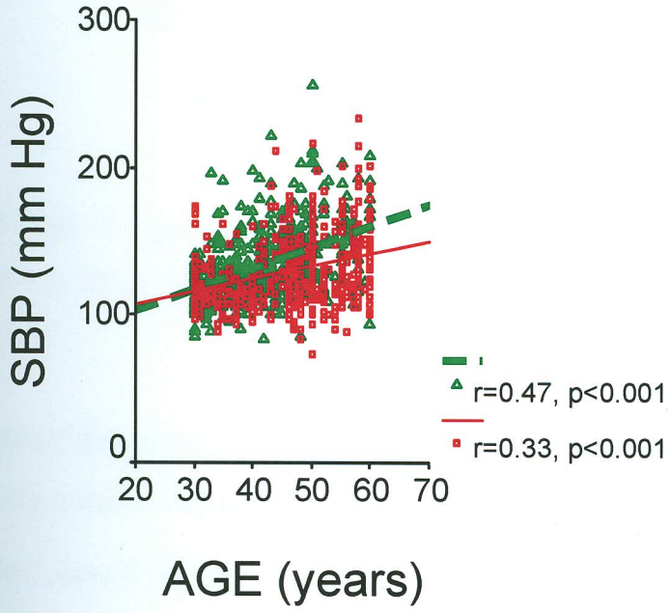
5.6 RELATIONSHIP BETWEEN SOME CORONARY RISK FACTORS.

Univariate scatter plots with regression lines for some coronary risk factors, in the rural and urban groups, are demonstrated in **Figure 2-13**

Blood pressure vs. age

Both systolic blood pressure (SBP; ***panel A***) and diastolic blood pressure (DBP; ***panel B)*** increased with increasing age **(Figure 2).** However, the slope of the

regression line was steeper for the urban than for the rural group ($P < 0.001$), so that for each decade there was an increase in systolic blood pressure of 15 mm Hg for the urban group versus 9 mm Hg for the rural group. The corresponding values for diastolic blood pressure were 6 mm Hg (urban group) and 2 mm Hg (rural group) respectively.



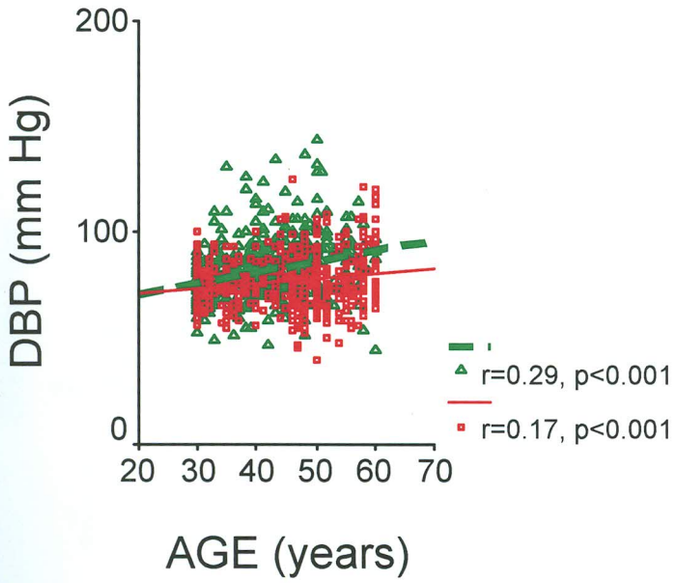


FIGURE 2. *Age-related increase in systolic blood pressure (SBP; upper A), and diastolic blood pressure (DBP; panel B), in the rural (■—■) and urban (▼-----▼) groups.*

Blood pressure vs. physical activity level

As illustrated in **Figure 3,** for both groups, systolic (SBP; panel A) and diastolic (DBP; panel B) blood pressure decreased with increasing physical activity (PAL). However, there was no group difference in the PAL related to decrease in blood pressure.

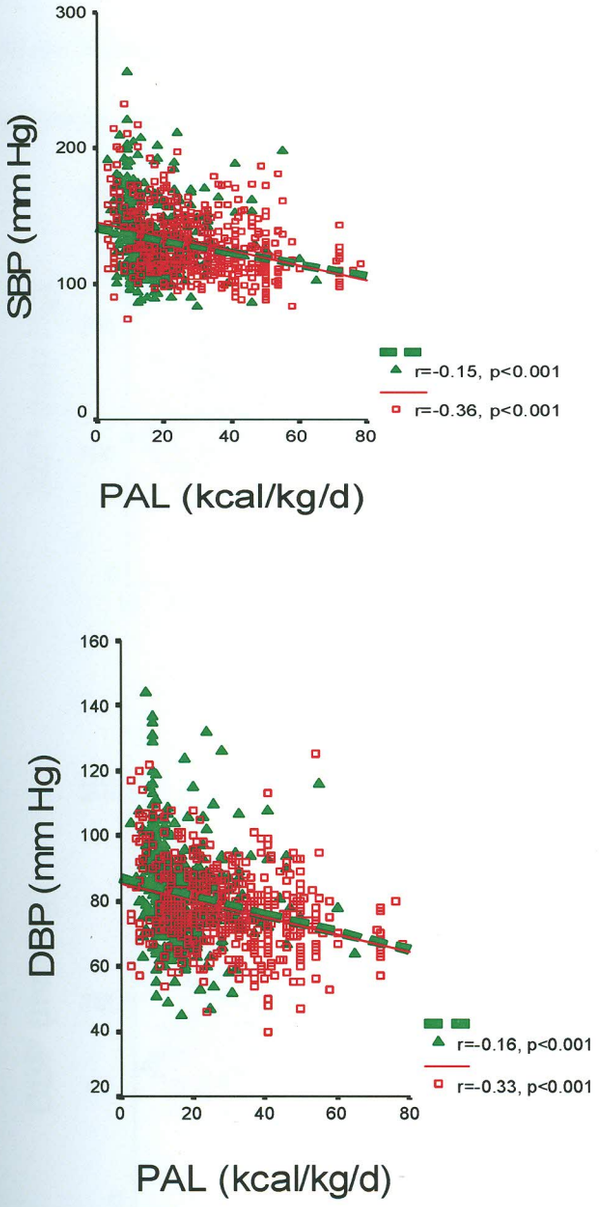


FIGURE 3. *Physical activity–related decrease in systolic blood pressure (SBP; panel A), and diastolic blood pressure (DBP; panel B), in the rural (■—■) and urban (▼-----▼) groups.*

Blood pressure vs. body mass index

For both groups, systolic (SBP; ***panel A***) and diastolic (DBP; ***panel B***) blood pressure increased with increasing BMI, but the slope of the increase did not differ significantly between the urban and rural group **(Figure 4).**

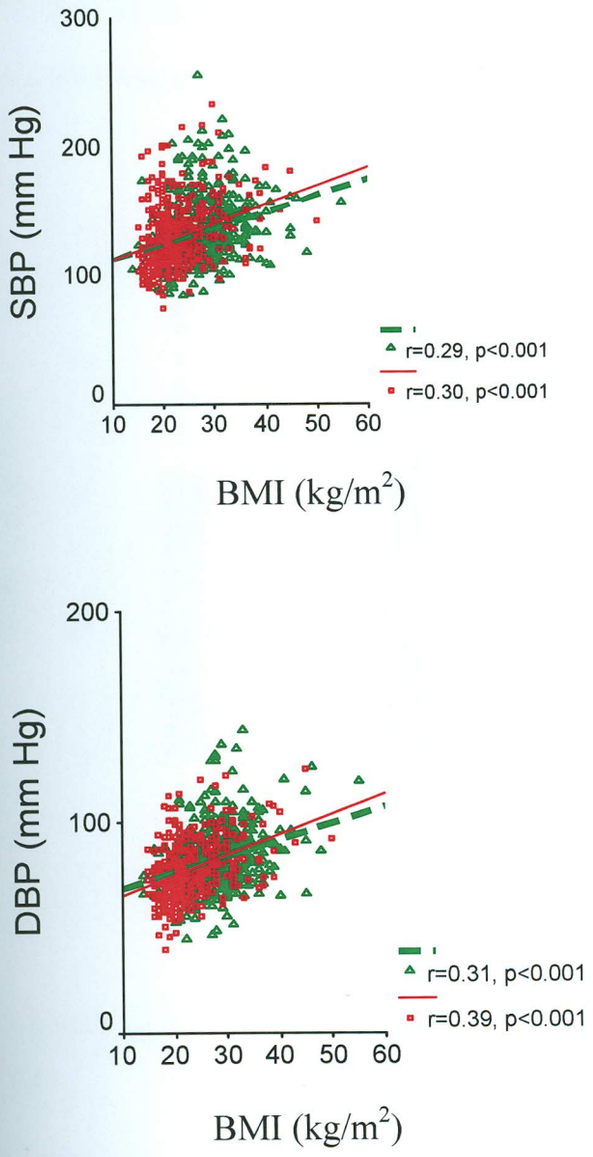


FIGURE 4. *Systolic blood pressure (SBP; panel A), and diastolic blood pressure (DBP; panel B) as related to body mass index (BMI) in the rural (■—■) and urban (▼-----▼) groups.*

Body mass index vs. age

As illustrated in **Figure 5,** the body mass index (BMI) increased with increasing age. For both groups, BMI increased only up to the age group 40-49 years. During the decade from 30-39 years to 40-49 years, the mean BMI of the rural group increased from 21 to 22 kg/m^2 and from 26 to 28 kg/m^2 in the urban group. For each age group, mean BMI was significantly higher in the urban than in the rural group.

