CHAPTER 2

LITERATURE REVIEW

2.1   Introduction

The term 'metabolic syndrome' is used to describe in one person the clustering of a specific group of risk factors associated with chronic diseases of lifestyle. Considerable evidence exists, as mentioned in Chapter 1, that insulin resistance is the underlying common factor in the development of the metabolic syndrome and that hyperinsulinaemia occurs as a response to insulin resistance (Flack and Sowers, 1991; Vague and Raccah, 1992; Colagiuri and Brand Miller, 1997; Liese *et al.*, 1998). According to Colagiuri and Brand Miller (1997), insulin resistance is common in most populations and has reached epidemic proportions in some. For this reason the metabolic syndrome is sometimes referred to as the insulin resistance or resistant syndrome.

In this Chapter, a brief outline of insulin resistance, its relationship with facets of the metabolic syndrome, characteristics of the metabolic syndrome and the effect of lifestyle in the developing of the metabolic syndrome, are given.

2.2   Insulin resistance

2.2.1   Expressions of insulin resistance / sensitivity

Insulin resistance is a state in which a given concentration of insulin produces a subnormal biological response (Kahn, 1978; Flier, 1983; Colagiuri and Brand Miller, 1997; Liese *et al.*, 1998). The term insulin resistance is often used alternatively to describe decreased insulin sensitivity (Colagiuri and Brand Miller, 1997).

Many methods have been used to assess insulin resistance, but according to Colagiuri and Brand Miller (1997) there is, unfortunately no uniform definition of insulin resistance.

Therefore, it is difficult to define and describe normal/abnormal insulin resistance. In the literature there is a reasonable agreement between two most commonly used methods to determine insulin resistance namely the euglycaemic hyperinsulinaemic clamp and the intravenous glucose tolerance test with minimal modelling (Colagiuri and Brand Miller, 1997). However, a major limitation in epidemiological research is the lack of a suitable standardised quantitative method for assessing insulin resistance. The calculation of indices remains the method to quantify insulin sensitivity or resistance in epidemiological studies. Donahue et al. (1988) used fasting insulin and glucose concentrations to calculate insulin sensitivity (IS). Matthews et al. (1985) used the same variables in a homeostasis model assessment (HOMA) to quantify insulin resistance (IR).

IS index = 10 000 X the reciprocal of [fasting insulin X fasting glucose] (Donahue et al., 1988).

HOMA IR = [fasting insulin X fasting glucose] / 22.5   (Matthews et al., 1985).

2.2.2 Physiology

For insulin resistance to be understood, it is necessary to give a brief summary of the cellular effects of insulin (for a review see Rosen, 1987; Zick, 1989; Houslay and Siddle, 1989). Insulin binds to specific receptors on the plasma membrane. The receptor serves two purposes. First, to recognise the hormone among all other substances in the blood and binding it with specificity and high affinity. Secondly, to transmit a transmembrane signal that results in an alteration in intracellular metabolic pathways (Kahn and White, 1988). The insulin receptor is composed of two subunits. According to Kahn and White (1985) the α-subunit is sensitive to proteolytic divarication/cleavage. The implication thereof suggests that the α-subunit acts largely extracellularly. The β-subunit appears to be involved in signal transduction across the membrane. Autophosphorylation of the β-subunit occurs within seconds with the activation of the intrinsic tyrosine-specific protein kinase. This rapid reaction is followed by a slower serine/threonine phosphorylation of the β-subunit (Mayor et al., 1991). The metabolic effects of insulin are summarised in Table 2.1.

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One of the physiological outcomes of the action of insulin is the lowering of blood glucose levels. At cellular level this is the result of insulin stimulated translocation of glucose carriers/transporters from an abundant intracellular pool (Kahn, 1992).

