REVIEW OF LITERATURE

REVIEW OF LITERATURE

The health research community is now well aware of the impending global pandemic of chronic degenerative diseases and the alarmingly increasing rates of these disorders in less developed countries and economies in transition However, the governments of these countries have not come to grips with the burden of these diseases especially cardio vascular disease (CVD) and the potential disaster it might cause. Many of these countries have achieved impressive gains in controlling, and in many instances preventing, infectious and communicable diseases, and they have improved the life expectancy of their citizens However, people in these countries are now subjected to many of the non-communicable chronic degenerative diseases, such as obesity, diabetes, hypertension and CVD, that occur in more developed counties

Globalization brings about not only changes in the prosperity of these countries but also ill health Rapid changes in diets and lifestyles that have occurred with industrialization, urbanization, economic development and market globalization, have accelerated over the past decade. This is having a significant impact on the health and nutritional status of populations, particularly in developing countries and in countries in transition While standards of living have improved, food availability has expanded and become more diversified, which in turn has contributed to shifting dietary patterns, for example, increased consumption of energy-dense diets high in

fat, particularly saturated fat, and low in unrefined carbohydrates These patterns are combined with a decline in energy expenditure that is associated with a sedentary lifestyle-motorized transport, labour-saving devices at home, the phasing out of physically demanding manual tasks at work, and leisure time that is predominantly devoted to physically undemanding pastimes.

Because of these changes in dietary and lifestyle patterns, chronic non communicable diseases – including obesity, hypertension and stroke –are increasingly significant causes of disability and premature death in both developing and newly developed countries, placing additional burdens on already overtaxed national health budgets There is very little money available for health care The health care funding ranges form US$4 (in Mozambique) to $870 (in Kuwait) per person per year The most populous nations India and China, spend $17 and $31 per person per year, respectively. These figures are in no way close to the budget allocation in many of the more-developed countries Yet, many of these countries aspire to treat the disease rather than preventing it in the first place In fact the richest country in the world (the USA) cannot afford a technology-based solution for CVD and other non-communicable diseases (Chockalingam 2000)

Prevention efforts must include health promotion at population level, health education at the level of patients, and continuing medical education at the level of health care providers In fact the knowledge gained by the more developed countries over the past century must be applied in less-developed

countries so that they too can benefit Of course, one must take into account the special risk factors that some ethnic populations have before applying any kind of strategies For example, people of south Asian origin have a high-risk even at "normal" total cholesterol concentrations, because they have low HDL cholesterol and high triglyceride concentrations Hence, before going into the various risk factors and the various CDD in particular it is necessary to look at the prevalence of these diseases The burden of CDD is rapidly increasing worldwide. It has been calculated that, in 2001, CDD contributed approximately 60% of the 56 9 million total reported deaths in the world and approximately 46% of the global burden of disease (WHO Report 2003) The proportion of the burden of CDD is expected to increase to 57% by 2020. Almost half of the total chronic disease deaths are attributable to CVD, obesity and diabetes are also showing worrying trends not only because they already affect a large proportion of the population, but also because they have started to appear early in life (WHO 2003)

PREVALENCE OF OBESITY

The prevalence of obesity is rising to epidemic proportions around the world at an alarming rate The rise in obesity is not restricted to more developed countries. With increasing westernization, prevalence of overweight and obesity appears to be rising amongst more affluent populations of less developed countries, even in those countries with current food security problems and significant rates of under nutrition Ghana, for example has

only slightly more underweight (BMI<18 4), than overweight (BMI>25) people This situation has been exacerbated due to the image of prosperity and success associated with weight gain in many of these societies It is a bitter irony that as developing countries continue their efforts to reduce hunger, some are facing the opposing problem of obesity A study carried out by the United Nations in 1999 found obesity in all developing regions, and growing rapidly, even in countries where hunger exists In China, the number of overweight people increased from less than 10% to 15% in just three years Even sub-Saharan Africa, where most of the worlds hungry live, is seeing an increase in obesity, especially among urban women. Thus, as poor countries become more prosperous, they face many of the problems common in industrialized nations Obesity is one of the most worrisome (WHO 2003)

The World Health Organisation (WHO) estimates that 1 2 billion people worldwide are affected by overweight and obesity, and the numbers are increasing at an unprecedented rate The secular trends of obesity worldwide have been depicted in **Table 1**. It is clearly evident from the table that with increasing time period, there occurs an increase in the prevalence of obesity among both males and females

In India, the problem of obesity is more prevalent in the upper middle class than among slum dwellers and more females than males have been found to be overweight in all age groups (NFI study) (Gopalan 1997). Thus, as against the prevalence rate of overweight of 1% for males and 4% for females in the

TABLE 1

SECUALR TRENDS OF OBESITY WORLDWIDE (BMI >30)

COUNTRY	YEAR	PREVALENCE (%)	
		Males	Females
Quebec			
	1992	10 0	10 0
	1998	13 5	11 7
England			
	1980	6 0	8 0
	1987	7 0	12 0
	1992	13 0	12 0
	1995	15 0	16 5
West Germany			
	1989	13 0	2 0
	1992	21 0	27 0
U.S.A.			
	1973	11 6	16 1
	1978	12 0	14 8
	1991	19 7	24.7
Brazil			
	1975	3 1	13.3
	1989	5 9	8 2
China			
	1991	0 4	0 9
	1992	1 2	1.6

Source WHO 1998

slums, the corresponding figures for the high-income group among the middle class were 32 2% and 50% (**Table 2**) This data is in line with observations reported by Visweswara Rao except that the rates among the high-income group in the NFI study are somewhat higher Visweswara Rao et al (1996) had reported a prevalence rate of 23 9% in urban males and 36.3% in urban females of the high socio-economic group as compared to 0.8% in rural males and 2.2% in rural females The NNMB report of 1996, covering nine Indian states, reported a prevalence rate of 3 6 % in rural males and 6 6 % in rural females (NNMB Report 1996)

In the NFI study the prevalence of abdominal obesity was found in 68 1 % of males and 58 0 % of females with the subjects where BMI >25 (**Table 3**). This indicates that the prevalence of abdominal obesity in subjects having BMI>25 is found to be on the higher side

Studies carried out in the department have shown the prevalence of overweight and obesity to be 8.6 % and 2 9 % among the hostel girls in the age group of 18-22 years (Mani and Tiwari 2002), where as it was found to be 14 2 % and 3.4 % in the urban population of Vadodara (Mani and Khan 2002). The study revealed the prevalence of obesity to be higher among females in comparison to the male subjects

TABLE 2

PREVALENCE OF OBESITY (BMI + 25) IN URBAN ADULTS BY SOCIO-ECONOMIC STATUS

ECONIMIC STATUS	PREVALENCE (%)	
	Males	Females
MIDDLE CLASS		
High	32 2	50 0
Middle	16.2	30 3
Low	7 0	27 8
Slum (Poor)	1 0	4 0

Source Gopalan (1997)

TABLE 3

PREVALENCE OF ABDOMINAL OBESITY (WHR) BY GRADES OF BMI

Grades of BMI	Prevalence (%) (With High WHR)	
	Males	Females
Undernourished (BMI < 18 5)	1 8	1 75
Normal (BMI 18 5-25)	17.8	20 0
Overweight/Obese (BMI > 25)	68.1	58.0

Source: Gopalan (1997)

PREVALENCE OF DIABETES

Diabetes is a major health problem from both national and worldwide perspectives. The prevalence of diabetes mellitus is on the rise at an alarming pace. The WHO has projected that the global prevalence of Type 2 diabetes mellitus will more than double from 135 million in 1995 to 300 million by 2025 (King and Rewers 1993) The WHO has also acknowledged that India has the maximum number of diabetic patients in any given country in the year 1995 (19 million) and this would increase to 57 million by the year 2025 (Premalatha et al, 2000) Thus, the countries with largest number of diabetics in the year 2025 will be India, China and the USA. (**Table 4**)

The prevalence of diabetes in India over a period of 30 years has increased substantially (**Table 5**) According to a recent PODIS study (n = 41251) carried out by the Indian Task Force on diabetes mellitus showed the prevalence to be 9 6% in the urban areas and 4.26% in rural areas, thus indicating the rising threat of the same in India. Various other studies carried out in different parts of India show the prevalence ranging between 0.5 - 11.6% (**Table 5**).

Studies carried out in the department have shown the prevalence of diabetes to be 8.8% in the urban population of Vadodara (Mani and Khan 2002), whereas it was found to be 5 3% in the urban population of Vallabh Vidyanagar (Mani and Gujarathi 2002)

TABLE 4

PREVALENCE OF DIABETES WORLDWIDE

	COUNTRY	1995	COUNTRY	2025
1	India	19 4	India	57 2
2	China	16 0	China	37 6
3	U S	13 9	U S	21 9
4	Russian Federation	8 9	Pakistan	14 5
5	Japan	6 3	Indonesia	12 4
6	Brazil	4 9	Russian Federation	12 2
7	Indonesia	4 5	Mexico	11 7
8	Pakistan	4 3	Brazil	11 6
9	Mexico	3 8	Egypt	-
10	Ukraine	3 6	Japan	8 5
All Other Countries		49 7		103 6
Total		**135.3**		**300.0**

Source Munichoodappa (2002)

TABLE 5

PREVALENCE OF DIABETES IN INDIA

STUDY	YEAR	PREVALENCE (%)
URBAN		
Cuttak	1971	1 2
New Delhi	1972	2 3
Madurai	1979	0 5
Multicentre	1979	0
Tenali	1984	4 7
Kudremukh	1988	5 0
Madras	1989	8 3
Madras	1992	8 2
Madras	1999	11 6
NUDS *	2001	13 9
PODIS **	2001	9 6
RURAL		
Bhadran	1986	3 8
Gangavathi	1989	2.2
Eluru	199	1 6
Madras	1992	2 4
PODIS	2001	4 26

Source Munichoodappa (2002)

* NUDS – National Urban Diabetes Survey
**PODIS – Prevalence of Diabetes in Indian Study

PREVALENCE OF HYPERTENSION

Hypertension is a silent killer It is estimated that over 800 million people in the world suffer from hypertension Ã study carried out by Kennedy et al , 2001 in United Kingdom showed the prevalence to be 19 5% among the European people residing in United Kingdom and 27 3% among the African-Caribbeans residing in United Kingdom In comparison to this, the African-Caribbeans residing in Jamaica showed the prevalence to be 12 4% respectively (**Table 6**) The National Health and Nutrition Examination Survey (1985) showed the prevalence of hypertension amongst all races to be 29.8% and it was found that the blacks had higher percent prevalence in comparison to the whites (**Table 6**)

A Multicentric study on hypertension carried out by the WHO (2001) in some urban and rural areas of Bangladesh and India showed the prevalence of hypertension in urban areas of Maharashtra to be 72% and 69% in Kerala, whereas in rural areas of Kerala showed the prevalence to be 55%. Similarly in urban area of Dhaka, the prevalence was 75% and 53% in rural area respectively (**Table 6**) The prevalence rates are lower among the rural areas in comparison to the urban areas, however the rural areas are also showing quite a large percent of prevalence A study by Fernando et al (1994) was conducted in suburban Sri Lankan community, to assess the prevalence of hypertension in a random sample of 633 subjects The prevalence was reported to be 15.25%

TABLE 6

PREVALENCE OF HYPERTENSION

PLACE	AGE GROUP (Yrs)	PREVALENCE (%)
Cameroon (Urban) #	25-74	16.8
Cameroon (Rural) #	25-74	5.7
Jamaica (African-Caribbean) #	25-74	12 4
UK (Manchester) (African-Caribbean) #	25-74	27 3
UK (Manchester) (European) #	25-74	19 5
USA (Blacks) •	18-74	38 2
USA (Whites) •	18-74	28 8
USA (All Races) •	18-74	29.8
Dhaka (Urban) ℗	70	75
Maharashtra(Urban) ℗	70	72
Kerala (Urban) ℗	70	69
Kerala (Rural) ℗	70	55
Dhaka (Rural) ℗	70	53

Kennedy et al 2001

• National Health and Nutrition Examination Survey 1985

℗ Bulletin of the World Health Organization, 2001

The trends of hypertension prevalence in India are depicted in **Table 7** In urban population, hypertension prevalence was 1 24%, 4 24% and 3 03% in adults of Calcutta (1949), Kanpur (1954) and Bombay (1959) respectively Recent studies show that the prevalence is 14 08% in Ludhiana (1985) and 10 99% in Jaipur (1995) In rural subjects hypertension prevalence increased form 1.99% (Delhi) and 0 52% (Bombay) in 1959 to 4 02% (Maharashtra) in 1993 and 7 08% (Rajasthan) in 1995 In addition to these studies, the study carried out in Vadodara shows the prevalence to be 11 7 % (Mani and Khan 2002), whereas it was found to be 5.7 % in Vallabh Vidyanagar (Mani and Gujarathi 2002)

PREVALENCE OF CORONARY HEART DISEASE

Current estimates show that 11 million of the 15 million deaths each year due to CVD occur in less-developed countries and economies in transition However, the projections for the next 20 years is even more staggering (Chockalingam 2000) (**Figure 1**).

Coronary heart disease (CHD) is the single leading cause of death in America as shown by the 2000 statistics (AHA, 2003). According to the National Heart, Lung, and Blood Institute's Atherosclerotic Risk in Communities (ARIC) Study it has been reported that every year 1,100,000 new and recurrent cases of coronary risk are noted and that over 44% die (Sharrett et al 2001)

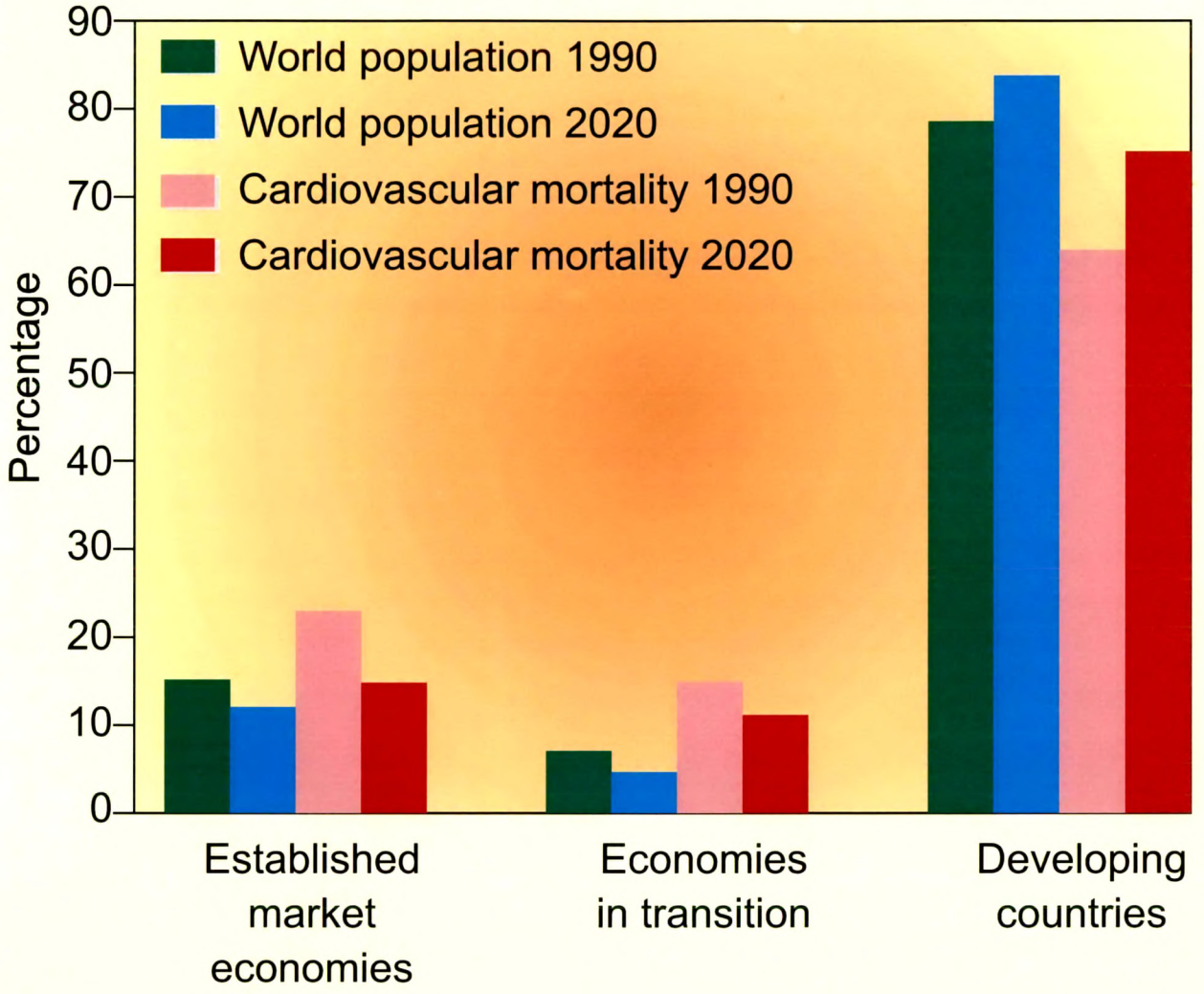
TABLE 7

PREVALENCE OF HYPERTENSION IN INDIA

Study	Year	Age-Group (Yrs)	Sample Size	Prevalence (%)
URBAN				
Calcutta	1949	18-58	2500	1 24
Kanpur	1954	18-60	2262	4 23
Bombay	1959	20-80	4120	3 03
Agra	1963	20-80	1934	4 35
Railway	1971	20-58	4232	9 24
Rohtak	1978	20-69	2023	6.43
Bombay	1980	20-80	5723	15 52
Delhi	1984	20-60	2455	3 18
Ludhiana	1985	20-75	1008	14 08
Jaipur	1995	20-80	2112	10 99
RURAL				
Delhi	1958	20-75	1052	1 99
Bombay	1959	30-60	5996	0 52
Haryana	1977	20-67	2045	3 57
Uttar Pradesh	1983	30-70	3332	0 36
Haryana	1983	20-69	905	5 41
Rajashthan	1984	21-60	912	5.59
Punjab	1985	20-75	3340	2 63
Rajasthan	1991	21-70	6840	3 83
Maharashtra	1993	16-60	448	4 02
Maharashtra	1993	20-69	4045	3 41
Kerala	1993	25-69	1130	17.88
Kerala	1994	20-70	1027	12 46
Rajasthan	1994	20-80	3148	7.08
TRIBAL				
Orissa	1986	20-70	4523	0 44
Himachal	1986	15-82	3103	2 42
Orissa	1994	20-70	935	2 56

Source: Gupta (1997)

FIGURE - 1
PROJECTION OF CARDIOVASCULAR MORTALITY



Source : Chockalingam (2000)

CHD prevalence has shown significant increase in India since 1950's The increase is significantly more in urban areas then in rural (**Table 8**) The prevalence increased in adult urban populations form 1 05% (Delhi) in 1960 to 9 67% (Delhi) and 7 90% (Jaipur) in 1995 In rural areas it increased form 2.03% (Haryana) in 1974 to 3 70 (Rajasthan) in 1995 Among the rural populations there is only a small increase in prevalence of CHD over the years, while in urban populations of India and other developing countries of Asia, who are being exposed to stress and modernization, CHD prevalence rtes have more than doubled in the last 30 years

OBESITY

Obesity is defined as a condition when adipose tissue makes up a greater than "normal" fraction of total body weight (Gray, 1989) Obesity is probably best defined as a degree of excess weight that imparts a heath risk (Oeser 1997).