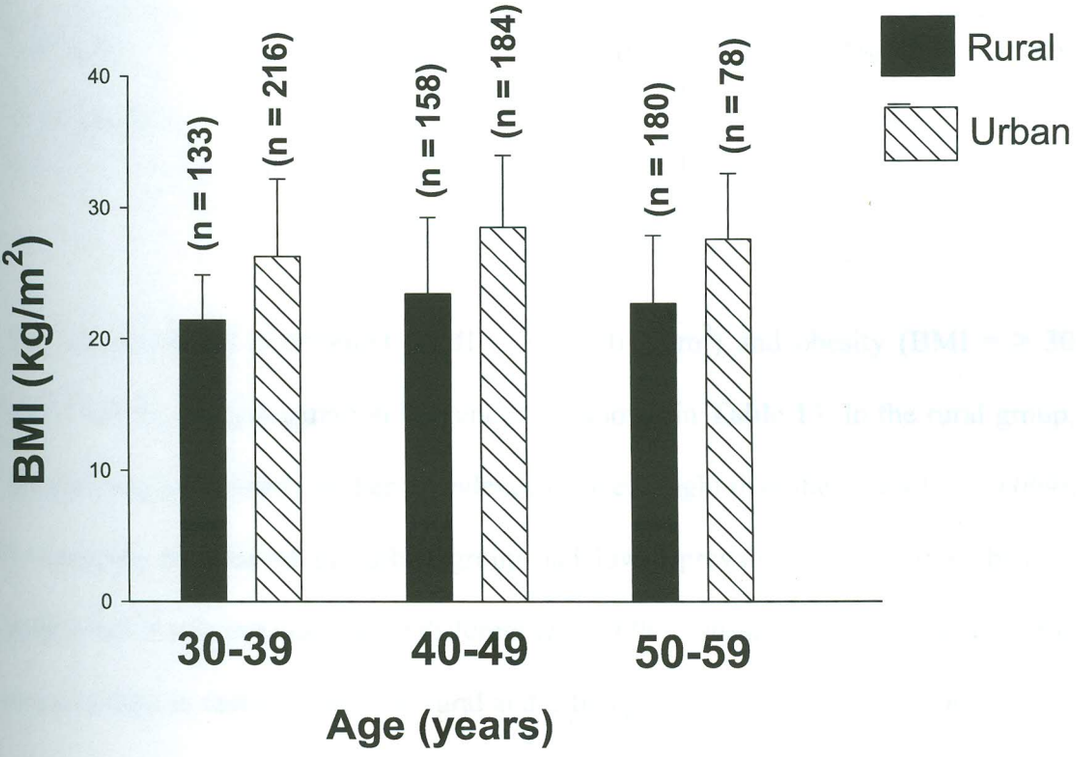


FIGURE 5. *Age-related increase in body mass index (BMI) in the rural and urban groups.*

The prevalence of overweight (BMI = 25 – 30 kg/m^2) and obesity (BMI = ≥ 30 kg/m^2) of the study population are shown in **Table 12**. The urban group had a much higher prevalence of both overweight and obesity compared with the rural group.

TABLE 12. Prevalence (%) of overweight and obesity in the study population

	All	Rural	Urban	P value
N	985	501	484	
Overweight 25 – 30 *(kg/m^2)*	29%	17%	41%	0.001
Obesity ≥ 30 *(kg/m^2)*	22%	10%	34%	0.001

The prevalence of overweight (BMI = 25 – 30 kg/m^2) and obesity (BMI = ≥ 30 kg/m^2) of the study population by gender are shown in **Table 13**. In the rural group, females had appreciably higher prevalence of overweight than the males ($P < 0.009$). In contrast, females of the urban group had lower prevalence of overweight than males, but it was not signifantly different ($P < 0.06$). Obesity was more prevalent in females than in males in both the rural and urban groups ($P < 0.02$, $P < 0.001$).

TABLE 13. Prevalence (%) of overweight and obesity in the study population by gender

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
Overweight 25 – 30 *(kg/m²)*	22%	13%[a]	37%[b]	45%[c,d]
Obesity ≥ 30 *(kg/m²)*	13%	7%[a]	45%[b]	25%[c,d]

a) vs. rural females; b) vs rural females; c) vs. rural males; d) vs. urban females

Waist circumference vs. body mass index

As expected, waist circumference increased with increasing BMI, and there was no difference in the slope of the regression lines for the urban and rural group **(Figure-6)**

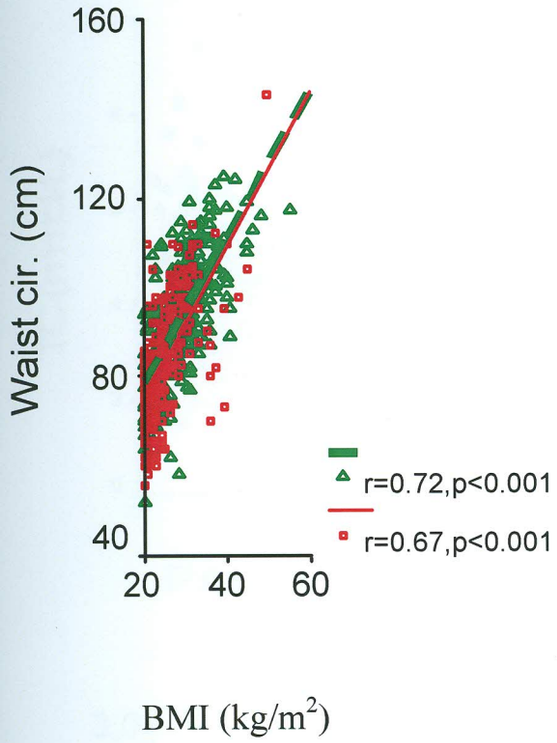
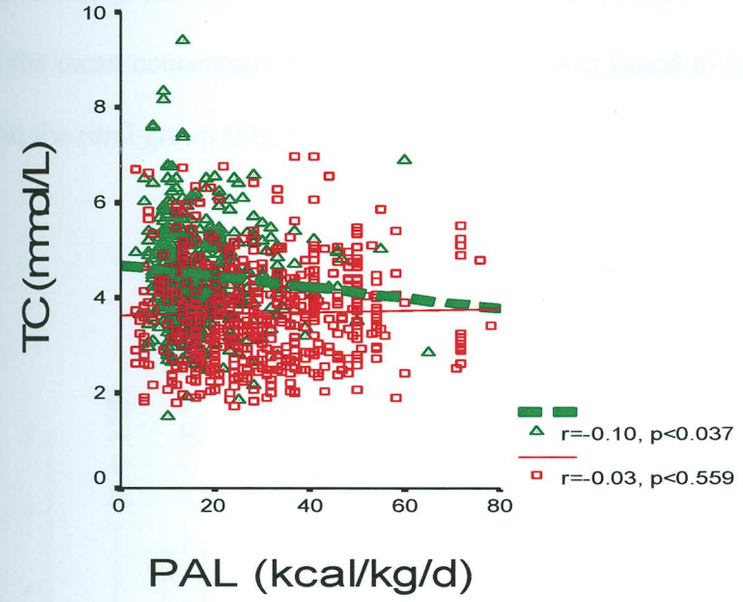


FIGURE 6. *Waist circumferences (Waist cir.) as related to body mass index (BMI) in the rural (■—■) and urban (▼-----▼) groups.*

Blood lipids vs. physical activity level

As shown in **Figure 7,** there was no consistent relationship between PAL and the concentration of blood lipids variables (TC and HDL-c; ***panel A and B***), although for the rural group, there was a statistically significant increase in HDL-c with increasing PAL.



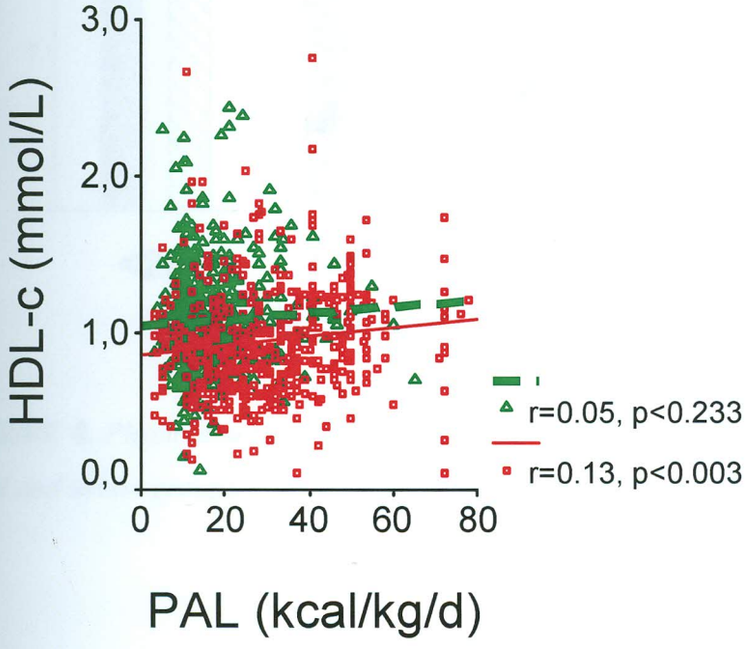


***FIGURE** 7. Total cholesterol (TC; panel B), and high-density lipoprotein cholesterol (HDL-c; panel B) as related to the physical activity level (PAL) in the rural (■—■) and urban (▼-----▼) groups.*

When dividing the material into three levels of physical activity, for each activity level the mean concentration of TC and HDL-c was found to be higher in the urban than in the rural group (**Figure 8 and 9**).