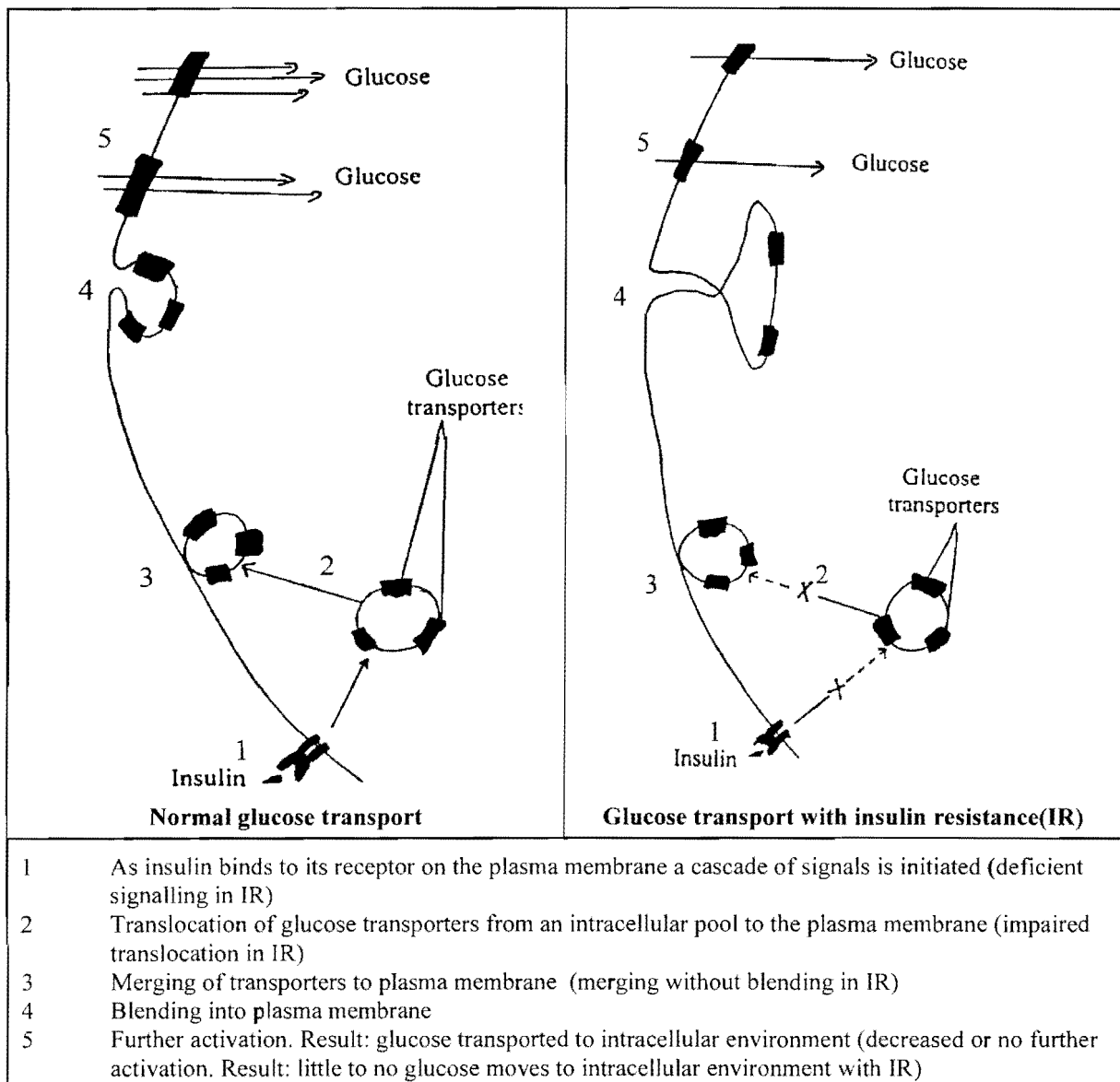**Table 2.1   Metabolic effects of insulin** [adapted from Greenspan and Baxter (1994)]

Target	Paracrine Effects	Outcomes and mechnisms
Pancreatic island cells	Pancreatic A cells: Pancreatic D cells:	* ↓ Secretion of glucagon * Somatostatin release: ↓ Secretion of glucagon
Target	**Endocrine Effects**	**Outcome**
Liver cells	Anabolic: Anticatabolic:	* Promotes glycogenesis * ↑ synthesis TG, TC,VLDL * ↑ protein synthesis * Inhibits glycogenolysis * Inhibits ketogenesis * Inhibits gluconeogenesis
Muscle cells	Promotes protein synthesis: Promotes glycogen synthesis:	* ↑ amino acid transport * Stimulates ribosomal protein synthesis * ↑ glucose transport * Enhances activity of glycogen synthetase * Inhibits activity of glycogen phosphorylase
Adipose tissue	Promotes TG storage:	* Induces lipoprotein lipase, making fatty acids available for absorption into fat cells. * ↑ glucose transport into fat cells, therefore increases availability of α-glycerol phosphate for TG synthesis * Inhibits intracellular lipolysis

↓ = decrease; ↑ = increase ; TG = triglycerides; TC= total cholesterol; VLDL = very low density lipoprotein.