The etiology of obesity is multifactorial Genetic, environmental, metabolic and behavioural issues may all contribute to the development and progression of obesity Furthermore, obesity is associated with common causes of morbidity and mortality such as coronary heart disease, type 2 diabetes, hypertension and coronary heart disease Hence, it has been aptly said that obesity is the mother of important CDD.

TABLE 8

PREVALENCE OF CORONARY HEART DISEASE

Study	Year	Age-Group (Yrs)	Sample Size	Prevalence (%)
URBAN				
Agra	1960	30-70	1046	1 05
Delhi	1962	30-70	1642	1 04
Chandigarh	1968	30-70	2030	6 60
Rohtak	1975	30-70	1407	3 63
Delhi	1990	25-65	13723	9 67
Jaipur	1995	20-80	2212	7 59
Moradabad	1995	20-70	152	8 55
Thiruvananthapuram	1995	20-70	506	12.65
RURAL				
Haryana	1974	30-70	1506	2.06
Vidarbha	1988	30-70	2433	1.69
Kerala	1993	25-65	1130	7 43
Punjab	1994	30-70	1100	3.09
Rajasthan	1994	20-80	3148	3 53
Uttar Pradesh	1995	20-80	162	3.09

Source: Gupta and Gupta (1996)

CLASSIFICATION OF OVERWEIGHT AND OBESITY

Several tools are available for the detailed characterization of the obese state, which include measures of body composition (e g underwater weighing), anatomical distribution of body fat (e g magnetic resonance imaging), energy intake (e g. prospective dietary record) and energy expenditure (e g doubly labeled water). However, the cost and the practical difficulties involved in such techniques limit their usefulness to research

The two most commonly and universally used techniques are

Body Mass Index

Body Mass Index (BMI) is a simple index of weight for height that is commonly used to classify overweight and obesity in adults The classification of overweight and obesity, according to BMI, is shown in **Table 9** as recommended by WHO (2003). The WHO classification is based primarily on the association between BMI and mortality.

A BMI of 30 or more is now widely accepted as denoting the classification of obesity However, BMI does not distinguish between weight associated with muscles and weight associated with fat. As a result, the relationship between BMI and body fat content varies according to body build and proportion Hence, another method to assess obesity which has been widely accepted is waist to hip ratio

TABLE 9

CLASSIFICATION OF OBESITY BASED ON BODY MASS INDEX

CLASSIFICATION	BMI (kg/m^2)	RISK OF CO-MORBIDITIES
Underweight	< 18 5	Low (but risk of other clinical problems increased)
Normal range	18 5 - 29 9	Average
Overweight	≥ 25 0	
Pre-obese	25 - 29 9	Increased
Class I	30 0 - 34 9	Moderate
Class II	35 0 - 39 9	Severe
Class III	> 40 0	Very Severe

Source. WHO 2003

Waist to Hip Ratio

Waist to hip ratio (WHR) is another method which is used to indicate the level of obesity, though it specifies the chances of abdominal obesity WHR >1 0 in case of men and >0 85 for females are said to be at high risk associated with central adiposity (**Table 10**)

Recently, waist circumference has been advocated to be a good indicator of body fatness because it is highly correlated with BMI, visceral fatness and total body fat (Katzmarzyk et al 1999) The WHR ratio may have a fallacy, especially in Indian women, where hip size is usually large and hence a fairly large waist may not produce an abnormal ratio Hence, absolute waist size is now considered a good parameter Men are said to be at high risk associated with central obesity when their waist measurement is >102 cm and women are said to be at high risk when their waist measurement if >88 cm (**Table 10**) BMI and waist circumference provide simple yet sensitive methods for the estimation of total and central adiposity in groups of adult women (Taylor et al 1999) Hence, use of both the methods, in combination help in establishing the degree of overweight and obesity.

ETIOLOGY OF OBESITY

Many factors contribute to the etiology of obesity, including genetics, environment, nutrition and the level of physical activity.

TABLE 10

CLASSIFICATION OF CENTRAL ADIPOSITY BASED ON WAIST CIRCUMFERENCE AND WAIST HIP RATIO

Risk Associated with Central Adiposity			
Risk:	Low	Moderate	High
Males			
Waist Circumference (cm)	< 94	94-102	> 102
Waist Hip Ratio (WHR)	< 0 9	0 9-1 0	> 1 0
Females			
Waist Circumference (cm)	< 80	80-88	> 88
Waist Hip Ratio (WHR)	< 0.75	0 75-0 85	> 0 85

Source: Chandalia (1998)

Genetic Factor

Early evidence of a genetic component underlying obesity came from a variety of animal models The first study of human beings employed twins, and established a high level of heritability (Rippe et al 1998) Since then, studies have focused on identifying specific genes and potential pathways for their contribution to obesity There are several known genetic mutations that have been associated with special and uncommon cases of severe obesity. A number of variants of the leptin gene, including those that cause leptin deficiencies and obesity, have been identified A gene called melanocortin-4 receptor that plays a key role in shutting off the urge to eat is defective in some families with a history of obesity Researchers have also identified a mutation in a gene for a protein called proopiomelanocortin, which results in a syndrome of obesity, red hair, and deficiencies in stress hormones About 5% of severely obese people have mutations that over-respond to agouti-related protein (AGRP) AGRP is a newly discovered protein that is controlled by leptin and regulates how many calories are consumed. Genetics also determine the number of fat cells a person has, and some people are simply born with more

Although genetic abnormalities may make it harder or easier to lose weight, the prevalence of obesity has dramatically increased over the past two decades, and genes could not have changed within that short amount of time The metabolism in humans evolved over centuries so that it could conserve energy and store fat during times of famine Most cases of obesity are now

observed in people with normal physiology who live in industrialized nations where food is overly plentiful, and it is easy to avoid expending enough energy to burn the excess calories One theory that combines genetic and environmental factors suggests that type 2 diabetes and the obesity that usually accompanies this disorder are derived from genetic actions that were once important for survival Some experts postulate the existence of a so-called "thrifty" gene, which regulates hormonal fluctuations to accommodate seasonal changes

Such a theory could explain the high incidence of type 2 diabetes and obesity found in Pima tribes and other Native American tribes with nomadic histories and Western dietary habits The traditional low-fat high-fiber foods of the Pima people may have protected this genetically susceptible population in the past from the high incidence of obesity and Type 2 diabetes they are experiencing now

Early studies estimated that hereditary influence accounted for upto 80% of the tendency to gain weight, but more recent data indicate that 33% of the BMI is attributable to genetics (Oeser 1997)

Since genetic factors account for only a third of the variance in body weight, environmental influences must therefore account for balance

Environmental Factors

Recent data of increase in the prevalence of obesity indicates that environmental factors are also important determinants for the development of obesity The process of modernization and economic transition has brought about a number of improvements to the standard of living. However, it has also had a number of negative consequences that have directly and indirectly led to the deleterious nutritional and physical activity patterns that contribute to the development of obesity In particular, the increase in dietary fat and the decrease in physical activity, a combination that has been termed "patho-environment", seem to underline this alarming epidemic of obesity (Ravussin and Tataranni1997). The various environmental factors, which contribute to the development of obesity, could be listed as increasing urbanization, socioeconomic status, nutritional factors and physical inactivity Nutritional factors and physical inactivity will be discussed later in this chapter Urbanisation and socio economic status are discussed below

Urbanisation

The prevalence of obesity has been found to be more among the urban areas in comparison to rural areas As more and more people turn towards urban civilizations in search of work etc , there is a series of change in their diet, physical activity, health and nutrition, which is collectively known as 'nutrition transition'. Since urban areas are much further ahead in the transition than rural areas, they experience higher rates of obesity. Cities offer a greater

range of food choices, generally at lower prices Urban work often demands less physical exertion than rural work And as more and more women work away from home, they may be too busy to shop for, prepare and cook healthy meals at home The fact that more people are moving to the city compounds the problem In 1900, just 10 percent of the world population inhabited cities Today, that figure is nearly 50 percent

According to United Nation's estimate, in the next 25 years, the rural population in the developing world is expected to increase by 6%, while the urban population will grow by 87% (UN Population Division 1988) It has been shown that as urbanization advances, the BMI distribution curve of the population shifts to the right (INCLEN 1996). One can speculate that this may result from a combination of increased energy intake, decreased energy expenditure and, perhaps reduced gastrointestinal nutrient losses

By the turn of the century nearly 35 per cent of India's population will be living in urban areas. Asia's urban population is expected to exceed 1.242 million by 2000 A D more than a five-fold increase from 226 million in 1950 (Gopalan 1997).

Urbanization involves changes in occupational patterns, life-styles, family structures and value systems These changes are reflected in changes in dietary practices and in the levels of physical activity (Gopalan 1997) In most countries, urban residents consume smaller proportions of carbohydrates and

greater proportion of protein and fat, particularly saturated fat (Popkin et al 1995). Majority of people in urban society adapt to the various changes in lifestyle and dietary pattern resulting in increased prevalence of overweight and obesity

Socio-economic Status

Socio-economic status (SES) is usually presented as a composite index combining income, education and occupation Studies have repeatedly shown that high SES is negatively correlated with obesity in developed countries, particularly among women, but is positively related with obesity the in population of developing countries (Sobal et al 1989 and Brown et al 1998) McMurray et al (2000) studied the effect of ethnicity and SES on body mass index of adolescents, from rural as well as urban settings and found that ethnicity and SES may be important factors that can influence body weight status

A study with the objective of finding the independent effects of income and education on the risk of obesity was carried out in the Brazilian adult population (Monteiro et al 2001) The study was carried in two regions - less developed and more developed In less developed region, level of education was not a risk factor, however, in the more developed one, better - educated men had slightly less chance to be obese. However, in case of females, income had direct association and education had inverse, in less developed region. In more developed region only the women's education influenced the risk of obesity, and the association between the two variables was inverse

and strong as in the less developed region The study indicated that in transition societies income tends to be a risk factor for obesity, whereas education tends to be protective and that both gender and level of economic development are relevant modifiers of the influence exerted by these variables

Laitinen et al (2001) carried out a study in Finland wherein family social class, maternal body mass index, childhood body mass index and age at menarche were found to be predictors of adult obesity The findings concluded that the family's social class during subject's childhood had a long-term influence on BMI, early maturation predicted overweight and obesity in adulthood

DIABETES MELLITUS

The syndrome of diabetes mellitus is characterized by chronic hyperglycemia and disturbances of the carbohydrate, protein and lipid metabolism, which are often associated with accelerated process of microvascular atherosclerosis in the eye and kidneys and an increased frequency of macro vascular disease – peripheral, vascular and coronary heart disease (Rossetti 2002)

Diabetes mellitus is a disease of ancient origin and over the years a number of definitions have emerged It is also defined as a chronic disease, which render the body unable to use carbohydrates properly causing it to rely too predominantly on protein and fat for fuel (Stenger 2001). It is also considered

to be a "disease of civilization" Studies have shown that risk factors like dietary choices, smoking, alcohol consumption, overweight/obesity and sedentary lifestyles; if effectively controlled can lead to a decrease in risk of developing further complications (Puska et al 1983, Fortmann et al 1995) Hence, it is a disease of metabolic dysregulation having several clinical forms, each having a distinct etiology, clinical presentation and course

Diabetes mellitus has a number of clinical forms and have been classified accordingly The latest classification encompasses both the clinical stages and etiological types of diabetes mellitus and other categories of hyperglycemia This classification is a result of improved understanding of the causes of diabetes mellitus All subjects with diabetes can be categorized according to clinical stage, and this is achievable in all circumstances. The stage of glycemia may change overtime depending on the extent of the underlying disease processes The disease process may be present but may not have progressed far enough to cause hyperglycemia The etiological classification reflects the fact that the defect or process which may lead to diabetes may be identifiable at any stage in the development of diabetes – even at the normoglycemia The etiological classification of National Diabetes Data Group and recent Who expert committee group on diabetes mellitus, 1999 in use is shown in **table 11**.

TABLE 11

ETIOLOGICAL CLASSIFICATION OF DISORDERS OF GLYCEMIA

Type 1 (beta cell destruction, usually leading to absolute insulin deficiency)

Autoimmune

Idiopathic

Type 2 (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance)

Other specific types

A Genetic defects of beta cell function

B Genetic defects insulin action

C Diseases of the exocrine pancreas

D Endocrinopathies

E Drug or chemical induced

F Infections

G Uncommon forms of immune mediated diabetes

H. Other genetic syndromes sometimes associated with diabetes

Gestational Diabetes (GDM) **

** Includes the former categories of gestational impaired glucose tolerance and gestational diabetes

Source American Diabetes Association (2002)

PATHOPHYSIOLOGY OF DIABETES MELLITUS

The pathophysiology of type 2 diabetes is complex and in most instances clearly requires defects in both β-cell function and insulin sensitivity Together, these abnormalities result in increased rates of glucose release by the liver and kidney as well as decreased clearance from the circulation

Two well-rehearsed theories as to pathogenesis exist First, the primary defect exists at the level β-cell and manifests itself as an impairment of insulin secretion Alternatively impaired tissue sensitivity to insulin represents the primary defect and initially the β-cell maintains an increased rate of insulin secretion that is able to offset insulin resistance With time, fasting hyperglycemia develops as pancreatic exhaustion occurs – there is insulinopenia relative to insulin resistance Patients with overt diabetes (regardless of whether they are lean or obese) thus exhibit a relative underproduction of insulin

For the last decade, a great deal of attention has been directed at further understanding the role of insulin resistance as an important contributor to the development and maintenance of the hyperglycemia of type 2 diabetes. Insulin resistance can be defined as a state of reduced responsiveness to normal circulating concentrations of insulin and is now recognized as a characteristic trait of type 2 diabetes (Saltiel 2000) Cross sectional studies have shown insulin resistance as a consistent finding in patients with type 2

diabetes (Cahill 1988) Moreover, since insulin resistance precedes the onset of the disease by 10-20 years, it is considered as the best predictor for the development of diabetes (Haffner et al 1990) Insulin resistance is also commonly associated with obesity, sedentary lifestyle and lack of physical activity (Gerich 2000, Elbein 1997, Ferrannin et al 1997)

Recently the vital role of the pancreatic islet, and specifically the β-cell, in the pathogenesis of type 2 diabetes has been studied It is well accepted that for hyperglycemia to exist in type 2 diabetes, β-cell dysfunction has to be present This alteration is manifested in a number of different ways including reductions in insulin release in response to glucose, and non glucose secretagogus, changes in pulsatility and oscillatory insulin secretion, an abnormality in the efficiency of proinsulin to insulin conversion, and reduced release of islet amyloid poly peptide (IAPP), also known as amylin (Kahn 2001). Data from the UKPDS suggests that the onset of β-cell dysfunction associated with diabetes occurs well before the development of hyperglycemia, and may commence many years before diagnosis of the disease (Holman 1998) However, this suggestion is based on an extrapolation of findings in subjects with established type 2 diabetes While this concept is gaining support, it has not been a universally accepted idea. Recent advances in our understanding of the modulating effect of insulin sensitivity on β-cell function have brought a new understanding and therefore a new interpretation to the assessments of insulin release in individuals at risk of developing type 2 diabetes Insulin sensitivity has long been recognized

to be an important factor determining the magnitude of the insulin response to β-cell stimulation (Olefsky et al 1973, Kahn et al 1993) Thus, when β-cell function is assessed, obese individuals who are insulin resistant manifest greater responses than age-matched lean subjects (Perley and Kipnis 1966, Polonsky et al 1988, Beard et al 1987)

The nature of this relationship is such that insulin sensitivity and β-cell function are inversely and proportionally related The relationship has also highlighted the fact that if two individuals have identical absolute insulin responses, the only way their β-cell function can be considered to be similar is if they have identical insulin sensitivity Conversely, if these same individuals differ in terms of insulin sensitivity, it has to be concluded that their β-cell function differs

Apart from the defects in insulin sensitivity and ß-cell function non insulin-dependent diabetes mellitus (NIDDM) / Type 2 diabetes is strongly inherited, as evidenced by a high concordance in identical twins and strong familial aggregation In unbiased studies, the concordance in identical twins is ~70%, whereas the lifetime risk to siblings is only half this rate (Elbein 1997) A history of NIDDM in a first-degree relative doubles the risk of diabetes Offspring of two diabetic parents have an 80% lifetime risk of diabetes (Kenny et al 1995, Rewers and Hamman 1995). Further evidence for a genetic role is suggested by the wide variation in incidence and prevalence among different ethnic groups. Thus, Pima Indians have a nearly 50% prevalence that is marked by a degree of insulin resistance not seen in Caucasians, and both

Hispanics and African-Americans are also at high risk (Kenny et al 1995).