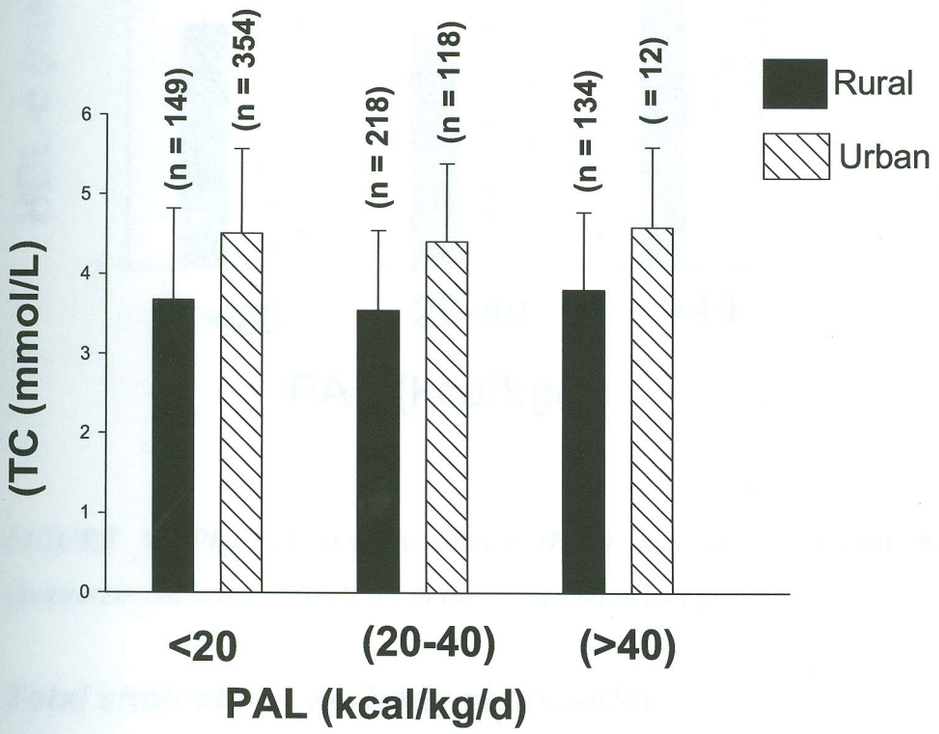


FIGURE 8. *Physical activity-related increase in serum total cholesterol (TC) in the rural and urban groups.*

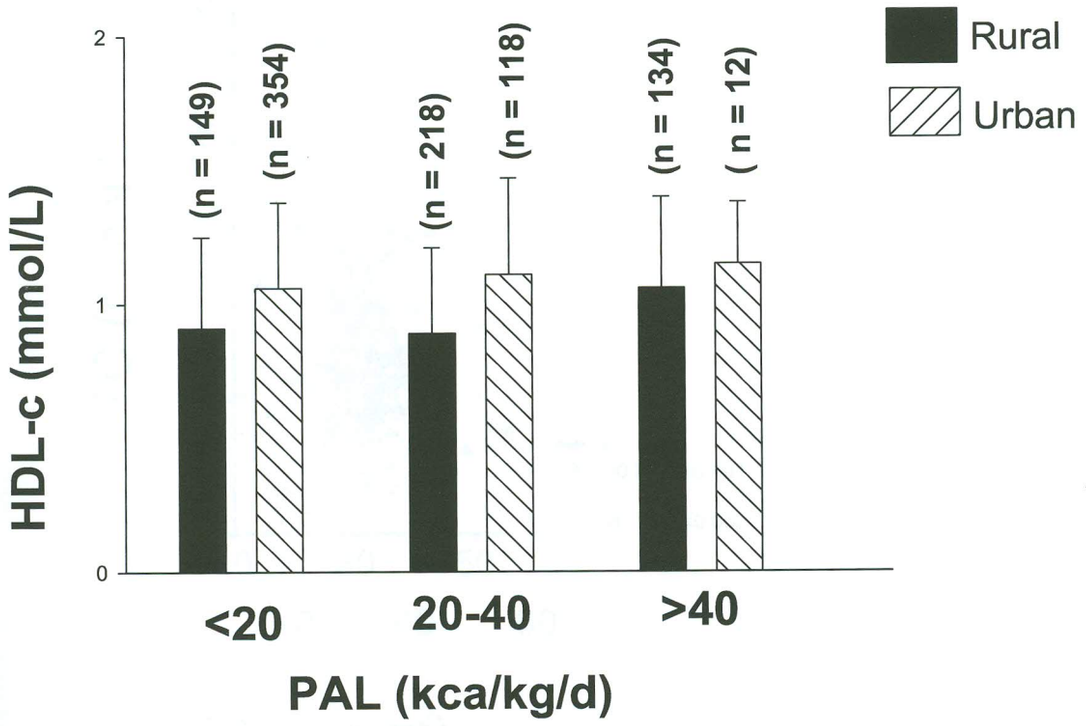


FIGURE 9. *Physical activity-related (PAL) increase in serum high-density lipoprotein cholesterol (HDL-c) in the rural and urban groups.*

Total cholesterol vs. body mass index

Total cholesterol (TC) increased with increasing body mass index **(Figure 10).** However, the slope the of regression line was steeper for the rural than for the urban group ($P < 0.01$)

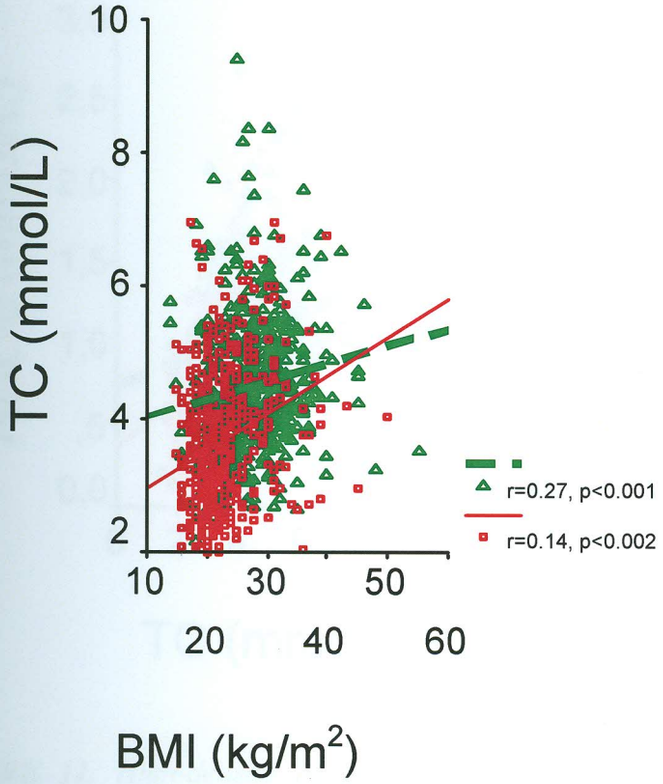


FIGURE 10. *Total cholesterol (TC) as related to body mass index (BMI) in the rural (■—■) and urban (▼----▼) groups.*

High-density lipoprotein cholesterol vs. total cholesterol

As demonstrated in **Figure 11,** there was an increase in high-density lipoprotein cholesterol (HDL-c) with increasing total cholesterol (TC) for both the rural and urban groups ($P < 0.001$). The TC-related increase in HDL-c was steeper for the rural than for the urban group. For the urban subjects, a twofold increase in TC was accompanied by 1.2 mmol/L increases in HDL-c. A similar increase in TC for rural subjects was accompanied by 1.7-mmol/L increase in HDL-c. Thus, in rural subjects an increase in TC was accounted for by a higher quantity of HDL-c than in urban subjects.

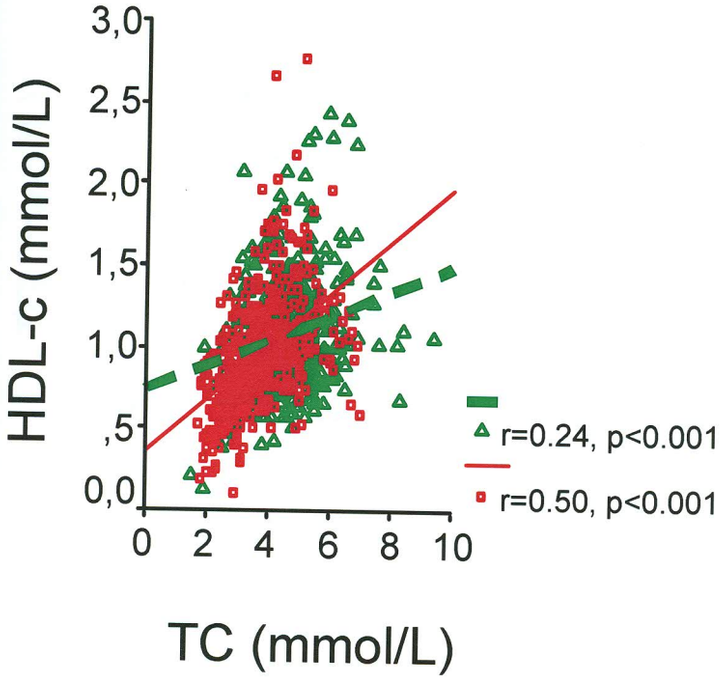
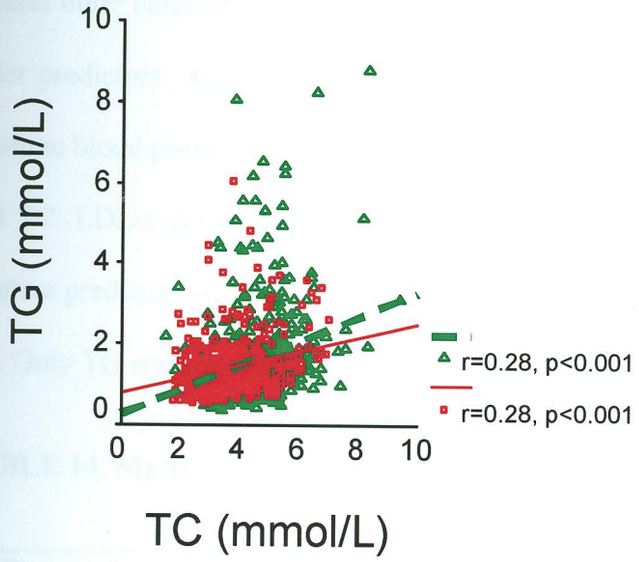
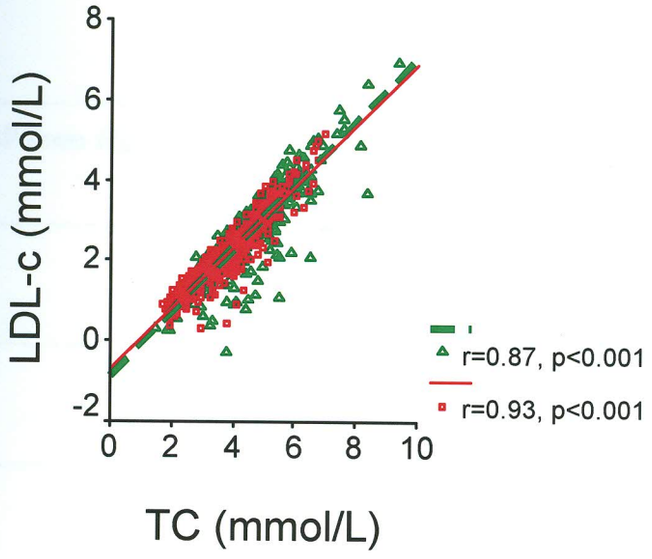


FIGURE 11. *High-density lipoprotein cholesterol (HDL-c) as related to total cholesterol (TC) in the rural (■—■) and urban (▼----▼) groups.*

Serum triglycerides and LDL-c vs. total cholesterol

For both rural and urban subjects, TG increased with increasing TC ($p<0.001$), and there was no difference in the slope of the regression lines between rural and urban subjects **(Figure 12, *panel A*)**. As expected, there was a strong positive relationship between LDL-c and TC **(Figure 12; *panel B*)**.