Mayor *et al.* (1992) hypothesised that high physiological levels of glucose and insulin could induce insulin resistance *via* the level of the glucose transport effector system. The occurrence of insulin resistance *via* a defect in the glucose transport system is illustrated in Figure 2.1.
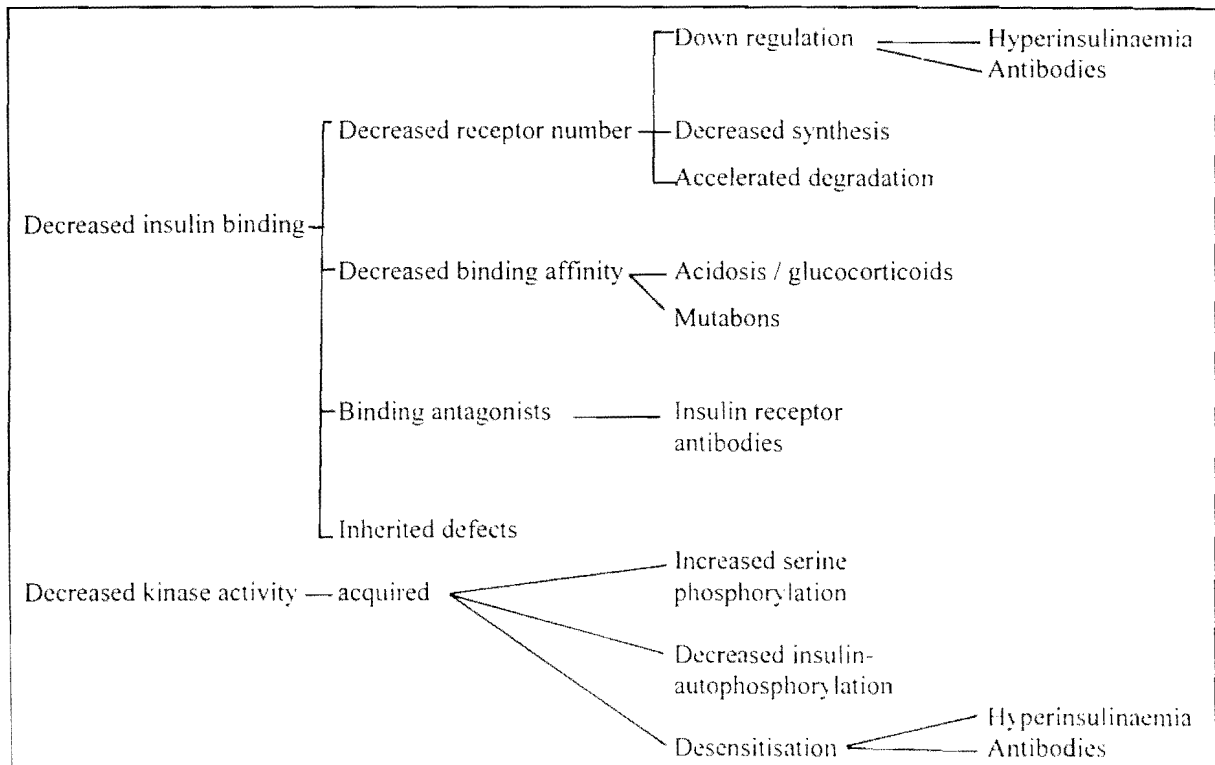
Other aspects of insulin resistance can involve a decrease in insulin sensitivity as well as