The physiology of NIDDM has provided some clues to possible defects Insulin resistance is nearly ubiquitous The offspring of two diabetic parents, who historically are at particularly high risk for future NIDDM, are insulin resistant many years before NIDDM development (Elbein 1997) In Pima Indians, San Antonio Hispanics and Utah Caucasians, insulin resistance is inherited in an autosomal fashion, suggesting that a single gene might influence this intermediate phenotype (Schumacher et al 1992, Stern et al 1996)

Individuals at risk for NIDDM also show various forms of pancreatic β-cell dysfunction (Polonsky et al 1996) Those with both impaired glucose tolerance (IGT) and NIDDM demonstrate loss of first-phase insulin release in response to an IV glucose load. Although this defect may result from glucotoxicity, more subtle defects of insulin secretion are present in family members at risk. Thus, the normal cyclic patterns of insulin release are lost in both NIDDM subjects and in relatives at risk (Polonsky et al 1996)

Among Pima Indians, the risk of future NIDDM is highest among those with both insulin resistance and a defect in insulin secretion. Defects of both insulin secretion and insulin sensitivity are apparent in offspring of NIDDM parents in Utah Caucasian pedigrees ascertained for multiple NIDDM siblings when insulin secretion is appropriately normalized for the degree of insulin resistance (Elbein 1997) Thus inherited defects of both insulin sensitivity and

β-cell function are likely to contribute to NIDDM susceptibility

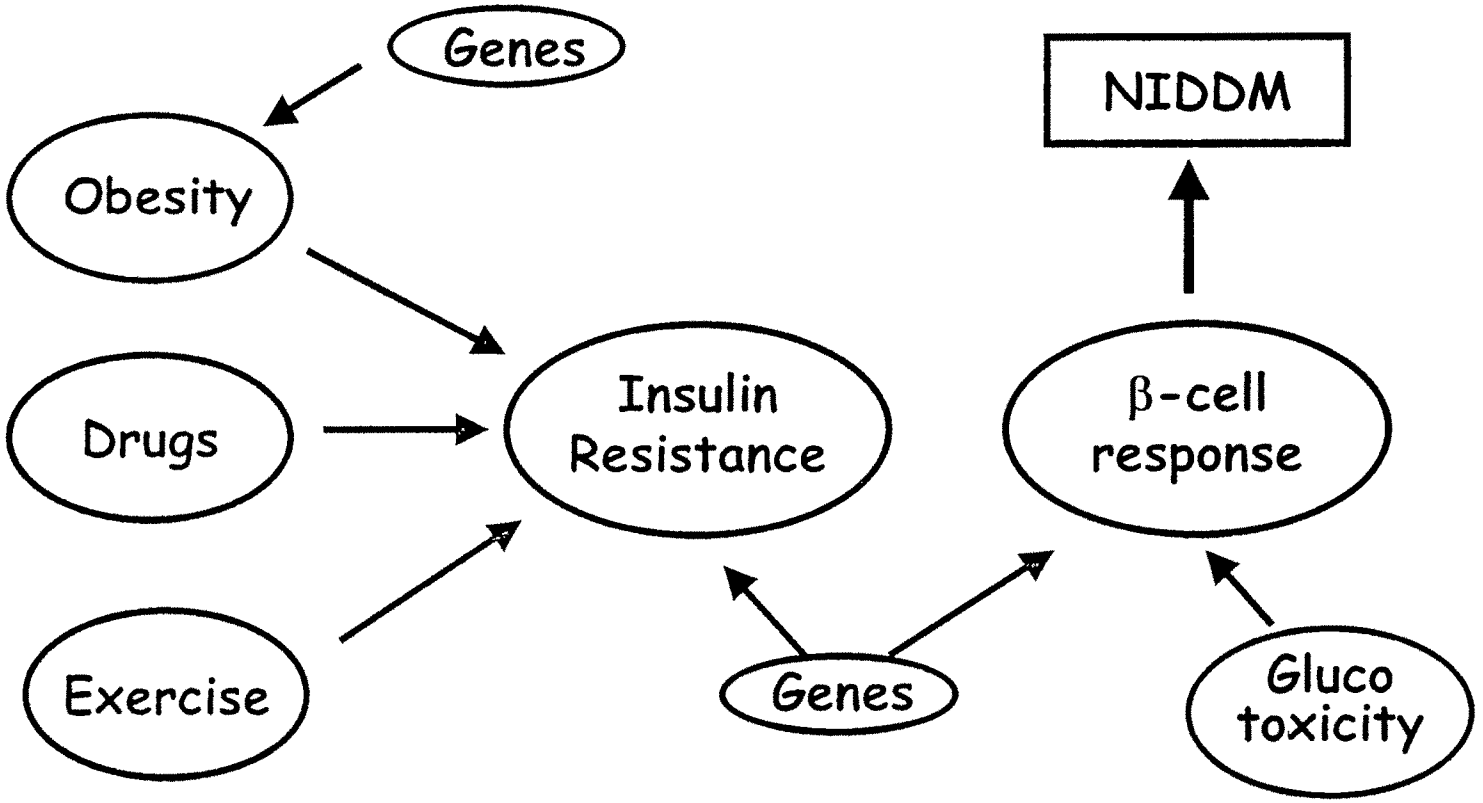
In contrast to defects that are at least partially inherited, NIDDM is also characterized by increased hepatic glucose production from both glycogenolysis and gluconeogenesis (DeFronzo et al 1992) This defect appears relatively late in the course of NIDDM development in most studies and thus is less likely to result directly from genetic susceptibility On the other hand, like the defect in insulin sensitivity, this defect may be closely related to obesity Both peripheral insulin resistance and the increased hepatic glucose output may result from high levels of circulating free (nonesterified) fatty acids (FFA) These high levels of FFA in turn appear to relate to the amount of visceral fat (Boden 1997) Thus, inherited susceptibility to obesity and particularly visceral obesity may contribute to both the hepatic and peripheral defects seen in NIDDM. Finally, both individuals with NIDDM and offspring of two NIDDM parents have reduced glucose effectiveness, i.e , the ability of glucose to mediate its own uptake independent of insulin. The potentially complex model of environmental and genetic susceptibility to NIDDM is summarized in **Figure 2**. The figure shows a model of diabetes pathogenesis and the interaction of multiple susceptibility loci and environmental factors The model presumes a cell defect as the final stage, which is most consistent with current hypotheses although not universally accepted.

HYPERTENSION

Hypertension is defined as systolic blood pressure greater than 140mHg and diastolic blood pressure greater than 90mmHg The classification of blood

FIGURE 2

MODELS OF NIDDM SUSCEPTIBILITY



Source. Elbein (1997)

pressure according to the Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), 2003 is given in **Table 12** Hypertension affects about 600million people all over the world (Joint National committee for Detection, evaluation and treatment of high blood pressure, 1993)

ETIOPATHOGENESIS OF HYPERTENSION

The different types of hypertension are.

1) Primary/Essential/Idiopathic Hypertension:

In this type of hypertension, the exact cause of the disease is not known. 90-94% of the cares are idiopathic and this is a long term and usually a progressive disorder.

The predisposing factors for this kind of hypertension are

a) Genetic, b) Stress, c) Obesity, d) High sypathatic tone, e) Increased intake of salt (NaCl)>6gm/day, f) Alcoholism, g) Smoking, h) Diabetes Mellitus

2) Secondary Hypertension:

Secondary hypertension occurs when some other disease or abnormality is involved in its causation. In 6-8%of the cases this hypertension is seen

The causes are:

Renal, Endocrinal, Vascular, Neurological, Drugs eg Corticosteroids etc

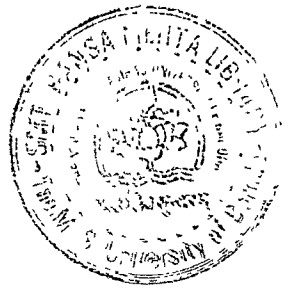


TABLE 12

CLASSIFICATION OF BLOOD PRESSURE

CATEGORY	SYSTOLIC BLOOD PRSSURE (mmHg)	DIASTOLIC BLOD PRESSURE (mmHg)
Normal	< 120	< 80
Prehypertension	120-139	80-89
Hypertension Stage I	140-159	90-99
Hypertension Stage II	≥160	≥100

Source: JNC 7 Report (2003)

3) White coat Hypertension:

This is a condition noted in patients whose blood pressure is elevated in the physicians clinic but normal at other times

Apart from the specific risk factors associated with primary or secondary hypertension, it seems to vary with race, heredity, environmental, geographical and dietary factors

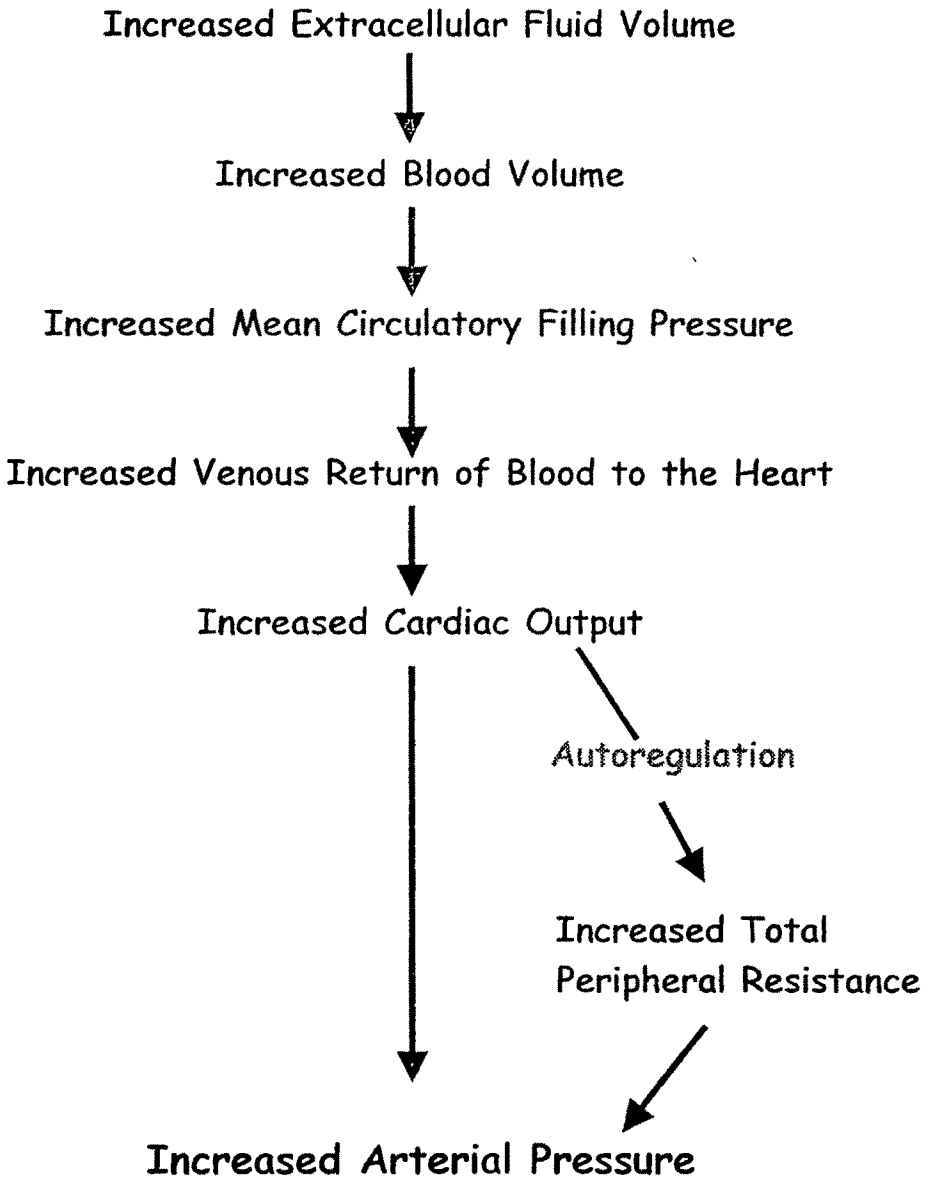
PATHOGENESIS OF HYPERTENSION

As we all are aware, that the nervous system has powerful capabilities for rapid, short-term control of arterial pressure, when the arterial pressure changes slowly over many hours or days, the nervous mechanisms gradually loose all or almost all of their ability to oppose the changes Apart from the nervous mechanisms, the kidneys play a dominant role in this control The renal-body system for arterial pressure control is a simple one when the body contains too much extracellular fluid, the arterial pressure rises. The rising pressure in turn has a direct effect to cause the kidneys to excrete the excess extracellular fluid, thus returning the pressure back toward normal

The overall mechanism by which increased extracellular volume elevates arterial blood pressure is given in **Figure 3** Increased extracellular fluid volume increases the blood volume which increases the mean circulatory filling pressure, which increases the venous return of blood to the heart, this in

FIGURE 3

MECHANISM SHOWING HOW EXTRACELLULAR VOLUME ELEVATES ARTERIAL PRESSURE



Source: Guyton and Hall (1996)

seconds while the blood flows through the small vessels of the lungs, catalysed by the enzyme *converting enzyme* that is present in the endothelium of the lung vessels

Angiotensin II is and extremely powerful vasoconstrictor, and has other effects as well that affect the circulation It persists in the blood only for 1 or 2 minutes because it is rapidly inactivated by multiple blood and tissue enzymes collectively called angiotensinase During its persistence in the blood, angiotensin II has two principal effects that can elevate arterial pressure. The first of these, vasoconstriction occurs rapidly Constriction of the arterioles increases the peripheral resistance, thereby, raising the arterial pressure Also, the mild constriction of the veins promotes increase venous return of blood to the heart, thereby helping the heart pump against the increasing pressure

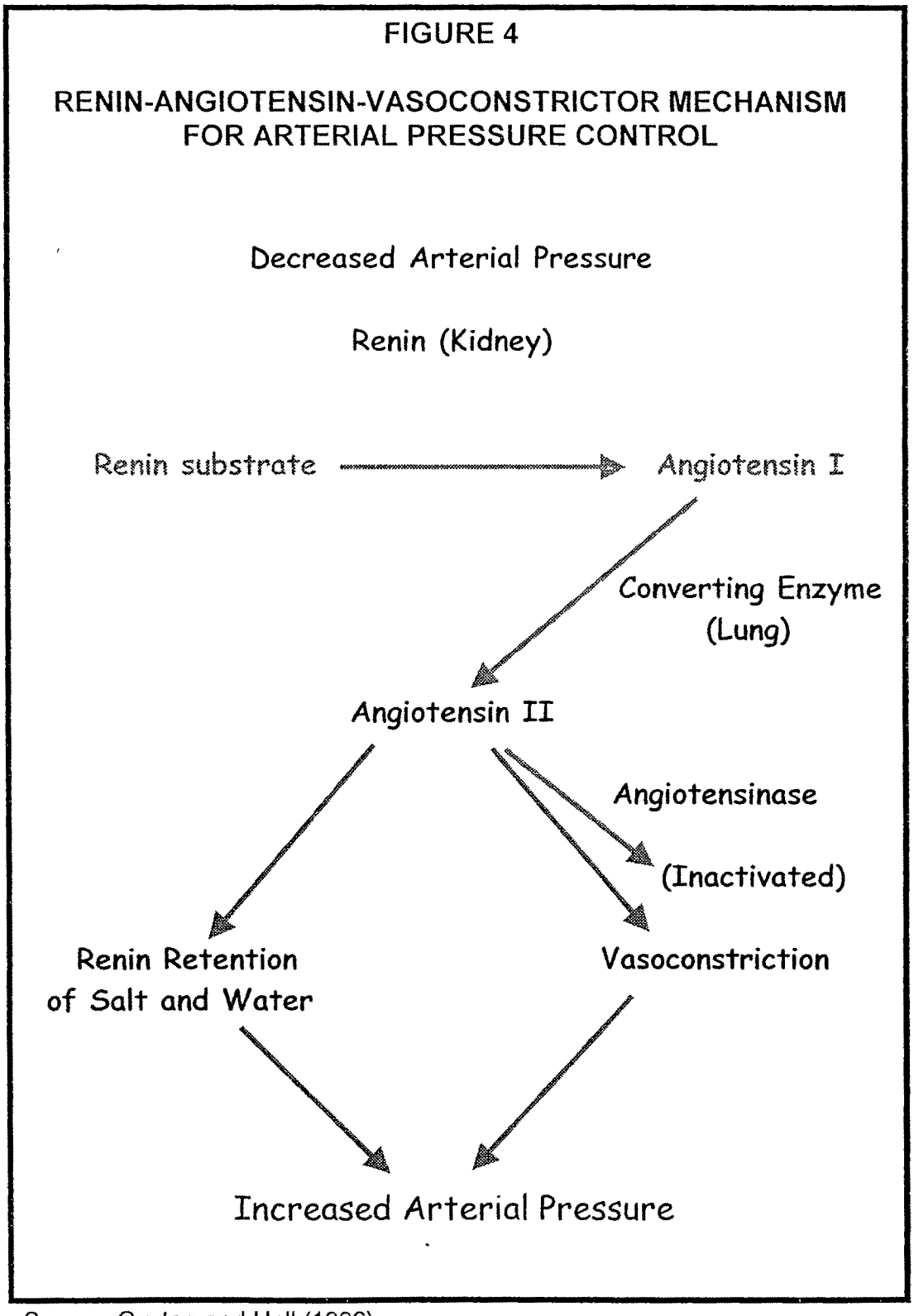
The second peripheral means by which angiotensin increases the arterial pressure is to act on the kidneys to decreases the excretion of both salt and water. This slowly increases the extracellular fluid volume, which then increases the arterial pressure over a period of hours and days (**Figure 4**)