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FIGURE 12. *Serum triglycerides (TG; panel A) and low-density lipoprotein cholesterol (LDL-c; panel B) in the rural (■—■) and urban (▼----▼) groups.*

5.7 MULTIPLE REGRESSION ANALYSIS

Multiple regression analysis was carried out to evaluate the contribution of some supposedly 'independent' variables to 'dependent' ones (**Table 14**). As illustrated in **Table 14**, the physical activity level (PAL) was a significant negative predictor of

several other coronary risk factors, but the apparent influence was low compared to other predictors. Age, BMI and TG were positive predictors to both systolic and diastolic blood pressure. Waist circumference predicted positively to DBP, BMI, TG, and TC. LDL-c predicted positively to DBP, BMI, and HDL-c. Only WHR was a positive predictor to HLD-c. BMI and HDL-c were positive predictors to LDL-c and TC. Only TG was a positive contributor to TC ($P < 0.001$).

TABLE 14. Multiple regressions for some coronary risk factors

Dependent variable	Independent variable	Standardized Regression Coefficient	P value
SBP ***(mm Hg)***	Age (years)	0.36	0.001
	BMI (kg/m^2)	0.25	0.001
	TG (mmol/L)	0.10	0.001
	PAL (kcal/kg/d)	-0.19	0.001
DBP ***(mm Hg)***	BMI (kg/m^2)	0.35	0.001
	Age (years)	0.17	0.001
	TG (mmol/L)	0.15	0.001

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	Waist cir. (cm)	0.10	0.006
	LDL-c (mmol/L)	0.06	0.047
	PAL (kcal/kg/d)	-0.18	0. 001
BMI ***(kg/m^2)***	Waist cir. (cm)	0.52	0. 001
	LDL-c (mmol/L)	0.13	0.001
	PAL (kcal/kg/d)	-0.23	0. 001
HDL-c ***(mmol/L)***	LDL-c (mmol/L)	0.23	0. 001
	WHR	0.11	0. 001
LDL-c ***(mmol/L)***	HDL-c (mmol/L)	0.46	0.001
	BMI (kg/m^2)	0.22	0. 001
	PAL (kcal/kg/d)	-0.08	0.016
TG ***(mmol/L)***	Waist cir. (cm)	0.16	0. 001
	PAL (kcal/kg/d)	-0.07	0. 046
TC ***(mmol/L)***	HDL-c (mmol/L)	0.48	0. 001

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	TG (mmol/L)	0.36	0.001
	BMI (kg/m^2)	0.16	0. 001
	Waist cir. (cm)	0.09	0. 007
	PAL kcal/kg/d)	-0.07	0. 008

SBP = systolic blood pressure, DBP = diastolic blood pressure, BMI = body mass index, Waist cir. = waist circumference, WHR = Waist-to-hip ratio, HDL-c = high-density lipoprotein cholesterol, TG = triglycerides, and TC = total cholesterol.

5.8 SOME LIFESTYLE RISK FACTORS RELATED TO CHD.

Diet pattern

Considering the whole study material, there was a low percentage (4) of subjects reporting low fat/ low carbohydrate intake (**Table 15**), but a high percentage (39) of subjects reporting high fat/low carbohydrate. There were no differences in percentage of subjects reporting low fat/high carbohydrate and high fat/high carbohydrate intake. In the rural group, there were only 1% of subjects reporting low fat/low carbohydrate, and 5% reported high fat/high carbohydrate intake. In contrast, there were high percentages of subjects reporting high fat/low carbohydrate (52%), and high fat/high carbohydrate (42%) intake. In the urban group, there were low percentages of subjects reporting either low fat/low carbohydrate, or low fat/high carbohydrate intake. In contrast to the rural group, there were a high percentage of urban subjects reporting high fat/high carbohydrate (59%), whereas the percentage of

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subjects reporting high fat/low carbohydrate was lower in the group (26% vs. 52%). Thus, the main contrast between the groups was that the major proportion of rural subjects reported either high fat/low carbohydrate intake, or low fat/high carbohydrate intake, whereas high fat/high carbohydrate seemed to be the predominant diet pattern of the urban group.

TABLE 15. Percentage of subjects in the study population reporting various patterns of fat and carbohydrate intake

Diet patterns	All	Rural	Urban	P value
N	985	501	484	
High fat/high CHO	29%	5%	55%	0.001
High fat/low CHO	39%	52%	26%	0.001
Low fat/low CHO	4%	1%	6%	0.001
Low fat/high CHO	28%	42%	13%	0.001

As depicted in **Figure 13,** the body mass index (BMI) was significantly higher in the high fat/high carbohydrate intake group than in the high fat/low carbohydrate intake group. The lowest BMI was found in the low fat/high carbohydrate intake group.

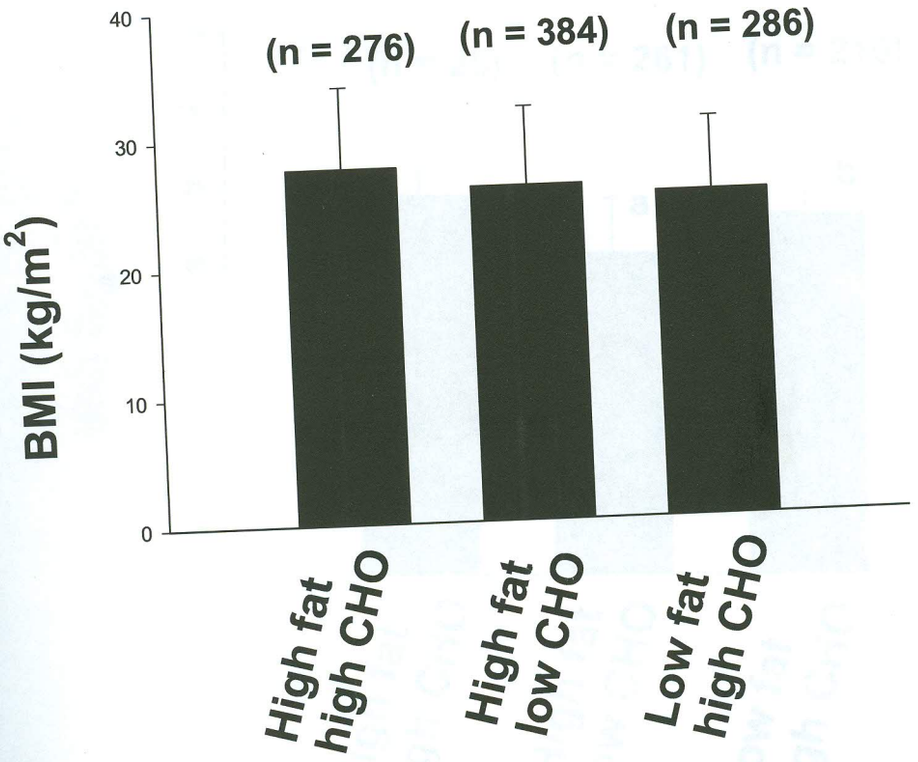


FIGURE 13. *Body mass index (BMI) in various diet pattern groups of the whole study population. Mean values ±SD, with numbers of subjects on top of the bars.*

As shown in **Figure 14,** in the rural group, the body mass index (BMI) was significantly higher in the high fat/high carbohydrate intake group than in the low fat/ high carbohydrate group, while the lowest BMI was in high fat/low carbohydrate groups *($P < 0.001$).*

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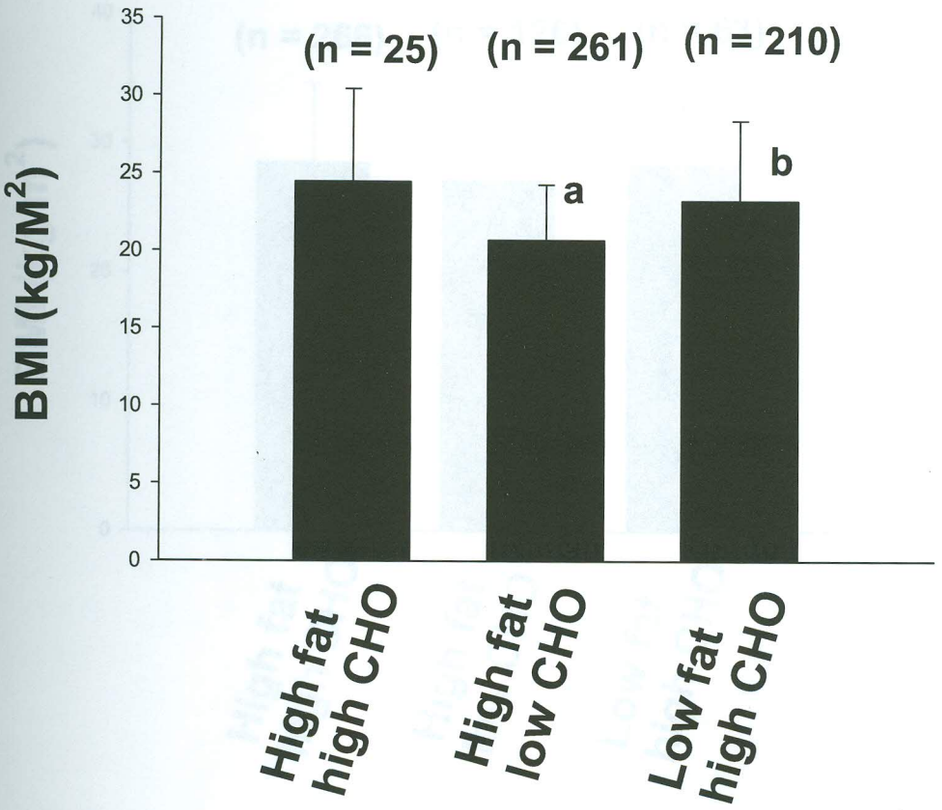


FIGURE 14. *Body mass index (BMI) in various diet pattern groups of the rural population. Mean values ±SD, with numbers of subjects on top of the bars.*

In contrast to the rural group, there were no group differences in body mass index (BMI) by reported fat and carbohydrate eating pattern in the urban population **(Figure 15)**, but the BMI was slightly lower in the high fat/low carbohydrate group than in the other two groups. Possible explanations of this apparent contradiction are discussed later on page (183).

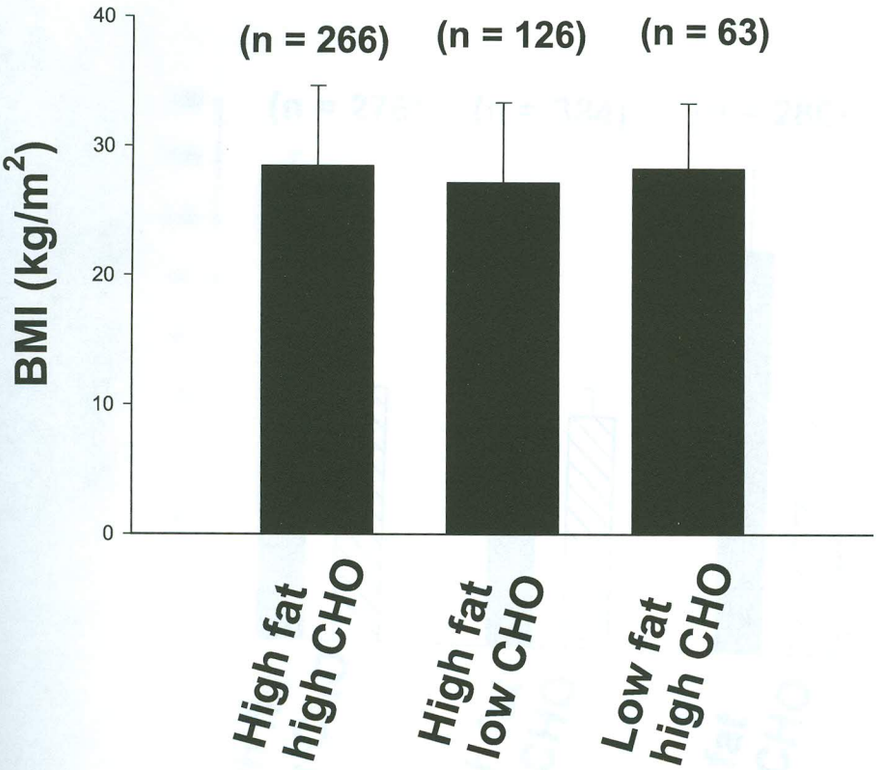


FIGURE 15. *Body mass index (BMI) in various diet pattern groups of the urban population. Mean values ±SD, with numbers of subjects on top of the bars.*

As illustrated in **Figure 16,** there were higher values of systolic and diastolic blood pressure in the high fat/high carbohydrate intake group than in the low fat/high carbohydrate group, while the lowest mean systolic and diastolic blood pressure was observed in the high fat and low carbohydrate group for the whole study population.

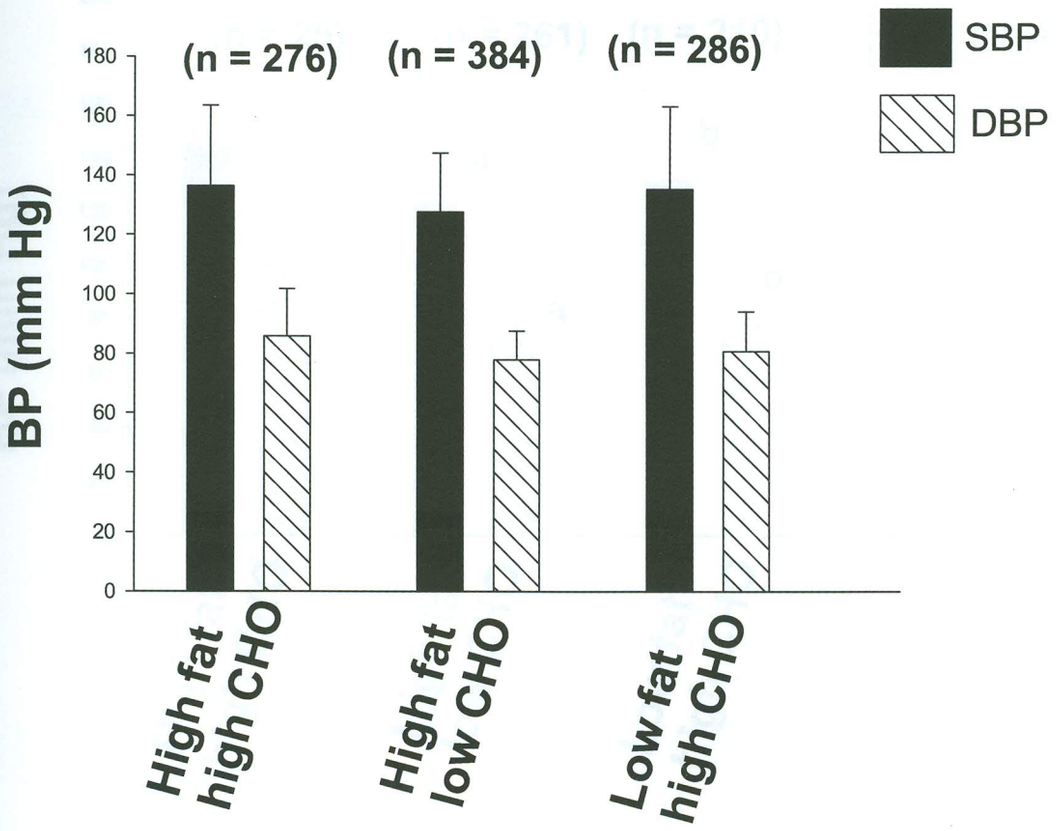


FIGURE 16. *Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in various diet pattern groups of the whole study population. Mean values ±SD, with numbers of subjects on the top of the bars.*

As demonstrated in **Figure 17,** in the rural population, both systolic and diastolic blood pressures were significantly higher in the high fat/high carbohydrate group than in the high fat/low carbohydrate group and the low fat/high carbohydrate group ($P < 0.001$). Among the diet groups, the high fat/low carbohydrate group had both the lowest systolic and diastolic blood pressures.

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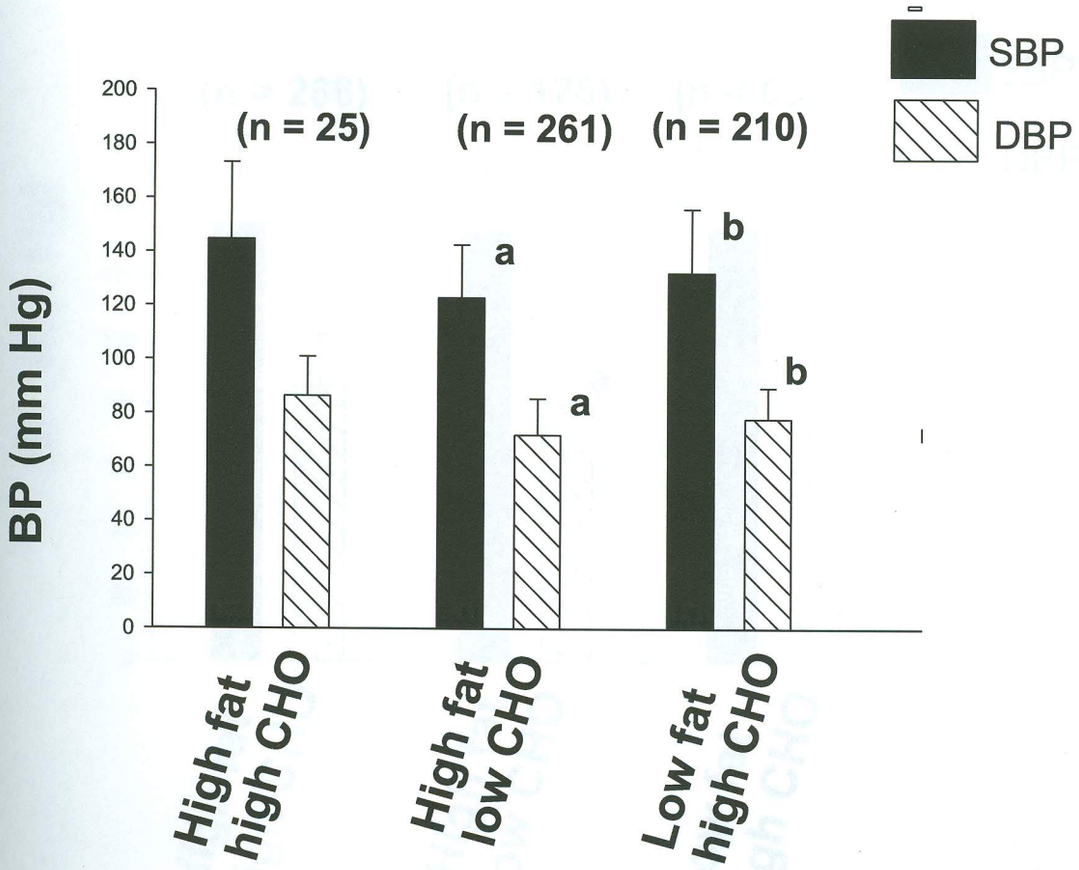


FIGURE 17. *Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in various diet pattern groups of the rural population. Mean values ±SD, with numbers of subjects on the top of the bars.*

Systolic and diastolic blood pressures as related to the diet pattern in the urban population are shown in **Figure 18**. In contrast to the rural group, there were no diet related differences in either systolic or diastolic blood pressure in this group.