CORONARY HEART DISEASE

Coronary artery disease, also called coronary heart disease or heart disease, is a leading cause of death for both men and women in India In recent years there has been a significant increase in the incidence of CAD/CHD in India

FIGURE 4

RENIN-ANGIOTENSIN-VASOCONSTRICTOR MECHANISM FOR ARTERIAL PRESSURE CONTROL



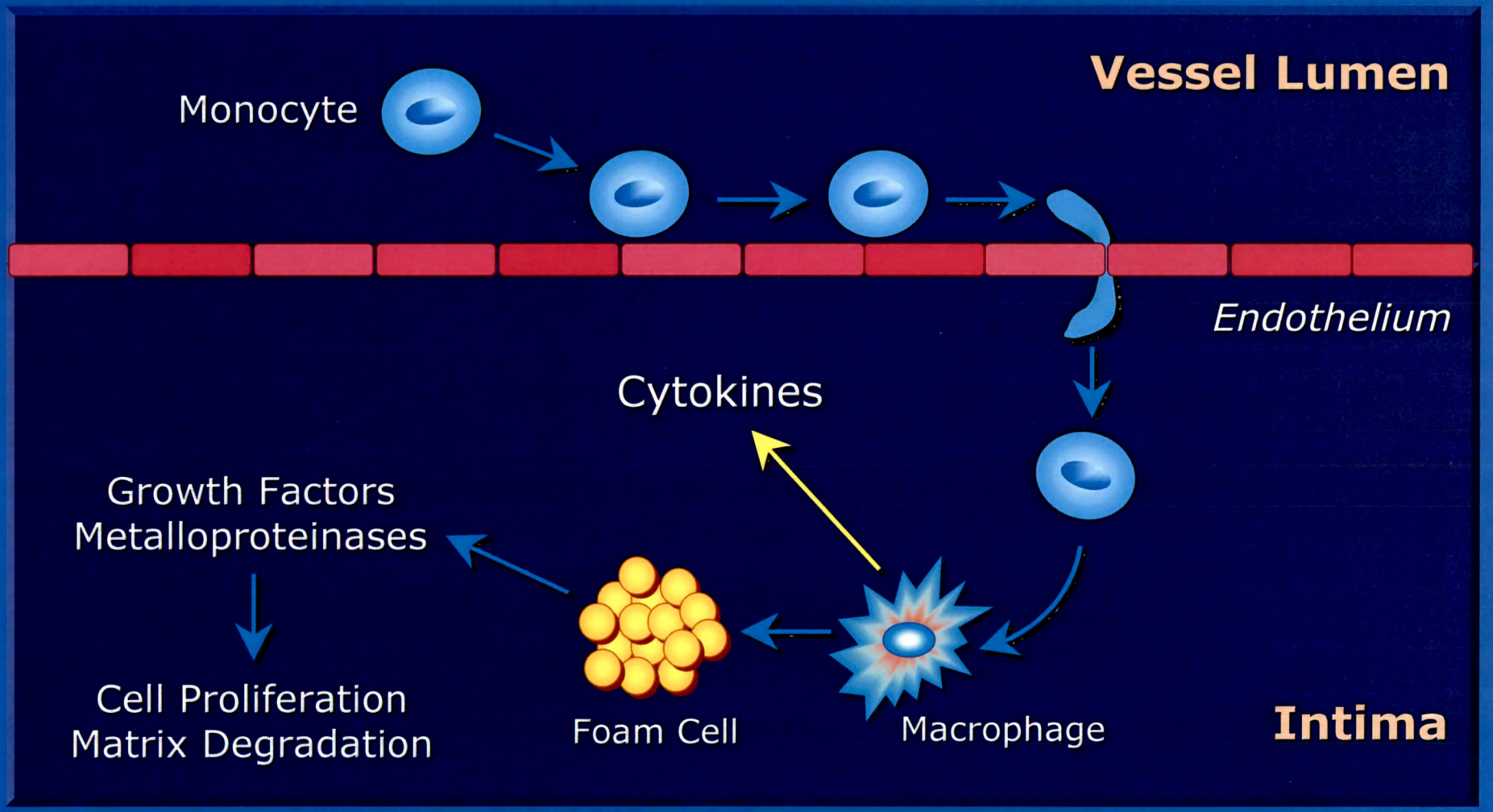
Source Guyton and Hall (1996)

The coronary arteries serve as the main blood supply for the heart muscle, which requires oxygen and other nutrients in order to function Healthy coronary arteries are clean, smooth and the artery walls are elastic and can expand to let more blood through when the heart needs to work harder

CAD occurs when these arteries become narrowed or clogged i e it is caused by atherosclerosis. Atherosclerosis involves the cellular infiltration of several cell types, including monocytes, T lymphocytes, and perhaps even mast cells Monocytes interact with the endothelial layer, attach firmly to the endothelium, and migrate into the subendothelial space, where the monocytes differentiate into macrophages Macrophages release a variety of chemicals, including cytokines, and also take up lipids, becoming foam cells Macrophages and foam cells secrete growth factors, which lead to cell proliferation and matrix production, as well as metalloproteinases, which lead to matrix degeneration Thus, macrophages and foam cells both contribute to lesion growth and may contribute to instability and thrombotic events (**Figure 5**) (Ross 1999)

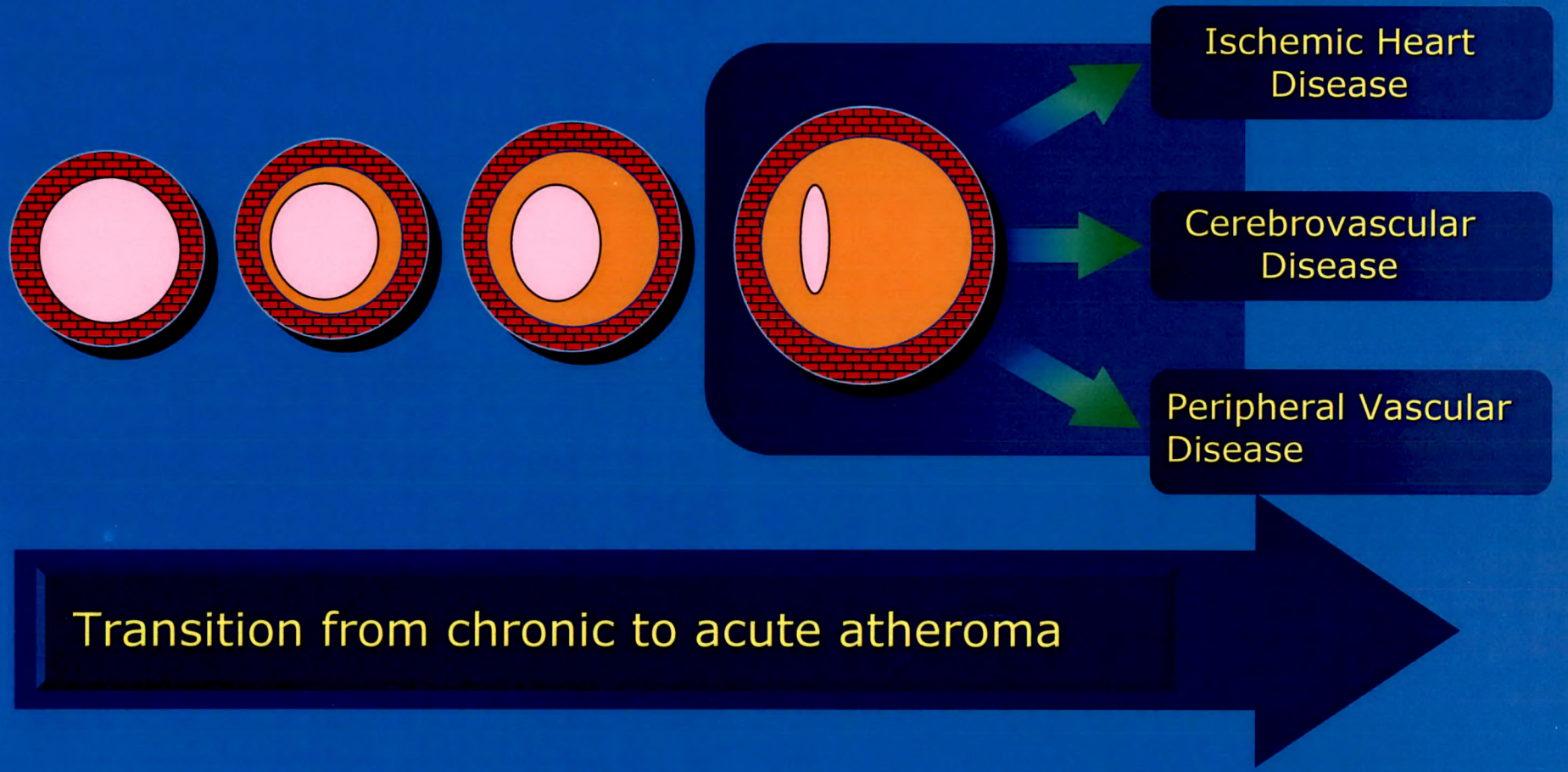
Once the atheroma is well established, it crosses the threshold to clinical manifestations In the coronary circulation, these manifestations include unstable angina and acute myocardial infarction, thrombotic complications of atheroma in the cerebrovascular or peripheral arteries include stroke and critical limb ischemia (Steinberg et al 1989) (**Figure 6**).

FIGURE 5
ATHEROSCLEROSIS - AN INFLAMMATORY DISEASE



Source: Ross (1999)

FIGURE 6
CLINICAL MANIFESTATIONS OF HUMAN ATHEROGENESIS



Source: Steinberg et al (1989)

All the major lipoprotein classes impact in some way or the other on the inflammatory process that leads to development of atherosclerosis. The triglyceride-rich lipoproteins-chylomicrons, very low density lipoprotein, and their catabolic remnants-and low-density lipoprotein cholesterol (LDL-C) are potentially proinflammatory, whereas high-density lipoprotein is potentially anti-inflammatory. Of all of the plasma lipoproteins, LDL-C has been most investigated in terms of its role in inflammation (Rye et al 1999, Doi et al 2000).

The modified LDL plays an important role in promoting the differentiation of monocytes into macrophages, a key step in the inflammatory process on the way to the development of atherosclerosis After modified LDL-C promotes the differentiation of monocytes into macrophages, the macrophages release a variety of chemicals, including cytokines

The activated macrophages also express a variety of scavenger receptors, several of which recognize the different forms of modified LDL-C. The macrophages take up the LDL-C through these scavenger receptors, accumulate the lipid, and are converted into the lipid-rich foam cells that are the hallmark of atherosclerosis Thus the evidence is now very strong that modified LDL-C particles are proinflammatory (Steinberg et al 1989)

HEALTH CONSEQUENCES OF VARIOUS CDD

OBESITY AND DIABETES MELLITUS

Obesity has been called the mother of chronic degenerative diseases because it is an independent risk factor for several non-communicable diseases. A positive association between obesity and diabetes mellitus has been observed repeatedly The risk of NIDDM increases continuously with BMI and decreases with weight loss Colditz et al (1995) reported that obese women above 40 years of age are more likely to develop NIDDM than the women who remained slim (BMI<22) Data from NHANES II, among US citizen, aged 29-29, reported the prevalence to be 2 9 times higher in overweight than non-overweight persons Obese persons tended to have a greater likelihood of glycosemia and an increasing prevalence of diabetes (Kannel 1979). Ten year follow-up (1986-1996) of middle-aged women in the Nurses Health Study and men Health Professionals Follow-up Study found that those with BMI>35 were approximately 20 times more likely to develop diabetes (Relative risk 17.0) (Field et al 2001) Yet another study carried out among Hispanics, the prevalence of diabetes was strongly associated with total and central obesity (Bermudez and Tucker 2001)

Studies carried out in South Indians have also found BMI to be strongly associated with glucose intolerance. It was also found that android pattern of body fat, measured as WHR, was found to be at a greater risk factor for

Type 2 diabetes then general obesity (Ramchandran and Snehalatha 1999)

Although a number of theories have been proposed concerning the link between obesity and type 2 diabetes, most focus on the cascade of metabolic abnormalities that are triggered by insulin resistance and the lipolytic properties of adipocytes (particularly abdominal adipocytes).

OBESITY AND HYPERTENSION

Obesity carries a penalty for the development of hypertension Both systolic and diastolic blood pressure increase with BMI, and obese individuals are at a higher risk of developing hypertension than are lean, subjects (Stamler et al 1989) Data from NHANES II (non-institutionalized, non-pregnant US residents, ages 20 to 29, 1976-1980), report the prevalence of hypertension (blood pressure, greater than 160/95) to be 2 9 times higher for overweight than for non-overweight. A study was undertaken by Kodali et al (1997) to investigate the role of regional adiposity and metabolic abnormalities in hypertension among Indian subjects, aged between 30-50 years, belonging to middle and low income group It was found that hypertensives had significantly higher body weight, body fat, BMI and WHR as compared to controls in both men and women.