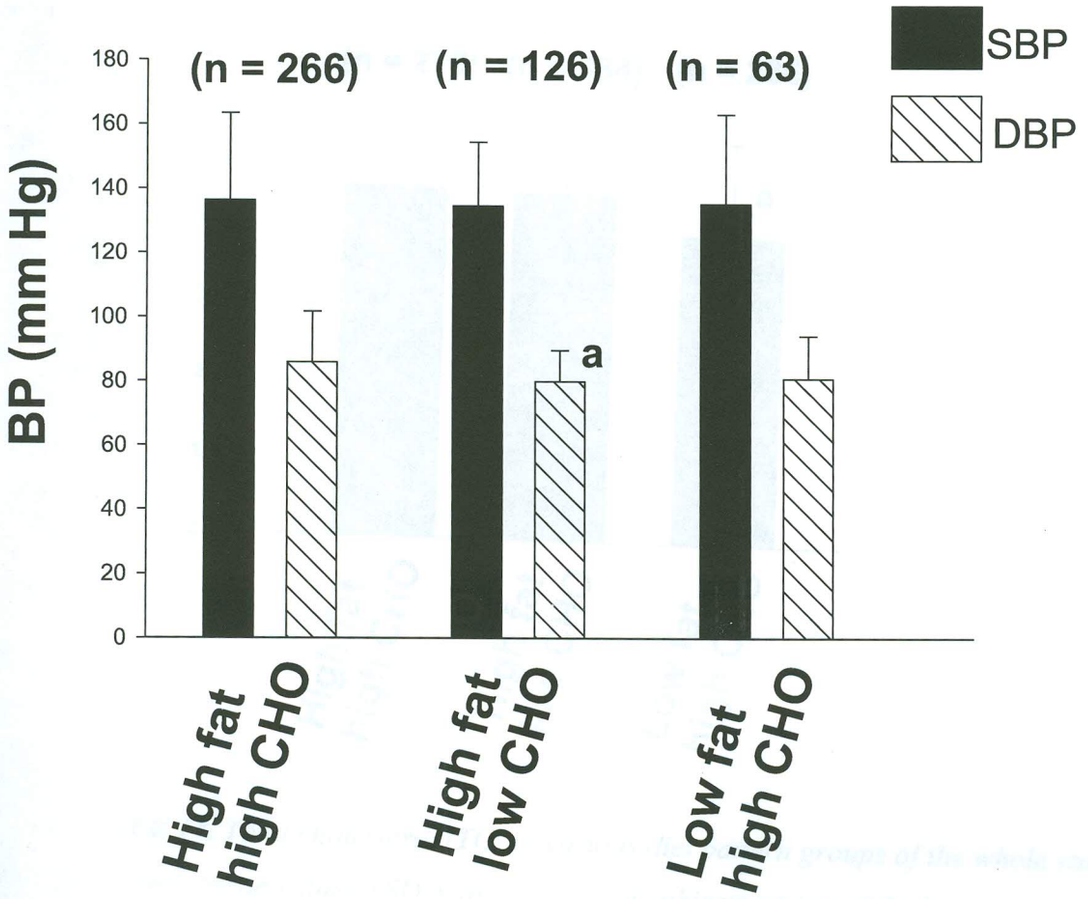


FIGURE 18. *Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in various diet pattern groups of the urban population. Mean values ±SD, with numbers of subjects on the top of the bars.*

Mean serum concentration of total cholesterol (TC) was similar in the high fat/high carbohydrate and the high fat/low carbohydrate intake groups in the whole study (**Figure 19**), whereas the low fat/high carbohydrate group had a lower serum concentration of TC *($P < 0.001$).*

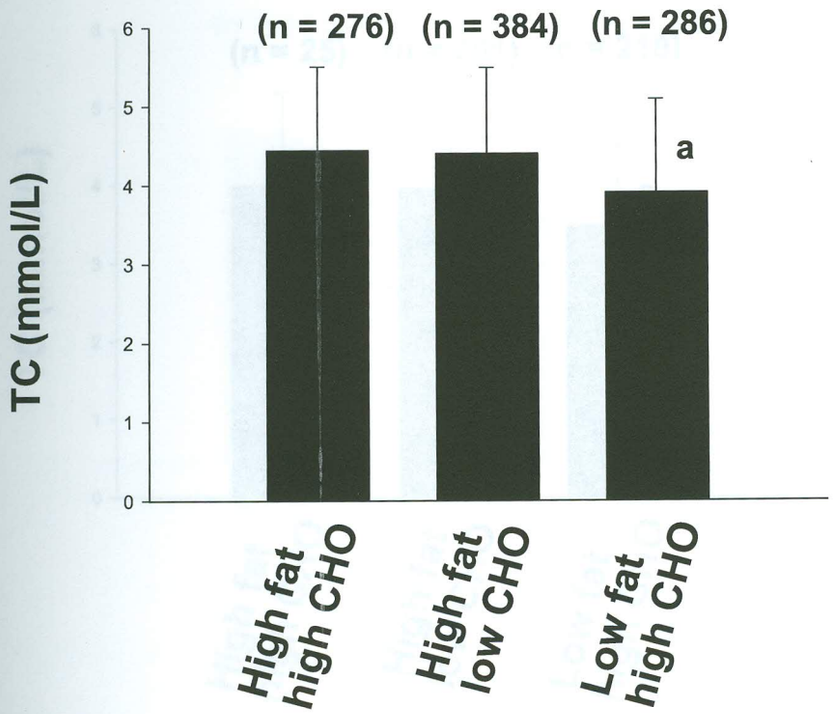


FIGURE 19. *Total cholesterol (TC) in various diet pattern groups of the whole study population. Mean values ±SD, with numbers of subjects on top of the bars.*

A similar diet pattern was observed in the rural population **(Figure 20),** whereas serum concentration of TC in the urban population did not respond to reported differences in diet pattern groups (**Figure 21**).

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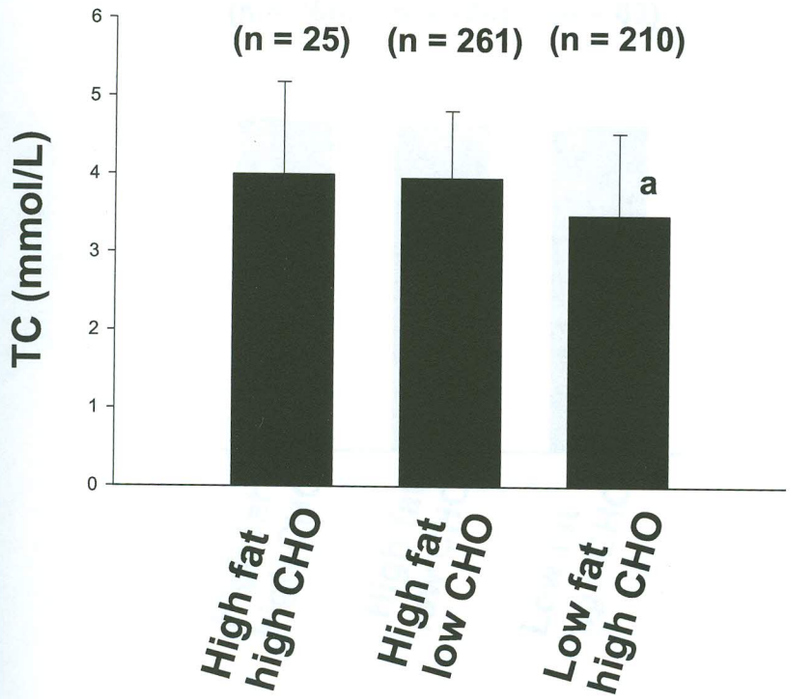


FIGURE 20. *Total cholesterol (TC) in various diet pattern groups of the rural population. Mean values ±SD, with numbers of subjects on top of the bars.*

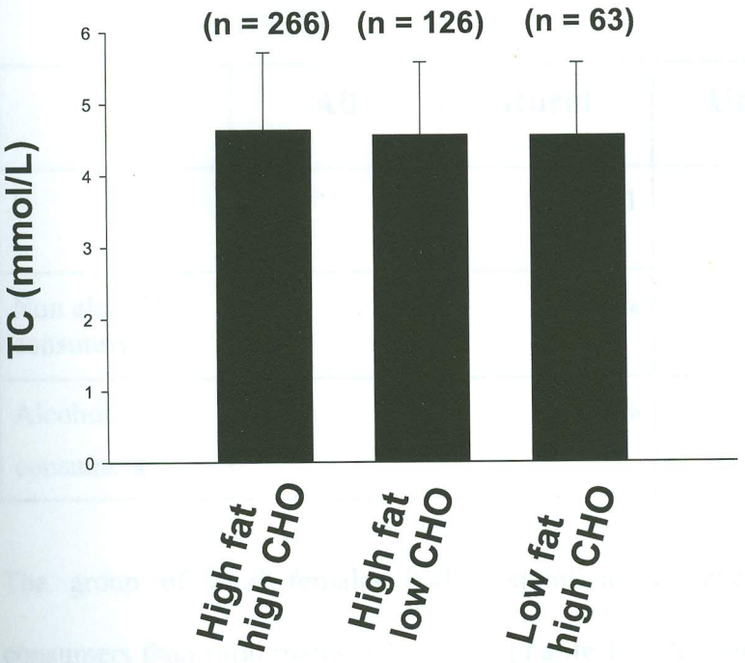


FIGURE 21. *Total cholesterol (TC) in various diet pattern groups of the urban population. Mean values ±SD, with numbers of subjects on top of the bars.*

Alcohol users

The prevalence of subjects reporting use of alcohol in the whole population was relatively low **(Table 16).** The rural group had a significantly lower prevalence of alcohol consumers than the urban group.

TABLE 16. Prevalence (%) of subjects reporting alcohol use

	All	Rural	Urban	P value
N	985	501	484	
Non alcohol consumers	77%	80%	73%	0.001
Alcohol consumers	23%	20%	27%	0.001

The group of rural females had a significantly lower prevalence of alcohol consumers than rural males, *(P < 0.01)* **(Table 17).** A similar situation was revealed in the urban group *(P < 0.01).* Urban males had the highest prevalence of alcohol use of all the groups in the study *(P < 0.001).*

TABLE 17. Prevalence (%) of subjects reporting alcohol use by gender

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
Non alcohol consumers	87%	74%	83%	65%
Alcohol consumers	13%	27% [a]	17%	36% [b]

a*) vs. rural females, b) vs. urban females*

Tobacco users

The prevalence of cigarette smokers (see some abbreviations and definitions and methods for definition of cigarette smokers) was low in both the rural and urban study population **(Table 18)**. However, the prevalence was significantly higher in the rural than in the urban group. Smokeless tobacco was prevalent in the rural group but not in the urban group. Interestingly, the prevalence of cigarette smokers was lower in the urban than in the rural group.

TABLE 18. Prevalence (%) of tobacco users of the study population

	All	Rural	Urban	P value
N	985	501	484	
Non smokers	80%	68%	91%	0.001
Cigarette smokers	13%	20%	9%	0.001
Smokeless tobacco users	7%	12%	None	-

Generally, cigarette smokers were mainly found among the male subjects. Indeed, the rural males had the highest frequency of cigarette smokers of all groups in the study *(P < 0.001)* **(Table 19).** In the rural group, the percentage of cigarette smokers was significantly higher among males than among females *(P < 0.01).* The group of urban males had a significantly higher frequency of cigarette smokers than the urban females *(P < 0.01).* More rural females used smokeless tobacco than rural males, but the difference did not reach statistical significance.

TABLE 19. Prevalence (%) of tobacco users of the study population by gender.

	Rural		Urban	
	Females	**Males**	**Females**	**Males**
N	256	245	255	229
Non smokers	80%	58%	98%	86%
Cigarette smokers	6%	31% [a]	2%	14% [b]
Smokeless tobacco users	14%	11%	None	None

a) vs. rural females, b) vs. urban females

CHAPTER 6. DISCUSSION

Most of the developing countries including Tanzania are undergoing epidemiological transitional phenomenon (Omran 1971, Pearson 1999). This epidemiological transition has followed rapidly the social, cultural and economic changes, where traditional societies have undergone westernization and urbanization, accompanied by a sedentary lifestyle, overconsumption of unhealthy diet, tobacco use and alcohol overuse, and stress. The impact of this trend would be an increase of diseases such as CHD events (Omran 1971, Pearson 1999, Edwards et al. 2000, Seedat 2000, Van der Sander 2000, Forrest et al. 2001). In fact, the urban inhabitants of Tanzania are more prosperous, sedentary, better educated, and have an excess of food intake, leading to chronic diseases. In contrast, the rural inhabitants are in general poor, illiterate and have physically demanding occupations, and some suffer from undernutrition. The findings in the present study indicate a favorable CHD risk factor profile among rural people and an unfavorable one among urban subjects. These observations may be indicative of an advanced stage of urbanization and westernization of the urban group of Tanzania, and support the work by Edwards et al. (2000), and Njelekela et al. (2001). Increased particular risk factors were also found among rural subjects. Due to a lack of longitudinal data, it remains to be clarified to what extent urbanization and western lifestyles are also taking place in the in rural populations of Tanzania. However, in earlier reports the prevalence of CHD risk factors among rural inhabitants has been documented to be low (Swai et al. 1993, Kitange et al. 1993).

6.1 Limitations in assessment

Methodological concerns

The specific aim of the study was estimate and compares the level of physical activity, at work, home and during leisure time, and to relate to the following risk factors, which are central for the incidence of CHD. Because exposure and outcome are measured simultaneously, it is not possible to determine whether the measured exposure preceded the outcome or resulted from it (Hennekens and Buring 1987). Though, biological mechanisms in the causation of CHD have been fairly well worked out, and findings from prospective studies can be used to assist in the analysis and interpretation of results in cross-sectional studies.

Association between exposure and outcome measures in epidemiological studies must be evaluated in terms of validity. The validity of those associations, in turn, is a matter of judging the roles of chance, bias, or confounding that could account for the observed associations in any epidemiological study (Hennekens and Buring 1987).

The size of the sample of the study population under study is a main consideration in determining whether an observed association between exposure and outcome is due to chance alone. In general, the smaller the sample size, the more likely it is that the observed association will not be reflective of the experience of the population from which the sample is drawn.

Bias in epidemiological studies refers to systemic errors that might be introduced in the design or implementation of the investigation that might distort the association between exposure and outcome (Hennekens and Buring 1987). A simple way to

describe the several types of bias that can exist in epidemiological studies is to divide them into main categories: selection and information bias.

Selection bias refers to systemic errors in procedures that are used to select study subjects or in factors that might influence subjects giving a systemic error in the identification of the study population (Hennekens and Buring 1987, Rothman K and Greenland 1998). A low response rate could introduce selection bias, especially if the responding or avoiding participation in the study has special characteristics that are associated with the exposure or outcomes measure. In the present study, selection bias was not a major concern in the rural as well as in the urban populations because of the high response rate (84 % and 81%, respectively). The most common reasons given for inappropriate selection in both populations were: there is no such people registration system in Tanzania, and illiteracy especially in the rural population.

Information bias refers to systemic error in the information obtained from participants. These errors, in turn, could be due to differences in the ways in which interviewers or data collectors elicit information from participants or to the participants themselves reporting information in a non-comparable manner. To avoid biases related to collecting data from participants, trained survey workers and myself performed blood pressure and anthropometrical measurements, blood sample collection as well as administering the questionnaire.

Bias due to misclassification error, i.e. misclassifying exposure or outcome, was reduced by applying standard WHO diagnostic criteria for defining e.g. high systolic and diastolic blood pressure, high total cholesterol, and obesity.

Another potential source of misclassification bias could be the classification of the physical activity level (PAL). The assessments PAL have the same inherent methodological limitations as some other studies done with black Africans (Zimmet et al. 1991, Sparling et al. 1994, Pereire et al. 1995 and 1998, Forrest et al. 2000). Activity grading is commonly used in epidemiological studies, but the grading is recognized to be crude and both an over- and an underestimation of PAL may occur. Several methods for measuring PAL have been used in population surveys. The assessment of PAL by questionnaire remains the method of choice for this kind of study (Wilson et al. 1986, Morris et al. 1990, Hong et al. 1994). In the present investigation, the estimation of PAL was obtained from participant responses to a questionnaire originally worked out for use in developed populations. However, it is now being used in studies worldwide, also in developing countries such as in Africa.

Reliability and validity of the questionnaire have been tested in native American populations but not in the indigenous African populations (Paffenbarger et al. 1993, Jones 1997; MOSPA). Other limitations related to the collection and analyses of PAL data were observed and should be considered. The data could have been more relevant if it also contained objective measurements and not only subjective self-reports. It seemed that some of the participants did not understand the importance of the study and were not familiar with the assignment. Regarding the duration, the subjects often could not ascertain how long (number of weeks, months or years) the reported physical activity was carried out. Even the estimation of physical activity in minutes or hours per day was not easy to indicate clearly from the given set of questions. Questions were made simple, logical, and relevant to both populations,

with the respondents' levels of education and language use taken into consideration. To reduce misinterpretations of the subject's physical activity types and levels, myself, and well-trained personnel with long experience in fieldwork, administered the questionnaire.

It is likely that the study has underestimated the true association between PAL and CHD risk factors. Similar situations have been recognized in previous studies done in Africa (Zimmet et al. 1991, Sparling et al. 1994, Pereira et al. 1995 and 1998, Forrest et al. 2000), as well as in other developing countries e.g. in Asia (Hong et al. 1994).

Data based on questionnaire responses are dependent on the subjective experiences of the respondent. Regarding smoking and drinking behavior, there may be a tendency to over/underreport, because participant may know that they should not smoke at all, and not drink much (health consequences).

The data presented in this study were collected from a representative sample of the rural and urban Tanzanian population. The sample group of 985 subjects could represent both rural (501 subjects) and urban (484 subjects) Tanzanian populations that are about 30 millions. However, it is important to have in mind that the whole of Tanzania is not the same. People from one place live in different ways with different customs, cultures and traditions compared to people from other places. While this may be true, there is no reason to believe there is a major difference lifestyle.

6.2 PHYSICAL ACTIVITY LEVEL

This study supports previous observations (Morris et al. 1953, Morris and Crawford 1958, Paffernbarger et al. 1986, Berlin and Colitz 1990) that the physical activity

level (PAL) is inversely related to the body mass index (BMI), body weight, diastolic and systolic blood pressure, waist-to-hip ratio (WHR), waist and hip circumferences, total cholesterol (TC), triglycerides (TG), and total cholesterol to high-density lipoprotein cholesterol ratio (TC/HDL-c ratio. The strongest inverse relationship was between PAL and BMI. Additionally, PAL was a significant negative predictor of several other coronary risk factors, but the apparent influence was low compared to other predictors. The rural group had significantly higher mean PAL, and lower mean values of selected risk factors than the urban group. Thus, the high PAL in the rural dwellers may explain the lower levels of the CHD risk factors observed in this area compared to those of the urban inhabitants. These variations may be explained partly by a difference in lifestyle. Generally, rural females and males live an active life. They work in agriculture or are involved in heavy physical activity, while most of urban females and males have sedentary work and habits. These findings support the observations by Mennen et al. (2000), among the Cameroon people, which reported higher PAL and lower levels of CHD risk factors among rural than urban subjects.

Evidently, the females PAL relative to household tasks and childcare tends to be inadequately estimated (Pereira et al. 1995, Kriska and Carpersen 1997, Forrest et al. 2000). For both groups of the present study, no significant difference in PAL was registered between females and males. Similar findings were observed among urban females in Nigeria (Forrest et al. 2000). Traditionally females do the childcare, cooking, and housework. Males take little part in domestic activities. For example, rural females with young children, during their daily activities at home or workplaces

(farms), usually tend to carry children on their backs much of the time. They also tend to fetch water and sometimes firewood nearly every day. In Tanzania, urban females of higher socio-economic status usually have help (housemaids) with childcare, cooking and housework, unlike those with lower socio-economic status. Thus, outside the workplace, urban females also have to do housework, cooking, childcare, and those with young children tend to carry children on their backs, as do rural females.

Leisure–time physical activity

In the present study data, there is no categorization between the various PAL`s reported. According to my observations, there were differences between physical activity forms, including occupational and leisure-time PAL. Although the urban population of the study had begun to adopt a more sedentary lifestyle, as observed in westernized societies, more occupational activity than leisure activity was seen. Gardening and small farming were common leisure time activities among urban residents. Dancing was also a preferred and common leisure time activity in both sexes and groups. Walking to the market or to visit friends was the most common leisure time activity in both groups. These findings agreed with the outcome of two studies done in West Africa (Fisch et al. 1987, Forrest et al. 2000). In comparison with western population, few urban inhabitants were engaged in biking, aerobics, jogging, playing soccer, tennis or weight lifting and none of the rural subjects did these activities.