The reason for the association between increased body weight and elevated blood pressure is unclear One possibility is that obesity is associated with

higher circulating levels of insulin, which enhances renal retention of sodium, resulting in increased blood pressure (Brenner et al 1988) Weight reduction has been associated with blood pressure lowering effect and this could be due to an improvement in insulin sensitivity and a decrease in sympathetic nervous system activity and occurs independent of salt restriction (Mertens and Van Gaal 2000)

OBESITY AND CARDIOVASCULAR DISEASE

Obesity carries a penalty in that it predisposes an individual to a number of cardiovascular risk factors including dyslipidemia, hypertension raised cholesterol and impaired glucose tolerance However, the Framingham study, a large general population based study that is strengthened by having long duration follow up data, disclosed an increasing risk of CHD with increasing levels of obesity, independent of the other standard risk factors. Thus obesity has been established as an independent risk factor for the development of coronary artery disease (Bahadori et al 1996)

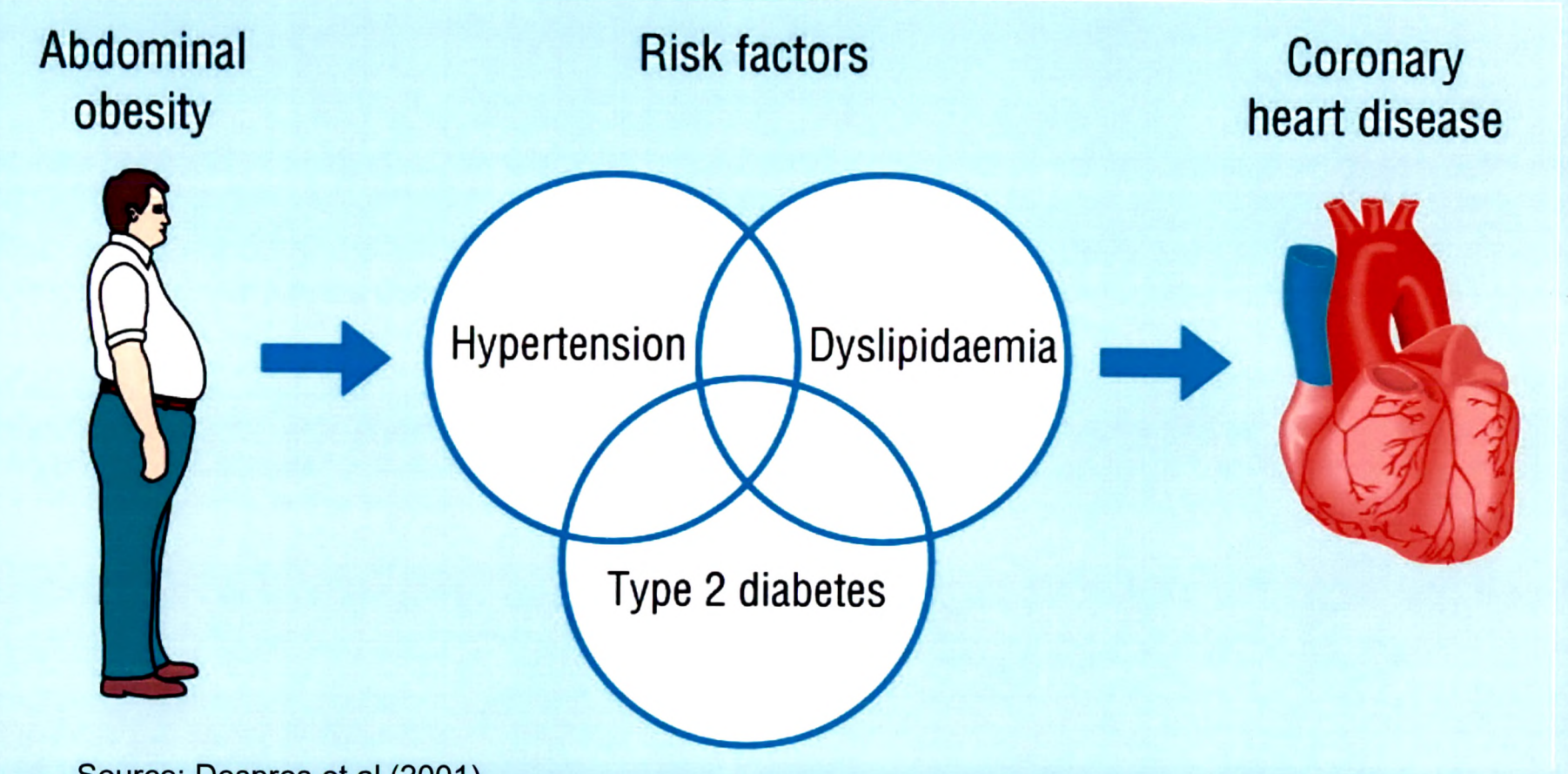
The distribution of fat deposits may be a better predictor of CHD than is the degree of obesity. Excess abdominal fat is more often related to disease than are fat deposits in the thigh or gluteral areas (Han et al 1995). In addition, mortality from CHD has been shown to be increased in the overweight, even at body weights only 10% above the average (Willett et al 1995)

In a fifteen-year follow-up of middle-aged men and women in Eastern Finland obesity was an independent risk factor for CHD mortality among men and also contributed to the risk of CHD among the women Starting at a BMI of 22 Kg/m^2, an increase in body weight equivalent to 1 BMI unit (Kg/m^2) was related to a 4% to 5% increase in CHD mortality. In other words, an increase in body weight of approximately 1 Kg increase the risk of CHD mortality by 1% to 1.5% (Jousilathi et al 1996) Baltimore Longitudinal Study of Aging showed that both WC and BMI were related to cardiovascular risk factors. It showed that when BMI is brought into the analysis, WC remains a significant predictor for most of the variables in younger men and women (<65 years), but significance is almost entirely lost in older men and women (+65 years). This could be due to the fact that the relationship of WC to intra-abdominal fat changes with age The relative distribution of sub-cutaneous to intra-abdominal fat probably changes, and abdominal wall laxness may increase with age so that a simple measurement of WC, although still predictive in itself of other risk factors, may both be as reliable a measure in older individuals (Iwao et al 2001). While some studies have shown WC to be a better predictor of cardiovascular disease risk factors than WHR, others have reported WHR to be a better indicator of cardiovascular risk (Perry et al 1998) (**Figure 7**)

Interestingly, Asian Indians have the highest rates of CHD of any ethnic group. Although the prevalence of classic risk factors is relatively low, there is a substantial prevalence in this population of high TG and low HDL-C levels,

FIGURE 7

INTERRELATION BETWEEN ABDOMINAL OBESITY AND CORONARY HEART DISEASE



Source: Despres et al (2001)

high lipoprotein levels, hyperinsulinaemia and abdominal obesity (Enas et al 1995).

DIABETES AND HYPERTENSION

As already mentioned above, a positive association exists between obesity and diabetes Apart form this diabetes also caries a penalty for hypertension as well as coronary heart disease.

Hypertension complicates diabetes in all populations and occurs with increasing frequency with advancing age. Both disorders are potent independent risk factors for cardiovascular, cerebral, renal, and peripheral atherosclerotic vascular disease (Jayakumar 2003) It is estimated that 30-75% of diabetic complications can be attributed to hypertension, which is approximately twice as common in diabetic patients as in non-diabetic individuals. Although diabetes and hypertension frequently occur together, their concurrence is considerably more than would be expected by chance alone. Patients with type II diabetes are frequently hypertensive at the time of diagnosis of diabetes, suggesting that hormonal or metabolic abnormalities associate with hypertension may exacerbate carbohydrate intolerance, or that both conditions are related to a common underlying mechanism The increase in blood pressure is generally correlated with obesity, decreased physical activity, and the advanced age characteristic of people with type II diabetes Isolated systolic hypertension is particularly common in type II diabetes and is frequently attributed to macrovascular disease and the loss of elastic

compliance in large arteries. In addition, systolic blood pressure may rise with age, further contributing to the high prevalence of systolic hypertension in type II diabetes populations It is seen that hypertension is more prevalent in diabetic men than diabetic women <50 years of age, and more common in women there after.

Multiple factors contribute to the genesis and maintenance of an elevated blood pressure in diabetes The hypertension seen in diabetes is characterized by expanded plasma volume, elevated peripheral vascular resistance, low plasma rennin activity, and other abnormalities in the rennin-angiotensin system Several experimental and clinical evidence indicate that hypertension in diabetes is volume dependent. First, hyperglycemia increases the osmolarity of the extracellular fluid, and an increased plasma volume has been demonstrated in both diabetic animals and humans Second, exchangeable sodium is frequently increased in patients with diabetes, and some diabetic patients have an exaggerated rise in blood pressure with a high-sodium diet. The maintenance of an elevated blood pressure is unclear because this increase also occurs in normotensive diabetic patients Renal insufficiency impairs the ability to excrete water and solute, perpetuating the volume expansion induced by hyperglycemia and/or sodium excess. Finally, alterations in the secretion or action of hormones that regulate sodium balance (e g , atrial natriuretic peptide, prostaglandins) may contribute to the volume overload

Considerable interest has been focused on the potential role of insulin resistance and hyperinsulinemia in the pathogenesis of hypertension in diabetes There are at least two possible mechanisms by which insulin may mediate an increase in blood pressure First, insulin stimulates renal sodium retention, which may predispose to volume overload Circulating levels of insulin are frequently elevated throughout the day in type II diabetes because of insulin resistance and these persistently high levels of insulin may play a role in initiating and maintaining the increase in total body sodium Second, the administration of insulin with subsequent stimulation of carbohydrate metabolism leads to an activation of the sympathetic nervous system and an increase in circulating norepinephrine levels, which may lead to vasoconstriction. The combined effects of volume expansion and vasoconstriction would be expected to produce a rise in systemic blood pressure.

DIABETES AND CORONARY HEART DISEASE

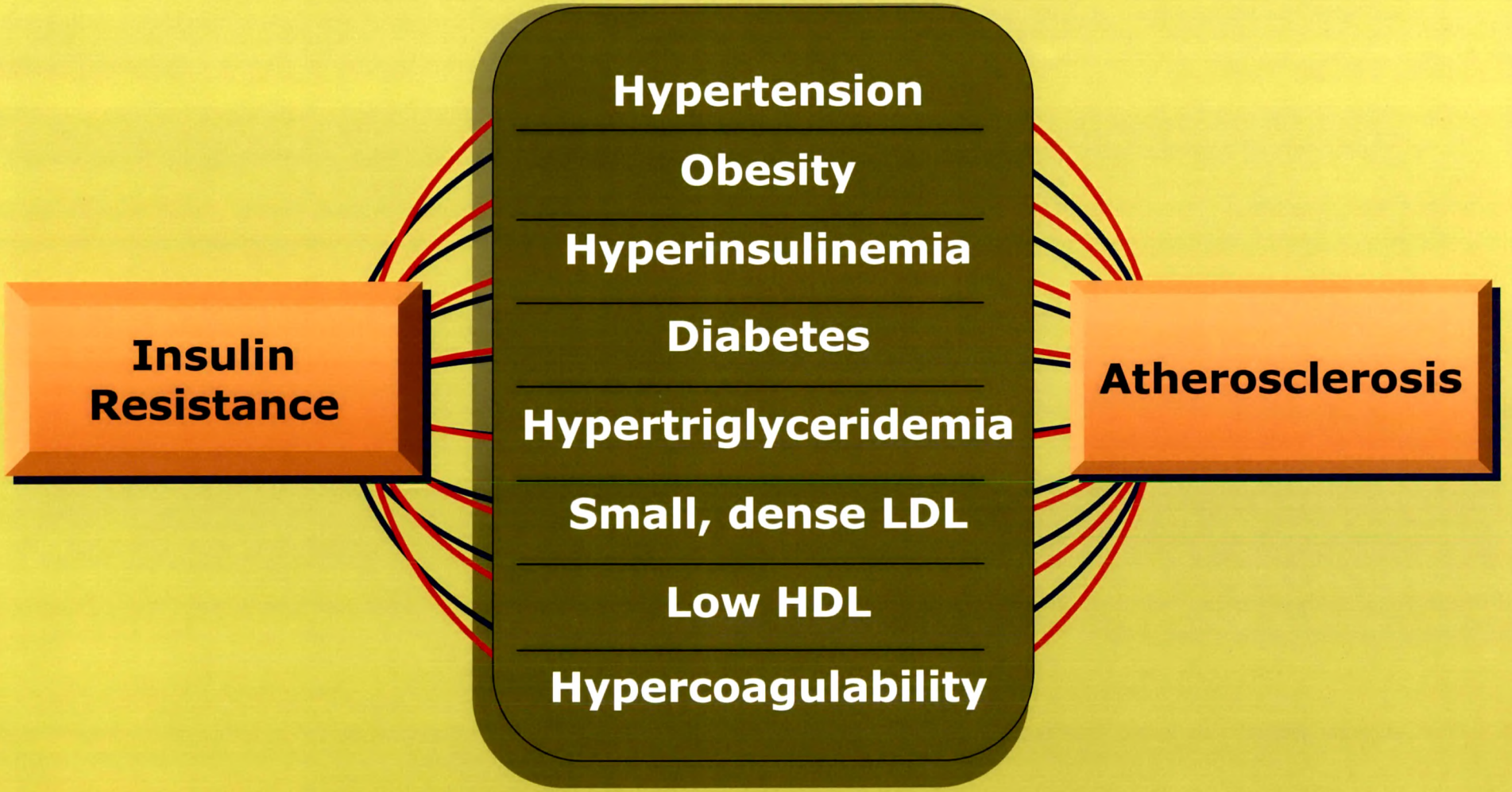
The association of CHD with manifest hyperglycemia (diabetes mellitus) needs no introduction. It is common knowledge that CHD is the major cause of morbidity and mortality in type 2 diabetes It is 2 - 4 5 times more prevalent in diabetics than in non-diabetics and abolishes the gender protection of premenopausal women against cardiovascular disease (Garber 2001) Insulin resistance, which is a major risk factor for the development of diabetes is, associated with panoply of abnormalities, including hypertension, hyperinsulinemia, hypertriglyceridemia with small, dense low-density

lipoprotein and low high-density lipoprotein, and hypercoagulability Obesity plays a role both in exacerbating insulin resistance and as an independent risk factor for atherosclerosis Therefore, any patient with insulin resistance has numerous reasons to be at very high risk for atherosclerosis (**Figure 8**)

The risk of CVD has been reported to increase continuously with glucose levels above 75mg/dl in a meta analysis of various studies in non diabetic populations (Gerstein 1997) Evidence is also beginning to accumulate that tells that it is probably the post prandial hyperglycemia which is more important factor for CVD than fasting hyperglycemia.

Post prandial state is associated not only with increased glucose levels but also increased triglycerides, small dense LDL-C, LDL-C oxidation, blood pressure etc There is also increased expression of adhesion molecules (Ceriello and Falleti 1996, Haller 1997). Some of these influences are interlinked and interact with other factors promoting CVD, for instance the post prandial hypertriglyceridemia causes qualitative changes in the LDL-C molecule making it predominantly of small dense variety which is more prone to oxidation and in the presence of hyperglycemia to glycosylation. These altered LDL-C particles cause atherogenesis as they are preferentially taken up by the macrophage rather than the LDL-C receptors Further higher triglyceride levels also lower the "good" HDL-C compromising the capability of this antiathergenic molecule to take up cholesterol from tissues for transfer to the liver the reverse cholesterol uptake (Garber 2001).

FIGURE 8
INTERRELATION BETWEEN ATHEROSCLEROSIS AND INSULIN RESISTANCE



Source:Lipids Online (www. lipidsonline .org)

The Bedford and Whitehall study (Donahue et al 1987) demonstrated excessive cardiovascular mortality in civil servants with a higher postglucose plasma glucose values this category was later defined as IGT, a stage intermediate between normalcy and diabetes mellitus which is known to be associated with more with macro rather than microvascular disease It is clear that post prandial/glucose load glycemia antedates diabetes and is a strong risk factor for the development of CVD Similar findings were demonstrated by the Honululu heart Study (Donahue et al1987), Helsinki policeman study etc (Balkau et al 1998), in the DECODE study higher tertiles of post glucose load plasma glucose levels were found to be associated with greater all cause mortality for each level of fasting hyperglycemia the post glucose load value gave a higher and additional risk (DECODE study 1999)

HYPERTENSION AND CORONARY HEART DISEASE

Hypertension is one of the major risk factors for coronary artery disease and stroke. The risk of stroke rises with every increment of diastolic pressure above 70mmHg. Its complication accounts for high morbidity and mortality in developed and developing countries

Co-morbid conditions such as obesity, lipid and glucose metabolism derangements, insulin resistance, arterial stiffness, and renal disease also contribute to the hypertension symptom complex that leads to stroke, coronary artery disease, and congestive heart failure

Several decades of population research from the Framingham Study have demonstrated the elevated blood pressure is a common and powerful contributor to the major cardiovascular diseases associated with accelerated atherogenesis (Kannel 2000)

Historically diastolic pressure has been regarded as the most important factor in the adverse sequelae of hypertension. However, large number of prospective population based investigators found that systolic blood pressure exerted a stronger influence than diastolic pressure and these studies also indicate that greater reliance should be placed on systolic pressure in evaluating hypertensive risk as a guide to hypertension control. In the Australian Blood Pressure Trial, correlations were found between baseline systolic but not diastolic pressure and levels of mortality form cardiovascular problems and other causes, as well as the incidence of stroke, coronary disease and severe hypertensive sequelae (Kannel 2000). Thus, it is clearly evident that accelerated atherogenesis is a key component of the hypertension syndrome

HYPERLIPIDEMIA IN CHRONIC DEGENERATIVE DISEASES

DYSLIPIDEMIA IN OBESITY

The negative effect of severe obesity on health and longevity is well documented. Obesity is closely related to several known cardiovascular risk

factors, such as hypertension, lipid abnormalities and impaired glucose metabolism, and it has a complicated association with smoking

Obese subjects on an average have higher serum TC, lower HDL-C, higher TG levels, higher blood glucose and a high plasma insulin level than lean persons (Jousilahti et al 1996) Numerous epidemiological studies (Kahn et al 1969, Kannel et al 1971, Gordon et al 1981) have shown that hypercholesterolemia when present for a longer duration leads to atherosclerosis, which in turn may precipitate CVD Framingham data indicate that weight gain raises both the cholesterol rich lipoprotein and the triglyceride rich VLDL and reduces HDL-C, producing an unfavourable L/H ratio (Kannel and Schatzkin 1983)

The etiology of these dyslipidemias remains under investigation, but most investigators favour the hypothesis that the highly lipolytic nature of adipocytes in general, and in particular visceral adipocytes, triggers a cascade of metabolic abnormalities resulting in dyslipidemia (Rippe et.al 1998)

Research has shown that android pattern of body fat, which pertains to the relative, excess of fat in the central body region, has been associated with increased atherosclerotic risk factor. Obese individuals are frequently characterized by a dyslipidemic state in which plasma TG are raised, HDL-C concentrations are reduced and low-density lipoprotein Apo B (LDL- Apo B) levels are raised This metabolic profile is most often seen in obese patients

with a high accumulation of intra-abdominal fat and has consistently been related to an increased risk of CHD (Despres et al 1990)

Excessive intra-abdominal fat accumulation is also associated with a greater proportion of small, dense LDL-C particles These small dense LDL particles may be caused by metabolic disturbances related to the accompanying high TG or low HDL levels Indeed, the hypertriglyceridemic state may be the combined result of an increased production and a reduced breakdown of triglyceride-rich lipoproteins This process results in lower HDL cholesterol levels and favours the triglyceride enrichment of LDL (Despres et al 1990, 1991). The Bogalusa Heart Study also showed that obese children and adults, particularly with abdominal obesity, have an elevated serum TG concentration (Freedman et al 2002) An increase in TG level in obesity are related to decreased HDL-C concentration The decreased HDL-C is associated with increased risk for CVD and heart attack in obese individuals (Bray GA 1992)

Hence it is clearly evident that the prevalence of several risk factors and diseases are dramatically increased in obesity. Adiposity carries a penalty of an adverse cardiovascular risk profile The greater the degree of overweight, higher the blood pressure, insulin resistance, triacylgycerol and ratio of total to HDL cholesterol.

DYSLIPIDEMIA IN DIABETES

Most data show that in type 2 patients with good or fair glycemic control, concentrations of LDL-C are similar to or slightly lower than those of non-diabetic individuals (Kannel 1985, Taskinen 1990, Howard, 1987) However, two abnormalities characterize lipoprotein metabolism in type 2 patients fasting and post prandial concentrations of triglyceride-rich lipoproteins, especially VLDL-C are higher and those of HDL-C are lower than among people without diabetes (Kannel 1985, Taskinen 1990, Howard 1987, Syvanne et al 1994)

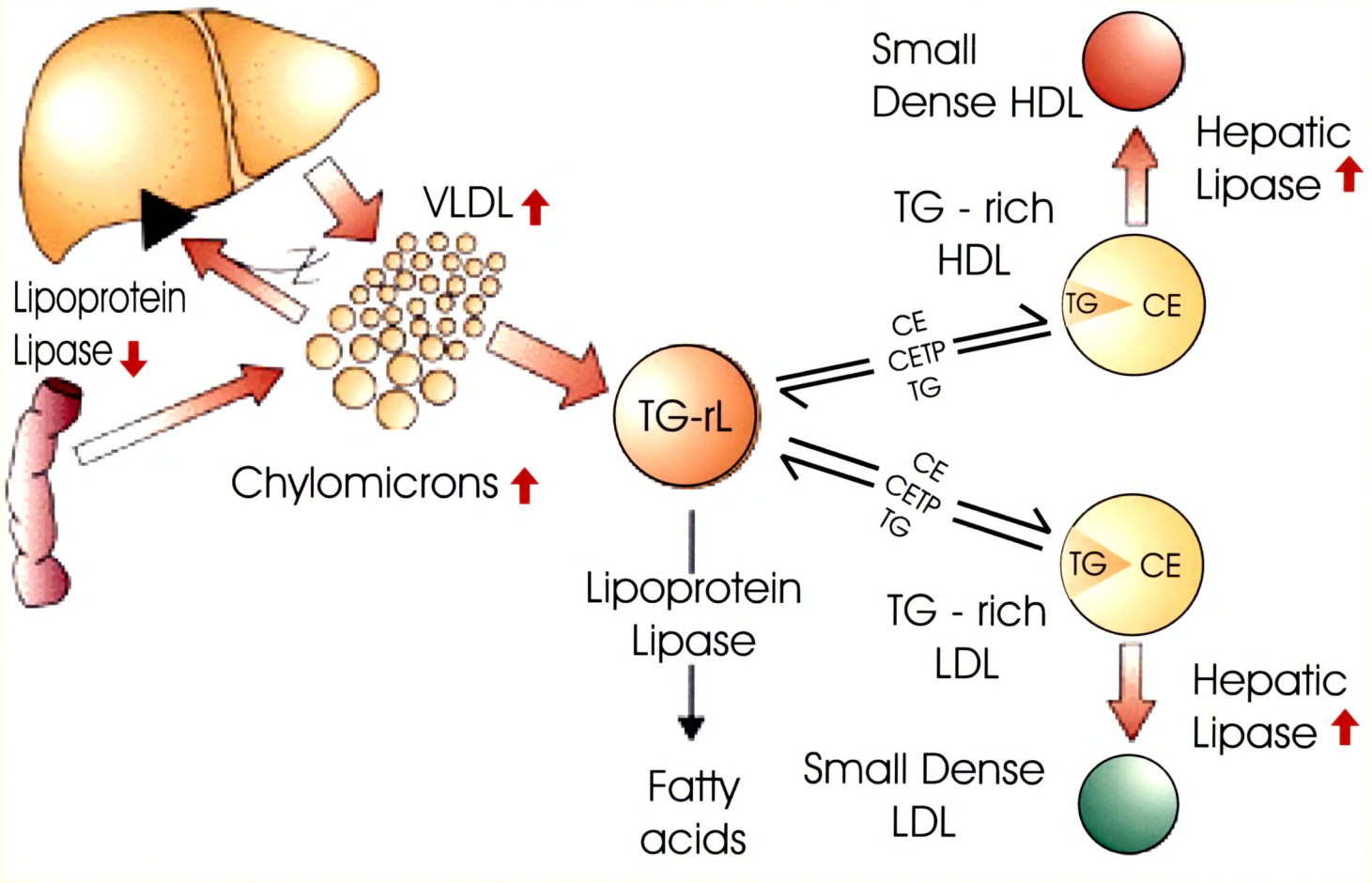
Although many mechanisms contribute to hypertriglyceridemia in type 2 diabetes, insulin resistance seems to be the common basis The insulin-resistant state impairs the normal suppression of fatty-acid release from adipose tissue in the postprandial state (Syvanne and Taskinen 1997) Consequently, the flux of free fatty acids to the liver increases and overproduction of VLDL-C from these substrates occurs when hyperinsulinemia is present Insulin is also involved in another defect of hepatic VLDL-C metabolism. Acute hyperinsulinaemia, such as that after a meal, suppresses the production of large, buoyant VLDL particles ($VLDL_1$) in the liver in non-diabetic people but not in NIDDM patients. We see $VLDL_1$ particles as analogous to chylomicrons, which should be released only in the fasting state when lipids from food are not available Thus, one function of insulin in non-diabetic people is to maintain the balance between intestinally derived and liver-derived triglyceride-rich lipoproteins In the NIDDM patient

this regulation fails, inappropriate production of VLDL-C by the liver occurs, and the balance favours hypertriglyceridemia **(Figure 9).**

The catabolism of triglyceride-rich lipoproteins is initiated by lipoprotein lipase, an endothelial enzyme that hydrolyses the triglyceride moiety of chylomicrons and VLDL, and releases fatty acids for energy production in muscle and for storage in adipose tissue. The activity of this enzyme is generally slightly lower in NIDDM patients than in non-diabetic people of similar age and degree of adiposity. the difference is more striking for patients with both NIDDM and CAD (Syvanne et al 1995) Lipoprotein lipase activity is low in untreated or poorly controlled NIDDM and increases with improved glycemic control In NIDDM, the passage of triglyceride-rich lipoproteins through the lipolytic cascade is delayed for two reasons there is a shortage of catalytic sites on lipoprotein lipase, and overproduction of triglycerides saturates the sites that are available Both mechanisms promote hypertriglyceridemia

The two components of diabetic dyslipidaemia, high concentrations of triglyceride-rich lipoproteins and low concentrations of HDL-C, are closely interwoven Hypertriglyceridaemia contributes to low HDL-C concentrations in two ways. The first process involves the transfer of 'surface remnants'--redundant phospholipids and apolipoproteins from lipolysis of triglyceride-rich lipoproteins--to HDL-C particles. Because lipoprotein lipase activity is decreased and lipolysis impaired in NIDDM, there are fewer surface remnants available to be incorporated into the HDL-C particle Second, the large

FIGURE 9
DYSLIPIDEMIA OF NIDDM



Source : Syvanne & Taskinen (1997)

amount of triglyceride-rich lipoproteins and their prolonged residence time in the circulation increase the exchange (mediated by cholesteryl-ester transfer protein) of esterified cholesterol from HDL-C to triglyceride-rich lipoproteins and of triglyceride to HDL particles. The result is enrichment of the HDL particle core with triglyceride The enriched HDL-C has a faster catabolic rate than normal HDL-C, which leads to a lower number of circulating HDL-C particles (**Figure 9**) Furthermore, the HDL-C particles in NIDDM are smaller owing to a high hepatic lipase activity--another feature of NIDDM. Hepatic lipase has a great avidity for triglyceride-rich HDL-C and hydrolyses the triglyceride in the HDL-C core, which leads to a smaller HDL-C particle size Another way of expressing this is that the small and dense HDL_3 predominates in NIDDM at the expense of the larger and cholesteryl-ester-rich HDL_2 (Syvanne and Taskinen1997).

There are considerable epidemiological data linking diabetic dyslipidaemia with the incidence of CHD in type 2 diabetes patients (Garg and Grundy 1990) and CHD accounts for upto to the observed mortality in these patients (Gowri et al 1999, Syvanne and Taskinen 1997) The relationship between hypertriglyceridemia and abnormalities in LDL-C particle size and composition has also been extensively investigated in diabetes (Grey et al 1997, Lahdenpera et al 1996) Compositional abmormalities that occur in LDL-C in type 2 diabetes may account for some of the increased risk of atherosclerosis in the population. Also studies show enhanced LDL-C oxiadation occurs in vivo, since high titres of auto antibodies to oxidatively modified LDL-C are

present in plasma (Bellomo et al 1995) Oxidative modification of LDL-C appears central to foam cell formation, the earliest lesion of atherosclerosis (Fuster et al 1992)

DYSLIPIDEMIA IN HYPERTENSION

Various studies including the Framingham (Castelli and Anderson 1986) as well as the Multiple Risk Intervention Trial (NIH Report, 1997) have shown that the cholesterol levels are high in hypertensive subjects

Similarly an Indian study also revealed that TC and LDL-C were higher in more than one half of the subjects (Joglekar and Nanivadekar, 1996) Yet another study carried out in Tirupati, India states that serum lipids can be considered as the risk factor for ischemic heart disease and hyeprtension (Latheef et al 1998) Increase in cholesterol and/or triglycerides was more severe in hypertensive than in normotensive patients The prevalence for hypertension was higher in patients with coronary artery disease than in patients without the disease or less) Furthermore, the association of hypertension with hyperlipidemia hints to an extremely unfavorable accumulation of renal and cardiovascular risk factors in a large number of renal graft recipients (Lenz et al 1999)

DYSLIPIDEMIA IN CORONARY HEART DISEASE

The association of TC, TG and HDL-C when studied on cardiovascular mortality showed that cardiovascular mortality was positively related to

cholesterol, where as HDL-C was inversely related to cardiovascular mortality among Polish US residents Thus indicating that in geographically and culturally diverse populations, the relation of lipids with CVD mortality is similar (Rywik et al 1999).

A significant relationship has been demonstrated between hypercholesterolemia and CAD in the Western world. However, in Chennai, India 75% of people of people with myocardial infarction had plasma cholesterol levels less than 200 mg/dl. In yet another study from India, even lower level of plasma cholesterol (<150 mg/dl) in patients with CAD have been reported Among the expatriate Indians living in the United Kingdom, their total plasma cholesterol has been found to be low compared to that in the natives Low levels of HDL-C is usually found among Indians in comparison to US population In general, the Indian men had 5 mg/dl lower than that in the European American and 15 mg/dl lower than among Japanese Americans (Chopra and Wasir 1998)

Apart form cholesterol and HDL-C, recent research shows that hypertriglyceridemia is an important independent cardiac risk factor The relationship of TG and CHD is complex wherein TG contribute directly or indirectly One of the direct effects of hypertriglyceridemia is an increase in large VLDL-C particles enriched with Apo E. This high content of Apo E enhances their uptake by macrophages to produce foam cells Hence, these large VLDL particles are atherogenic and above their cholesterol content

Hypertriglyceridemia leads to delayed removal of post-prandial lipoproteins which are considered to be atherogenic There is competition between VLDL-C and post-prandial lipoproteins for lipoprotein lipase i e the hydrolysis of chylomicron triglycerides is retarded in hypertriglyceridemic patients The post prandial lipoproteins, induce the accumulation of lipids in macrophages leading to the formation of foam cells which are characteristic of atherosclerosis. This would further raise the risk of CHD

Another effect of increase in TG is the induction of excess, small dense LDL-C These are considered more atherogenic than normal LDL-C because they readily filter into the arterial walls

Various epidemiological studies done globally reveal that TG, on their own have an important role to play in predicting atherogenesis One of the initial studies to support this data was the Prospective Cardiovascular Munster (PROCAM) Study done between 1979 to 1985 which enrolled 19,698 persons in the age groups 16-65 years (Assman et al 1996) In addition, this study also stated that increase in TC and LDL-C and TG as well as decrease in HDL-C levels were directly proportional to the increase in the risk of CHD (Assman et al 1998). Further boost was given to the theory of TG as an independent marker in CHD by the Framingham heart Study (Castelli 1986), Paris Prospective Study (Fontbonne et al 1989), Helsinki Heart Study (Manninen et al 1992), Copenhagen Male Study (Jeppesen et al 1998) etc

Many researchers have found that patients with hypertriglyceridemia frequently have low plasma levels of HDL-C (Manocha and Srivastava 2002) This further increases the risk for CHD and a significant part of the risk associated with raised triglycerides due to decreased HDL-C Elevated plasma TG levels increase the transfer of cholesterol esters form HDL particles to triglyceride-rich lipoproteins, an action, which results in lowering of HDL-C concentration However, once TG rise beyond a certain level, they do not further cause a transfer of cholesterol esters from HDL-C Hence the inverse correlation between triglycerides and HDL-C is strong only up to a distinct elevated range beyond which any further rise in TG is not associated with a further fall in HDL-C (Lechleitner et al 1990, Tato et al 1997).

Although the CVD risk associated with individual lipoproteins has been examined, it would be valuable to have a measure that reflects the combined risk of all lipoprotein changes observed in various CDD. Some investigators have recently suggested that a measure of Non-HDL-C, which reflects total cholesterol minus HDL-C (i e all apolipoprotein B – containing atherogenic lipoproteins), might be a useful marker of this combined risk (Havel and Rapaport, 1995, Frost and Havel 1998, Garg and Grundy 1990) In the Quebec Cardiovascular Study carried out on healthy men, Non-HDL-C was a strong risk factor for IHD and a better predictor than the traditional lipid risk factors. Thus, the study suggested that Non-HDL-C should be used as risk factor for ischemic heart disease (IHD) because it includes VLDL-C, IDL and Lp(a) (Cantin et al 1999) A recent study conducted in a cohort containing

both diabetic and nondiabetic individuals showed that Non-HDL-C was a somewhat better predictor of CVD than LDL-C (Cui et al 2001) Findings form the Lipid Research Clinics Programme Follow-up Study also showed that Non-HDL-C emerged as a somewhat better predictor of CVD morality than LDL-C (Cui et al 2001) Further more the Adult Treatment Panel of the National Cholesterol Education Programme has recommended using Non-HDL-C in assessing CVD risk in patients with diabetes (Executive summary of the NCEP 2001). In patients with diabetes, known cardiovascular disease or high-risk scores on cardiovascular disease measurement scales, the target LDL-C should be less than 100 mg/dl and the Non-HDL-C should be less than 130 mg/dl The Strong Heart Study results show that Non HDL-C is a significant predictor of CVD in diabetic men and women And thus may be particularly useful in treating patients with diabetes (Lu et al 2003)

Apolipoproteins

There are various risk factors, which act synergistically leading to the development of cardio vascular diseases. In profiling the risk of these non-communicable diseases it has been customary to utilize the measurement of fasting blood sugar (FBS), TG, TC, HDL-C, LDL-C etc., which have already been discussed above. However, LDL-C may not be an accurate predictor of heart attack or other cardiac events in healthy adults Instead, the investigators suggest that blood levels of two proteins found in cholesterol – Apo B and Apo A1 may be better 'markers' for heart risk in persons without

the signs and symptoms of heart attack

As we are aware that the ApoA1 and ApoA2 are the major proteins present in HDL-C and Apo B is the major protein of LDL-C and higher levels of Apo B suggest an increased number of LDL particles If Apo B level is increased relatively to LDL-C level, this suggests that the LDL-particles are smaller and denser, a factor associated with increased risk. Thus, Apo B might be a good indicator of heart disease because it reflects the number of lipoproteins that are associated with the development of atherosclerosis Although LDL-C and HDL-C are known risk factors, it is suggested that Apo B, ApoB/ApoA1 and ApoA1 should also be regarded as highly predictive in evaluation of cardiac risk. (Walldius et al 2001) Another study carried out in Italy also confirm that Apo A1 and Apo A1 /Apo B ratio are better than HDL-C in assessing the severity of coronary damage (Garfagnini et al 1995)

In a study carried out among Indian population, overall Apo B and TG levels showed larger univariate difference between the normal group (no CAD) and the group with CAD The variable with strongest predictive power for CAD was the ratio of Apo A1 to Apo B These results indicate that Apo A1 and Apo B provide a better marker for predicting the presence of CAD as compared to traditional lipid measures. Overall the levels of these apolipoproteins seem to be lower in Indian population as compared to those reported from most Western population (Bahl et al 1994).