In the present study education level was explored but not reported in the result chapter. In westernized communities as well as in developing societies, PAL,

especially leisure time PAL, has been related to education level and socio-economics status (Dreyer et al. 2001). The higher the education level and socio-economics status attainment of the participants, the greater was the participation in leisure time physical activity and vice versa. In this study, leisure time PAL was not found to be associated with education level or socio-economics status among urban subjects. Higher education level and socio-economics status attained by urban subjects did not affect their participation in leisure-time PAL. Very few urban inhabitants were engaged in biking, aerobics, jogging, playing soccer, tennis or weight lifting during leisure-time. Similar situations were observed among Nigerian urban males of high education level and socio-economics status (Forrest et al. 2001). Tanzanian urban residents of high education level and socio-economics status, generally practice a sedentary lifestyle during leisure time (personal observation).

Habitual lifestyle related to physical activity

Between the two Tanzanians populations studied, rural and urban, several demographic parameters should be considered in interpreting their daily life related to the PAL data. All rural residents had a traditional, natural African life-style in agricultural settings. They resided in poor and short term housing with no electricity or water. Most of them were people with very low socio-economic status. They were either farmers or farmers and fishermen, and very few were employed. A majority of those who were employed was exposed to hard physical labour, besides their daily work on the farm. In addition, females did housework and worked daily on the farms. In rural areas, there was almost no regular public transport. Bicycles were often used to travel, and walking was common. They could walk from morning to evening

crossing mountains and hills to their destinations, e.g. taking animals for grazing, farm, market, or hospital. Not only that, those people are used to carrying heavy loads on their backs or heads e.g. babies, water, and firewood. Fetching water and firewood were part of their daily activities throughout the year.

Many of the urban subjects were born and raised in the villages and had moved to urban areas for school or work when they were grown. Consequently, they had spent their childhoods in rural areas where physical activities were common. Some of them resided in permanent housing with indoor water and electricity; thus, they did not have to fetch water and firewood like the rural residents. There were people of different socio-economic status, from lowest to highest. The majorities were employed in white-collar jobs, some were in blue-collar jobs and the rest were involved in small businesses. In urban areas public transportation was available in some places and irregular in others. Few urban dwellers had access to personal, office or family vehicles. Due to transport irregularities, walking to and from the stations and homes is common. Despite this, the walking distance to and from their homes, station and working place was relatively short, compared to the rural subjects. Few participants were engaged in biking to work as means of transport. During their leisure time some were spending time in front of the television, driving a car or were just sitting and chatting. Compared with other urbanized populations, time in front of the television or in the car seems to be considerably less.

Due to the lifestyle facts mentioned above, it seems that both rural and urban populations attained higher life-long PAL compared with other populations of Westernized communities. An argument can be made for an overall higher life-long

PAL in both the rural and the urban populations of this study. Although objective data are not available, comments from the few studies concerning African communities done in South Africa on physical activity related with CHD and its risk factors, support this argument. Seftel (1978) and Walker (1991) pointed out that among most blacks PAL was higher compared to the whites in South Africa. Similarly, Sparling et al. (1994) reported that the amount of routine daily PAL in the black urban South African population was higher throughout their lifetimes than in the majority of e.g. American and European populations. Accordingly, the PAL, which black Africans obtain everyday at work, is relatively higher than that of people from communities of more favorable higher socio-economic class. Work requiring heavy physical labour such as farm and industry work, has nearly disappeared in those westernized communities. New technologies have replaced heavy physical labour. Farm and industry work are still performed manually in many African communities.

6.3 BODY MASS INDEX

In studies of the association between PAL and CHD risk factors, BMI might perhaps be considered as an independent variable, because it is a determinant of other CHD risk factors e.g. blood pressure and TC, and it is also inversely associated with PAL (Rothman 1986). On the other hand, people with low PAL, would be expected to put on weight, in this sense PAL would be factor for a contributor to increased BMI.

In this study, the strongest inverse correlation was observed between PAL and body mass index (BMI). BMI was also positively related to weight, waist and hip circumferences, TC, LDL-c, waist-to-hip ratio, and TC/HDL-c ratio, and TG.

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In this study, the strongest inverse correlation was observed between PAL and body mass index (BMI). BMI was also positively related to weight, waist and hip circumferences, TC, LDL-c, waist-to-hip ratio, and TC/HDL-c ratio, and TG.

The mean values of BMI were at the normal range of the recommended standard in Western populations (Rotimi et al. 1995, Bailey and Ferro-Luzzy 1995, Simmons et al. 1996), but considerably lower than BMI values found in the USA (Kuczmarski et al. 1994). Rural-urban differences in BMI were observed in this study, the rural populations having lower mean BMI than the urban populations. This could be due to higher PAL in the rural population, which may contribute significantly to lower BMI. However, the BMI decrease with increasing PAL was observed in both groups. Also other studies have demonstrated an association between decreased BMI and increased PAL (Ballon and Keesey 1991, Duncan et al. 1991, Seidell et al. 1991).

The female groups had higher BMI values than male groups, probably due to their lower mean values of height. Similar differences between the sexes have been observed among rural and urban populations in Gambia and Cameroon (van de Sander et al. 2000, Mennen et al. 2000), and South Africans (Mollentze et al. 1995).

In this study the mean BMI value of the rural population ($23kg/m^2$) was at the normal distribution level (Simmons et al. 1996). In the rural population, however there were subjects with a BMI value of ≤ 18.5. Compared to BMI values of people in the developed countries this may be considered as underweight, probably due to undernutrition and chronic energy deficiency (Nube et al. 1998). On the other hand normal values of BMI for specific subjects were recorded, due to their lower height and weight. Similar findings have been found among Indian males and females with smaller body size (Singh et al. 1997). Lower mean BMI values in populations of developing countries have also proposed by other investigative groups (WHO study group 1990, ICG 1996), with a lower limit of 18.5 and upper limit of 23, or normal

range for adult BMI between 18.5 - 25 kg/m^2 (FAO 1994, WHO 1995). Thus, in developing countries, the BMI of adults was suggested to be less comparable to developed countries. Nonetheless, BMI has increased and is still increasing in developing countries, concomitant with increasing economic change probably as a consequence of overconsumption and decreased PAL (Dalton 1997, Hu et al. 2000).

In contrast, the mean of BMI of the urban populations (27) was above the upper end of distribution for typical Western populations, $\leq$ 25 (Simmons et al. 1996). These findings provide further evidence that developing communities, and particularly urban populations, are much affected by urbanization due to improvement in socio-economic standards, westernization of food processing, lifestyle, including diet and PAL.

An increase in BMI with increasing age has been observed (Malhotra et al. 1999, Hu et al. 2000, Forrest et al. 2000). Similar tendencies were found in the rural and urban populations of this study, but the increase was more pronounced among the urban than the rural population. Between 30 and 49 years of age, BMI increased by 2 in the urban population but only 1 for the rural population. Possible reasons for this could be the economic status and the PAL differences between these two populations. The fact is that the majority of the urban group aged 30-49, attained higher income strata, and lower PAL compared to the rural population of the same age. A study done among urban Nigerians has also demonstrated an association between increased BMI, and high socio-economic status in male seniors who attained low PAL (Forrest et al 2000). Again, these findings give further evidence that urbanization, in

combination with an increasing income, is an important factor for BMI increase in African countries.

Generally, in many studies conducted in developed societies high BMI has been used as a substitute classification of obesity and as a predictor of CHD (Després and Lamarche 1993). Severe obesity with a body-mass index of 30 or more is common and represents a major health problem in developed as well as developing populations (Kutty et al. 1993, Abate 2000). In this study overweight and obesity were prevalent, but significantly higher in urban groups than in the rural groups. Females had a higher prevalence of obesity. Similar findings have been reported in other African countries (Bovet et al. 1991, Walker 1991, Seedat 1996 and 1998, Khattab et al. 1999), as well as in Tanzania (Njelekela et al. 2001). Furthermore, these findings were compatible with result from studies conducted in the USA, despite the fact that the current study's female population was significantly leaner (Wings et al. 1989).

The increase of obesity prevalence has been noted in many developing countries, followed by an increase in urbanization, adopting westernization of food processing, dietary habits, and sedentary lifestyles (Ghannem and Fredj 1997, Forrest et al. 2000, van der Sander 2000, Doll et al. 2002). In the current study, regular consumption of meat, fish, coconut milk, and fried chips was reported and more common in the urban than in the rural areas. This could be a partial cause of the high prevalence of overweight and obesity in the urban population. A relationship between obesity and similar type of diet has previously been documented in the urban population of Tanzania (Njelekela et al. 2001).

Multivariate analyses have revealed BMI–related increases in both systolic and diastolic blood pressure, and BMI as an independent predictor of hypertension (Stamler 1991, Reeder et al. 1992, Mikhail et al. 1999, Brown et al. 2000, Wilsgaard et al. 2000, Sharma et al. 2001). In the present study, 5% of rural and 11% of urban obese individuals had blood pressure exceeding 140/90 mmHg, possibly an indication of the effects of urbanization on blood pressure increase. It has been noticed; however that rural black Africans are less obese when they migrate to urban areas, but when they change their lifestyles, the incidence of obesity increases, as does the prevalence of hypertension (Seedat 1996, and 1998). This could be one of the reasons for the higher prevalence of hypertension and obesity among urban groups. In addition, the prevalence of obesity and hypertension was more prevalent in females than in males in both rural (7% in females and 3% in males) and urban (12% in females and 9% in males) groups. Matching trends have also been demonstrated among urban black females of sub-Saharan Africa (Seedat 1996, 1998, and 2000), Northern-African (Ibrahim et al. 2001, Mokhtar et al. 2001), African-American females (Kumanyika 1997, Jones 1999), and Norway (Wilsgaard et al. 2000). In contrast, obesity has been observed not to be associated with hypertension among obese females in developing communities, particularly in Africa, probably due to higher PAL (Walker 1991, Muna et al. 1993). The same observation has shown among certain obese people in developed societies as reported by Després and Lamarche (1993).

Generally, total cholesterol levels increase with increasing BMI, and obese persons tend to have total cholesterol levels at the high-risk level (Reeder et al. 1992, Denke