A study carried out among obese subjects showed that plasma TG and LDL-C were significantly higher, whereas HDL-C/LDL-C and Apo A1/Apo B ratios, were significantly lower in moderately to severely obese women than in non obese post menopausal controls (Vermeulen 1990) A study carried out in Australia also showed that BMI and WHR were positively correlated with Apo B and TC levels, and negatively correlated with Aop A1 and HDL-C levels (Kinlay et al 1991) Yet another study showed that obese patients without CAD had significantly higher Apo A1/Apo B ratios that obese patients with CAD, indicating a favourable distribution of cholesterol-containing particles (Bahadori et al 1996)

Despite the increased risk of atherosclerosis in diabetes, levels of serum TC, TG, LDL-C and HDL-C were similar in 57 men with IDDM and 81 nondiabetic controls. However, substantially lower serum levels of Apo B, the principal apolipoproteins of LDL-C were found in IDDM (Winocour et al 1986) In a study carried out on diabetic patients significant increases of TG, TC, LDL-C and Apo B levels were observed in patients whose diabetes was the most poorly controlled (HbA1: 12.9 ± 1 3%, Fructosamine: 4.6 ± 0 9mmol/l). These parameters were significantly correlated with HbA1 and even more significantly with fructosamine (Willems and Dorchy 1990).

Apart form levels of these apolipoproteins in various diseases, MONICA-Israel study found that Apo A1 and B levels varied with age In women aged 45-64 years higher levels of Apo A1, Apo B, TC, LDL-C and a lower ratio of HDL-

C/TC were found than their younger counterparts (24-44 years) (Brunner et al 1988)

Besides these diseases there are various modifiable risk factors which have some role to play in the development and progression of these chronic degenerative diseases and particularly CHD Some of these factors have been discussed below.

SMOKING

Smoking is a leading preventable cause of premature death all over the world As many as 30% of all coronary heart disease (CHD) deaths in the United States each year are attributable to cigarette smoking, with the risk being strongly dose-related (US Dept of Health and Human Services, 1989, 1990). Smoking also nearly doubles the risk of ischemic stroke Smoking acts synergistically with other risk factors, substantially increasing the risk of CHD (Ockene and Miller 1997).

Smoke from a cigarette contains from 0 5 to 3 0 mg of nicotine, depending on the different brands When the smoke is inhaled practically all the nicotine is absorbed, and the plasma nicotine levels may increase up to 40-50 ng/ml of plasma. Nicotine is a stimulator of both sympathetic ad parasympathetic ganglia, and nicotine inhaled in cigarette smoke increases the arterial epinephrine concentration The cardiac effect of nicotine administration in normal subjects increases in heart rate, cardiac output, blood pressure, and

coronary blood flow Nicotine may further predispose to the initiation of arrhythmia, particularly when the myocardium is damaged Apart form nicotine it is said that carbon monoxide is responsible in smokers developing atherosclerosis in comparison to non-smokers (Astrup and Kjeldsen 1973) Cigarette smoke also contains 3-6% carbon monoxide, about 20-30 ml depending on the temperature of combustion The toxic effect of carbon monoxide was its ability to bind to haemoglobin at a much higher degree than oxygen, thus displacing oxygen in oxyhaemoglobin and depriving blood of its oxygen transport ability. It is said that this carbon monoxide in tobacco smoke is responsible for the development of atherosclerosis in smoker in comparison to non-smokers Carbon monoxide also leads to hyperlipemia

Cigarette smoking alters the serum lipids and lipoproteins and these changes are related to the duration and amount of smoking. Active smoking increase LDL-C and VLDL-C where HDL-C content is lowered, resulting in decreased ratio of HDL-C/TC and HDL-C/ LDL-C (Whig et al 1992) Smoking has been shown to lower HDL-C levels (Shah and Sadaria 2003) Results of Bogalusa heart study have shown an association of cigarette smoking and alcohol consumption with levels of serum lipid and lipoproteins in both adults and adolescents, while cigarette smoking is associated with decreased HDL-C and increased LDL-C levels, moderate alcohol consumption is related to increased level of HDL-C (Freedman et al 1985) Smoking induces an acute rise in metabolic rate and tends to reduce food intake related to non-smokers (Dallosso and James 1984). Cigarette smoking may be regarded as a

significant risk factor for the development of Ischemic Heart Disease (IHD)

Many epidemiologic studies and reviews (Ciruzzi et al 1998, Law et al 1997, Wells AJ 1998) have pointed to the effect of passive smoking on the risk of coronary heart disease Even so, the extent of the association between passive smoking and coronary heart disease is not fully known, as passive cigarette smoking is associated with a smaller increase in the relative risk of coronary heart disease than is active cigarette smoking (Jiang et al 1999)

ALCOHOL

Many studies have shown an inverse association between alcohol consumption and coronary heart disease, with a possible flattening at higher consumption levels (Rimm et al 1996)

Similar observation is also noted in a study carried to assess whether among diabetics the inverse correlation exists among light to moderate consumption and CHD The results suggest that light to moderate alcohol consumption is associated with similar risk reductions in CHD among diabetic and nondiabetic men (Ajani et al 2000).

However, one cannot neglect the fact that excessive alcohol intake is a risk factor for CHD, hypertension and all other cardiovascular diseases Excess intake leads to increase in blood pressure because of increase in sympathetic nerve activity, which increase cardiac output and increase heart rate And it

alters cell membrane permeability allowing more calcium to enter the cell by inhibition of sodium (Malhotra and Patel 2003) A study carried out in Scotland showed a strong positive correlation between alcohol consumption and risk of mortality from stroke in men drinking excessive alcohol (Hart et al 1999).

Apart form the amount of alcohol consumed a large population-based sample was carried out to show a relationship between pattern of alcohol drinking and progression of atherosclerosis in carotid arteries This study shows that heavy acute loads of alcohol seem to relate to enhanced progression of carotid atherosclerosis, independent of the total average level of alcohol consumption It is plausible that the metabolic and physiological stress that occurs in the body during and after heavy drinking may facilitate atherosclerotic changes, but the actual mediating process is not clear Thus this study indicates that drinking style, and not only the total amount of alcohol consumed, may have an impact on the development of atherosclerotic disease and especially its progression (Kauhanen et al 1999).

One of the classic example of an inverse association between moderate alcohol consumption and CHD is the 'French Paradox', where in the French people are found to be at a lower risk of suffering from CHD inspite of consumption of red wine, which is said to have a protective effect.

Many studies are being carried out to assess whether the protective effect is confined to specific beverages (such as red wine) or relates to ethanol A

study carried out in the Czech Republic showed that the protective effect of alcohol intake is due to ethanol rather than to specific substances present in different types of beverages (Bobak et al 2000). Another study that compared results form 10 prospective cohort studies showed that that all alcoholic drinks if consumed in moderation are linked with lower risk, so that much of the benefit is from alcohol rather than other components of each type of drink (Rimm et al 1996)

SEDENTARY LIFESTYLE / PHYSICAL INACTIVITY

Modernization has led to a sedentary lifestyle, one of the major reasons for the growing number of such diseases. Sedentary lifestyle is associated with a greater risk for the development of various CDD Modest levels of physical activity help to control blood lipid abnormalities, diabetes and obesity as well as blood pressure lowering effect in certain hypertensive groups

The Surgeon General's Report on Physical Activity and Health (USA, 1996) made one thing perfectly clear. a sedentary lifestyle is damaging to health and bears responsibility for the growing obesity problems. It used data from the Behavioral Risk Factor Surveillance System (BRFSS) and the Second National Health and Nutrition Examination Survey (NHANES II) and showed that sedentary lifestyle was the most prevalent (58%) modifiable risk factor for CHD reported, followed by cigarette smoking, 25%; obesity, 22%; hypertension, 17%; and diabetes, 5% The study showed that sedentary

persons are approximately twice as likely as physically active persons to die from CHD (Powell et al 1989)

It has been suggested that physical activity is likely to protect against obesity regardless of an individual's genetic predisposition to it (Samaras et al 1999) Exercise and physical activity have several benefits

- Exercise can improve glycemic control and insulin sensitivity, and may prevent the development of type 2 diabetes in high-risk groups (Tremblay et al 1991).
- Long-term aerobic exercise regimens have had a beneficial effect upon the systemic blood pressure.
- Prolonged exercise programs cause a greater decrease in abdominal fat than lower body fat (Despres et al 1991)
- Regular physical activity decreases the risk of CVD mortality, particularly the risk posed by CHD (Shetty 1997).
- Regular exercise has been shown to improve control of lipid abnormalities, diabetes mellitus, hypertension, and obesity, with the greatest benefits realised by sedentary individuals who begin to exercise (Bray 2000)

Though diet modification is the most important aspect of controlling weight gain, the addition of an exercise program to diet modification results in more weight loss than dieting alone and seem to be especially helpful in

maintaining weight loss and preserving lean body mass (Oeser 1997) Energy expenditure through physical activity is an important part of energy balance equation that determines body weight Decrease in energy expenditure through decreased physical activity is likely to be one of the major factors contributing to the global epidemic of overweight and obesity (WHO Report, 2003)

STRESS

Psychological stress in the workplace is generally regarded by the public as an important cause of coronary heart disease While epidemiological studies have amply demonstrated a strong, consistent relation between coronary disease and cigarette smoking, high blood cholesterol, hypertension, diabetes, and family history (Kannel et al 1976 and Kannel et al 1986), the epidemiological evidence supporting the relation between coronary disease and job stress is relatively sparse Blue-collar workers have shown higher rates of coronary disease than white-collar workers in some studies (Marmot et al 1978, Buring et al 1987 and Pocock et al 1987), but other studies suggest this may be explained by more adverse levels of traditional coronary risk factors (Hebert et al 1992) The effect of type A personality on coronary artery disease has been extensively studied, and the role of social support in patients with coronary disease has come under increasing scrutiny (Hlatky et al 1995). These studies did not, however, directly assess the role of job-related stress in coronary disease

Results from the Whitehall II study showed an association between effort-reward imbalance and incidence of coronary heart disease, as indicated by self reports (Williams et al 1992) It was found that employees reporting high job strain and high effort-reward imbalance had a twofold higher risk of death from cardiovascular disease than their colleagues scoring low in these dimensions

DIETARY FACTORS

Diet and nutrition are important factors in the promotion and maintenance of good health through out the entire life course Nutrition is coming to the fore as a major modifiable determinant of chronic disease with scientific evidence increasingly supporting view that alterations in diet have strong effects, both positive and negative, on health through out life Most importantly, dietary adjustments may not only influence present health, but many determine whether or not an individual will develop such diseases as cardiovascular disease and diabetes much later in life (WHO 2003) Dietary factors are considered to be a major modifiable risk factoring the management of CDD. A consistent and positive relation between saturated fatty acids intake, plasma cholesterol and CHD has been found Saturated fat is the principal dietary determinant of LDL-C levels (Krauss et al 2000) Saturated fatty acids suppress LDL receptor activity, thus forcing LDL-C to accumulate in the serum, which is a risk factor for CHD Thus, saturated fatty acids alter homeostasis of lipoprotein metabolism, which results in elevation of LDL-C

This leads to increased accumulation and poor clearance of cholesterol and its esters form arterial walls (Oliver 1982). It has also been established that dietary trans-unsaturated fatty acids can increase LDL-C and reduce HDL-C (Lichtenstein et al 1999, Judd et al 1994) Such fatty acids are found in prepared foods containing partially hydrogenated vegetable oil. In addition, there may be a high content of trans fatty acids in oils used to prepare fried foods in most restaurants and fast-food chains

The major mono unsaturated fatty acid (MUFA) present in animal and plant fats are oleic acid, present in olive oil Studies have shown that MUFA do not lower HDL-C levels but reduce LDL-C levels This lowers the L/H ratio, thereby reducing coronary risk (Keys 1965)

Another fatty acid i.e PUFA has been found to lower the serum cholesterol and thus reduce the incidence of myocardial and sudden death (Ulbricht and Southgate 1991). The cholesterol lowering action of polyunsaturated fatty acid (PUFA) is a result of their strong antilipogenic ability, which lowers liver lipoprotein synthesis and increases lipoprotein catabolism and removal Two types of PUFA occur in the diet, n_6 and n_3 PUFA. The predominant n_6 fatty acid is linoleic acid, which has been known to have cholesterol lowering action. n_3 fatty acids are found in high concentration in fish oils n_3 are protective against CHD as these lower the serum cholesterol levels and increase HDL-C levels (Ulbricht and Southgate 1991)

Recent evidence has put PUFA as culprits in CVD process, because of their increased susceptibility to damage form free radicals, which might be one to the initiators of endothelial damage that ultimately results in atherosclerosis and CVD. Over consumption of PUFA such as vegetable oils increase the need for antioxidant nutrients to protect against free radical damage

Apart form these fatty acids dietary cholesterol can also increase LDL-C levels, although to a much lesser extent than saturated fat. Epidemiological data have suggested that increased dietary cholesterol intake is associated with an increase in coronary disease risk independent of plasma cholesterol levels (Shekelle and Stamle 1989)

Dietary fat also appears to be an important determinant of diabetes risk, independent of total caloric intake Increased intake of dietary fat was associated with occurrence of diabetes among second-generation Japanese-American men (Franz et al 2002) In observational epidemiological studies, a high saturated fat intake has been associated with a higher risk of impaired glucose tolerance and higher fasting glucose and insulin levels (WHO 2003) Results form two recent studies suggest that increased intake of PUFA fat may be associated with reduced risk of type 2 diabetes, independent of BMI, total energy intake, physical activity, and other potential confounders (Hughes et al 1995, Louheranta et al 1999). Several studies have identified fat as a contributor to insulin resistance independent of obesity, but other studies do not support this (Franz et al 2002) Nevertheless, it appears that all types of

fat, except n-3 fatty acids, may have an adverse effect on insulin sensitivity Results are more consistent for an adverse effect of saturated fats These effects may be enhanced among individuals with obesity or low levels of physical activity

Excess carbohydrate can also be converted to fat, but human subjects do not use this metabolic pathway to any appreciable extent, unless large excess of a low fat, high carbohydrate diet is consumed Isocaloric substitution of any type of carbohydrate for dietary fat leads to a transient increasing in fasting TG levels

Intake of refined CHO may lead to Hypertriglyceridemia It has also been reported that substitution of simple sugars for starch results in increased concentrations of serum cholesterol and TG, and that high intakes of sucrose or fructose raise TG levels more than glucose (Mac Donald et al 1967) Recent studies have provided preliminary evidence for reduced risk of diabetes with increased intake of whole grains and dietary fibre (Liu et al 2000, Wolever et al 1997) In both the Nurses Health Study (Liu et al 2000), and the IOWA Women's Health Study (Meyer et al 2000), increased intake of whole grain food was associated with significant reductions in the incidence of type 2 diabetes. A higher glycemic load was related to increased incidence of diabetes

Similar observations were noticed for CHD diseases, that diets low in complex carbohydrates, fibre, minerals and vitamins are associated with increased risk of cardiovascular disease (Krauss et al 2000) The reason behind this is that soluble fibres modestly reduce total and LDL-C levels beyond those achieved by a diet low in saturated fat and cholesterol Additionally, dietary fibre may promote satiety by slowing gastric emptying and helping to control caloric intake and body weight (Anderson et al 1994) Apart from its preventive role in CHD, diabetes and hypertension, increased fibre intake has been found to be beneficial in the prevention of obesity, which in turn is the risk factor for various CDD Dietary fiber modifies food eating pattern and energy balance Fullness might be associated with bulk because high fiber diets have a greater volume than high fat diets, which could lead to a decreased energy intake. Fiber slows gastric emptying which might trigger satiety; reduce hunger and prolong fullness Evidence suggests that obesity is much less prevailed in population who consume fiber rich diets as opposed to those who consume low fiber diet It was also found that subjects who had greater BMI values also had diets containing the most fat and least dietary fibers (Medeinos et al 1996) However, the effect of dietary fibre depends on its type Pectin, gums and soluble fibres have a serum cholesterol lowering effect Wheat fibre does not decrease TC in diabetics (Mani et al 1986, Mani et al 1987)

Various studies have been carried out regarding the protein intake It is shown that plant proteins have been known to be less cholesterolemic than animal

proteins (Park et al 1987)

Cholesterol oxidation and turnover are evidently increased when, for example, casein is replaced by a vegetable protein It has been suggested that there would be a fall in total cholesterol of 8 mg/dl if the diet, already with 30% of protein from vegetable source, were to include 50% of protein from vegetables (Carroll et al 1978)

However, it is seen that excessive intake of calories from any source namely, CHO, protein, fat or alcohol increases the levels of TG and TC in blood (Ghafoornisa 1986). Excess calories increase VLDL-C production and decrease VLDL-C removal, resulting in increased TG levels. Also, excess calories leads to increase in body weight which is associated with the development of most prevalent CDD.

Apart from the deleterious effect of excess calories, fat, type of fat etc recent research has laid emphasis on the probable role of antioxidants in the prevention or management of various CDD

ANTIOXIDANTS

Antioxidants are a group of compounds that are produced by the body and that occur naturally in many foods Antioxidants work together in the body to maintain our health and vigor well into the late decades of life They do this by protecting us from damage caused by free radicals, which can injure

healthy cells and tissues These free radicals react with billions of cells in the body and may lead to the development of a number of chronic diseases including cancer, cataracts and heart disease.

Hydroxyl radicals react with carbohydrates by randomly abstracting a hydrogen atom form one of the carbon atoms, producing a carbon-centered radical This leads to chain breaks in important molecules such as hyaluronic acid in a process involving intermediates such as peroxyl radicals. Proteins have many reactive sites that can be damaged during oxidative stress Aggressive radicals such as hydroxyl radical can fragment proteins in plasma and these reactions usually produce irreversible modifications in amino acids

Oxidative modification of LDL-C appears to have an important role in foam-cell formation and atherogenesis This link between the oxidation of LDL-C and atherogenesis provides a convenient and simple rationale for the beneficial effect of antioxidants on the incidence of coronary artery disease A number of clinical studies have explored this link between LDL-C oxidation and atherogenesis

Carotenoids have been implicated in preventing the oxidation of LDL-C and consequently reducing the formation of atherosclerotic lesions, in protecting against the development of cortical cataract, and in reducing the oxidative stress induced by smoking

There is widespread evidence that Vitamin E can function in general as a biologic antioxidant to protect cellular membranes from oxidative destruction by neutralizing free radicals Phospholipids in cellular and subcellular membranes contain PUFA that are susceptible to peroxidation. Vitamin E is the fat-soluble antioxidant capable of protecting these fatty acids by interrupting free radical reactions that otherwise can cause membrane damage in subcellular organelles

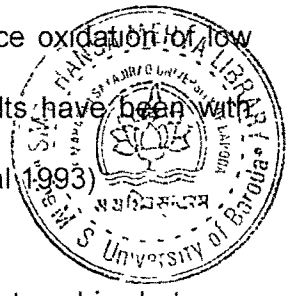
Ascorbic acid scavenges aqueous superoxide and hydroxyl radicals and acts as a chain-breaking antioxidant in lipid peroxidations Ascorbic acid may also act indirectly in protecting lipid membranes by regenerating the active form of membrane-bound Vitamin E The vitamin appears to be important for antioxidant protection in plasma as well as in other extracellular fluids, for membranes, and intracellularly

Observational and Interventional Studies of Antioxidants in the Management of Various Diseases

Epidemiological studies have generally reported that increased intake of antioxidants through diet or supplements, particularly vitamins E and C and beta carotene, is associated with a lower risk of coronary heart disease (Rimm et al 1996, Lonn and Yusuf 1997)

Other antioxidants, such as other carotenoids, flavonoids, selenium,

magnesium etc found in natural food products may reduce oxidation of low density lipoprotein cholesterol The most compelling results have been with vitamin E supplementation (Rimm et al 1996, Stampfer et al 1993)



Many observational studies have investigated the relationship between coronary heart disease and dietary intakes (Rimm et al 1996, Stampfer et al 1993, Donnan et al 1993, Knekt et al 1994, Botton et al 1992) Four large scale studies (Rimm et al 1996, Stampfer et al 1993, Knekt et al 1994, Botton et al 1992) involving 5000-40000 subjects were studied All four found an association between Vitamin E intake and a measure of CHD The male health professionals study and the female nurses health study found a 35-40% reduction in the incidence of major coronary events, non-fatal myocardial infarction and death from cardiac causes in the subjects who had Vitamin E intake in the top quintile as compared with those in the lowest quintile. The median intake for the male subjects in the top quintile was 419 IU/d (276 mg/d) while the median intake of the female subjects in the top quintile was 208 IU/d (137 mg/d) Both these are far higher (10-20 times higher) compared to the RDA for Vitamin E which is 10 mg/d Daily use of single supplement consisting of at least 100 IU (66 mg) of vitamin E for two or more years was associated with 37% decrease in heart attack risk among men and 41% decrease in women The benefit was greatest in subjects taking 100-250 IU of supplemental Vitamin E (i.e 66 mg - 165 mg/d) with little additional effect above 165 mg/d. Therefore the question whether usual dietary intakes will be adequate to protect against oxidative stress encountered day-to-day

remains open although the Edinburg Artery Study (Donnan et al 1993) found an association between dietary intakes of Vitamin E in the range of 9-20 mg and peripheral artery disease

The data on beta carotene are also indicative of a beneficial effect although the benefits may be confined to only particular sub-groups like present and past smokers. The male health professional and female nurses study referred to earlier have shown that high beta carotene intakes are associated with reduced coronary risk in smokers Current smokers in the top $1/5^{th}$ of β-carotene intake had a 70% reduction in heart disease risk while past smokers showed a 40% reduction In lifelong non-smokers no significant effect was observed (Rimm et al 1996). Another multicentric study in nine locations (known as EURAMIC - the European Multicentric Study on Antioxidants, Myocardial Infarction and Breast Cancer) found a significant association between low β-carotene concentrations in the adipose tissue and increased risk of myocardial infarction This effect was again seen mainly in current smokers (Euramic study of ILSI 1995)

On the contrary data support for an association between intakes of vitamin C and CHD is not consistent While the NHANES study found a relative risk of 0.66 for CHD mortality in the subjects who were in the highest tertile of vitamin C intake compared to the others (Enstrom et al 1992), the physicians health study and the nurses study referred to earlier found no association between vitamin C intake and risk of coronary heart disease (Blot et al 1992,

Enstrom et al 1992) Also, the Dutch and the Swedish study did not show any association between vitamin C intake and coronary mortality (Knok et al 1987, Lapidus et al 1986) The former (i e. NHANES study) also found that subjects whose vitamin C intake exceeded 50 mg/day had a lower rate of death from all cardiovascular diseases It is interesting also to note that as vitamin C production has risen in the US, the CHD mortality has fallen Increase in production however is not necessarily synonymous with increased intakes

Large randomised placebo controlled trials of vitamin E among Finnish male smokers (n=29,133) who were randomly assigned to tocopherol (Vitamin E) 50 mg daily or placebo and carotene 20 mg daily or placebo for 5-7 years did not prevent death from cardiovascular disease or myocardial infarction, but the incidence of angina pectoris was modestly reduced (Rapola et al 1996) In the subgroup of individuals with previous myocardial infarction, modest benefits on non-fatal coronary events but no effect on cardiac mortality were reported (Rapola et al 1997) The major limitation of this trial was the vitamin E dose used (50 mg/day), which is much lower than the doses suggested by most of the epidemiological data to be cardioprotective

A second large primary prevention trial conducted in China reported a marginally significant reduction in total mortality (9%, 0% to 70%) for a combination of vitamin E, beta-carotene, and selenium, with a trend towards reduced cerebrovascular mortality (Blot et al 1993)

The Cambridge Heart Antioxidant Study (CHAOS) is a secondary prevention study of 2002 patients with coronary atherosclerosis randomised to Vitamin E 800 IU daily or 400 IU daily or placebo It reported marked reductions in non-fatal myocardial infarction (77%, 53% to 89%, P<0 001) and in the combined end point of any major cardiovascular event (47%, 17% to 66%, P=0 005) (Stephens et al 1996).

The primary prevention trials for carotene evaluated in the Physicians Health Study (PHS) (ATBC Study Group 1994), Beta Carotene and Retinal Efficacy trial (CARET) (Omenn et al 1996), and Alpha Tocopherol Beta carotene Cancer Prevention Study (ATBC) (Hennekens et al 1996) failed to show any reduction in the risk of cardiovascular events and cancer

There have been no large trials of Vitamin C supplementation In a trial of 578 patients admitted to a geriatric hospital, supplementation with 200 mg of Vitamin C daily did not reduce mortality at six months (Wilson et al 1973). In the Chinese trial discussed above there was no reduction in total mortality and in mortality from cerebrovascular disease in people randomised to a combination of Vitamin C and molybdenum (Blot et al 1993).

There is some evidence available to show that high intake of flavonoids may offer protection from CAD. The association between consumption of red wine and reduced risk of coronary heart disease observed in the French population, which is more commonly known as the "French Paradox" is one such example of the beneficial effect of phenolic flavonoids such as catechins,

epicatechins, quercitins, anthocyanins etc. present in red wine CAD mortality per 100,000 is 78 in the region where red wine is widely consumed as against 380 in UK and 102 for France in general. High consumption of red wine, olive oil and fresh fruits and vegetables, all of them rich in anti-oxidants are considered to contribute to this

The strongest evidence comes from the study on elderly subjects in Zutphen, Netherlands (Hertog et al 1992) Five food flavonoids were measured in vegetables, fruits and beverages commonly consumed in Netherlands (the flavonols - quercetin, kaempferrol and myricetin and the flavones epigenin and luteolin) were measured The relationship between the baseline intake of these and subsequent CHD mortality and incidence of MI was studied in 805 men (65-84 years) over a five year period from 1985-1990. Mean flavonoid intake was 25.9 mg/d. Quercetin and kaempferol constituted the major proportion of the flavonoids (95%) The main sources of flavonoids in this population was black tea (61% of intake), onions (13%) and apples (10%). Mean daily consumption of these were tea 3 4 c, onions 9.4 g and apples 68.8 g. The flavonoid intake at baseline was found to be significantly and inversely associated with mortality from coronary heart disease.

Similarly, the Zutphen Elderly Study evaluated the association between catechin intake and the incidence of and mortality from ischemic heart disease and stroke. Catechins, which belong to the flavonoid family, are the main components of tea and may be responsible for the alleged protective effect The mean catechin intake was mainly from black tea, apples, and

chocolate. The results showed that catechins, whether from tea or other sources, might reduce the risk of ischemic heart disease mortality but not of stroke (Ilja et al 2001)

In the US male health professional's study, higher intake of flavonols was associated with a risk reduction in CVD mortality (RR=0.63) in men with previous CVD (Rimm et al 1996) However, a study from California, USA, tea intake was not related to CHD (MI) or to mortality from CVD, yet another study from a Welsch population showed a direct association of heavy tea drinking with CHD, although what factors besides tea drinking could have contributed to this are not fully described (Tijburg et al 1997) Therefore, the possibility that flavonoids have a beneficial effect on CHD needs to be considered and further investigations in humans are needed

Hence, keeping in mind the various factors leading to the development of various CDD, the present study was planned ***'to study the risk factor analysis in the development of chronic degenerative diseases in an industrial set up in Vadodara'***.

At a glance .....

- Rapid changes in diets and lifestyles that have occurred with industrialization, urbanization, economic development and market globalization, have accelerated over the past decade This is having a significant impact on the health and nutritional status of the population, particularly in developing countries and in countries in transition

The key findings in this area include:

Gopalan (1997): Urbanization involves changes in occupational patterns, life-styles, family structures and value systems These changes are reflected in changes in dietary practices and in the levels of physical activity

Popkin et al (1995): In most countries, urban residents consume smaller proportions of carbohydrates and greater proportion of protein and fat

Sobal et al (1989) and Brown et al (1998): Majority of people in urban society adapt to the various changes in lifestyle and dietary pattern resulting in increased prevalence of overweight and obesity. Studies have repeatedly shown that high SES is negatively correlated with obesity in developed countries, particularly among women, but is positively related with obesity the in population of developing countries

- Obesity has been called the mother of chronic degenerative diseases because it is an independent risk factor for several non-communicable diseases

The key findings in this area include:

Colditz et al (1995): A positive association between obesity and diabetes mellitus has been observed repeatedly The risk of NIDDM increases continuously with BMI and decreases with weight loss Obese women above 40 years of age are more likely to develop NIDDM than the women who remained slim (BMI<22).

Kannel (1979): Data from NHANES II, among US citizen, aged 29-29, reported the prevalence of diabetes to be 2 9 times higher in overweight than non-overweight persons.

Field et al (2001): Ten year follow-up (1986-1996) of middle-aged women in the Nurses Health Study and men Health Professionals Follow-up Study found that those with BMI>35 were approximately 20 times more likely to develop diabetes (Relative risk 17 0).

Bermudez and Tucker (2001): showed that the prevalence of diabetes was strongly associated with total and central obesity among Hispanics.

Ramchandran and Snehalatha (1999): Studies carried out in Southern Indians have also found BMI to be strongly associated with glucose intolerance. It was also found that android pattern of body fat, measured as WHR, was found to be a greater risk factor to Type 2 diabetes then general obesity.

Bahadori et al (1996): Obesity carries a penalty in that it predisposes an individual to a number of cardiovascular risk factors including dyslipidemia, hypertension raised cholesterol and impaired glucose tolerance.

Iwao et al (2001): Baltimore Longitudinal Study of Aging showed that both WC and BMI were related to cardiovascular risk factors.

- Aberrations in the atherogenic lipid parameters are observed among subjects suffering from various CDD

The key findings in this area include:

Jousilahti et al (1996): Obese subjects on an average have higher serum TC, lower HDL-C, higher TG levels, higher blood glucose and a high plasma insulin level than lean persons

Kahn et al (1969), Kannel et al (1971), Gordon et al (1981): Numerous epidemiological studies have shown that hypercholesterolemia when present for a longer duration leads to atherosclerosis, which in turn may precipitate CVD

Kannel and Schatzkin (1983): Framingham data indicate that weight gain raises both the cholesterol rich lipoprotein and the triglyceride rich VLDL and reduces HDL-C, producing an unfavourable L/H ratio

Grey et al (1997), Lahdenpera et al (1996): The two components of diabetic dyslipidaemia, high concentrations of triglyceride-rich lipoproteins and low concentrations of HDL, are closely interwoven. The relationship between hypertriglyceridemia and abnormalities in LDL-C particle size and composition has also been extensively investigated in diabetes

Fuster et al (1992): Oxidative modification of LDL-C appears central to foam cell formation, the earliest lesion of atherosclerosis.

Castelli and Anderson (1986), NIH Report (1997): Various studies including the Framingham as well as the Multiple Risk Intervention Trial have shown that the cholesterol levels are high in hypertensive subjects

Castelli (1986), Fontbonne et al (1989), Manninen et al (1992), Jeppesen et al (1998): Apart form cholesterol and HDL-C, recent research shows that hypertriglyceridemia is an important independent cardiac risk factor. Further boost was given to the theory of TG as an independent marker in CHD by the Framingham heart Study

Cantin et al (1999): In the Quebec Cardiovascular Study carried out on healthy men, Non-HDL cholesterol was a strong risk factor for IHD and a better predictor than the traditional lipid risk factors Thus, the study suggested that non-HDL cholesterol should be used as risk factor for ischemic heart disease (IHD) because it includes VLDL, IDL and Lp(a)

Cui et al (2001): Findings form the Lipid Research Clinics Programme Follow-up Study also showed that Non-HDL cholesterol emerged as a somewhat better predictor of CVD morality than LDL

- Apo A1 and Apo B provide a better marker for predicting cardiovascular risk as compared to traditional lipid measures

The key findings in this area include:

Walldius et al (2001): showed that Apo B might be a good indicator of heart disease because it reflects the number of lipoproteins that are associated with the development of atherosclerosis. Although LDL-C and HDL-C are known risk factors, it is suggested that Apo B, ApoB/ApoA1 and ApoA1 should also be regarded as highly predictive in evaluation of cardiac risk.

Garfagnini et al (1995): A study carried out in Italy confirmed that Apo A1 and Apo A1 /Apo B ratio are better than HDL-C in assessing the severity of coronary damage

Bahl et al (1994): In a study carried out among Indian population, overall Apo B and TG levels showed larger univariate difference between the normal group (no CAD) and the group with CAD The variable with strongest predictive power for CAD was the ratio of Apo A1 to Apo B. These results indicate that Apo A1 and Apo B provide a better marker for predicting the presence of CAD as compared to traditional lipid measures

- General habits of the individuals such as smoking and alcohol consumption have been found to be a risk for bringing about metabolic alterations in the disease profile of the individuals.

The key findings in this area include:

Ockene and Miller (1997): Smoking acts synergistically with other risk factors, substantially increasing the risk of CHD

Shah and Sadaria (2003), Whig et al (1992): Active smoking increase LDL-C and VLDL-C where HDL-C content is lowered, resulting in decreased ratio of HDL-C/TC and HDL-C/ LDL-C.

Freedman et al (1985): Results of Bogalusa heart study have shown an association of cigarette smoking and alcohol consumption with levels of serum lipid and lipoproteins in both adults and adolescents, while cigarette smoking is associated with decreased HDL-C and increased LDL-C levels, moderate alcohol consumption is related to increased level of HDL-C

Rimm et al (1996): Many studies have shown an inverse association between alcohol consumption and coronary heart disease, with a possible flattening at higher consumption levels.

Diet and nutrition are important factors in the promotion and maintenance of good health through out the entire life course Dietary factors are considered to be a major modifiable risk factoring the management of CDD. Apart from the deleterious effect of excess calories, fat, type of fat etc recent research has laid emphasis on the probable role of antioxidants in the prevention or management of various CDD.

The key findings in this area include:

Krauss et al. (2000): Saturated fat is the principal dietary determinant of LDL-C levels

Lichtenstein et al (1999), Judd et al (1994): It has also been established that dietary trans-unsaturated fatty acids can increase LDL-C and reduce HDL-C

Keys (1965): Studies have shown that MUFA do not lower HDL-C levels but reduce LDL-C levels This lowers the L/H ratio, thereby reducing coronary risk.

Ulbricht and Southgate (1991): n_3 are protective against CHD as these lower the serum cholesterol levels and increase HDL-C levels.

Lonn and Yusuf (1997), Rimm et al (1996): showed that increased intake of antioxidants through diet or supplements, particularly vitamins E and C and beta carotene, is associated with a lower risk of coronary heart disease

Hertog et al (1992): There is some evidence available to show that high intake of flavonoids may offer protection from CAD. The strongest evidence comes from the study on elderly subjects in Zutphen, Netherlands, where the flavonoid intake was found to be significantly and inversely associated with mortality from coronary heart disease