a decrease in insulin responsiveness. A decrease in insulin sensitivity means that more insulin is needed to produce the same effect and implies a change in the receptor number or affinity (Pillay and Makgoba, 1991).
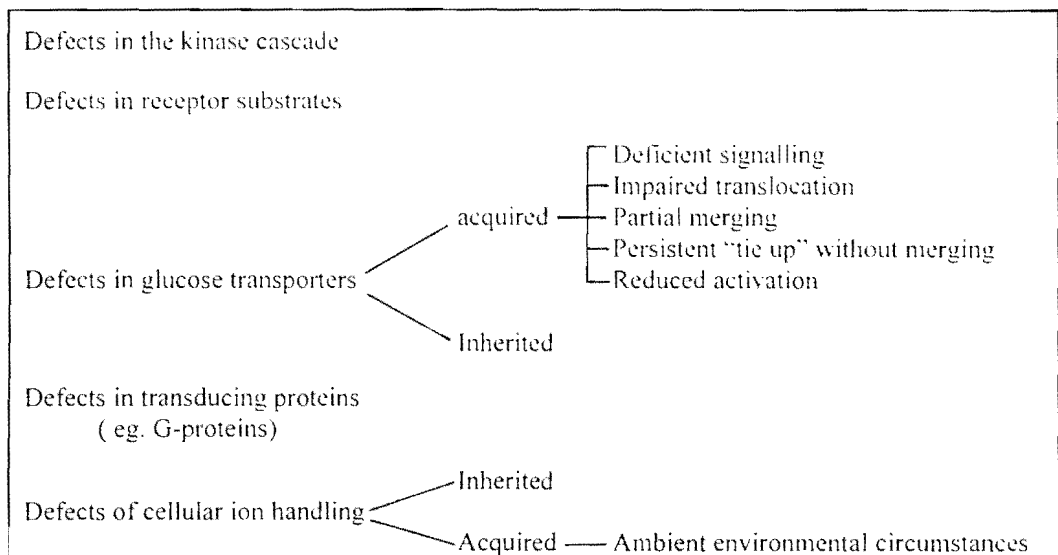

1	As insulin binds to its receptor on the plasma membrane a cascade of signals is initiated (deficient signalling in IR)
2	Translocation of glucose transporters from an intracellular pool to the plasma membrane (impaired translocation in IR)
3	Merging of transporters to plasma membrane (merging without blending in IR)
4	Blending into plasma membrane
5	Further activation. Result: glucose transported to intracellular environment (decreased or no further activation. Result: little to no glucose moves to intracellular environment with IR)

Figure 2.1   Illustration of the events involved in insulin stimulated glucose transport in muscle and adipose cells [Adapted from Kahn (1992)].

Decreased responsiveness means the decrease in the maximal insulin response which implies a change in a rate-limiting step, usually at a post-receptor level (Pillay and Makgoba, 1991). According to a review article on the molecular mechanisms of insulin resistance by Pillay and Makgoba (1991), the mechanisms involved in insulin resistance on receptor and post-receptor level can be summarised as indicated in Figures 2.2 &2.3.

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Down regulation ——————— Hyperinsulinaemia
Antibodies

Decreased receptor number — Decreased synthesis
Accelerated degradation

Decreased insulin binding —

Decreased binding affinity — Acidosis / glucocorticoids
Mutabons

Binding antagonists ——————— Insulin receptor antibodies

Inherited defects

Decreased kinase activity — acquired — Increased serine phosphorylation

Decreased insulin-autophosphorylation

Desensitisation ◄——— Hyperinsulinaemia
Antibodies

Figure 2.2   Some mechanisms of receptor-mediated insulin resistance [Adapted from Pillay and Makgoba (1991)].

Defects in the kinase cascade

Defects in receptor substrates

Deficient signalling
Impaired translocation
acquired — Partial merging
Persistent "tie up" without merging
Reduced activation

Defects in glucose transporters

Inherited

Defects in transducing proteins
(eg. G-proteins)

Inherited
Defects of cellular ion handling
Acquired —— Ambient environmental circumstances

Figure 2.3   Some mechanisms of post-receptor-mediated insulin resistance [Compiled from Pillay and Makgoba (1991), Kahn (1992) and Resnick (1993)].

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2.2.3 Pathophysiology: Association of insulin resistance with risk factors of chronic diseases of lifestyle

A genetic predisposition appears to be involved in many of the risk factors for the chronic diseases of lifestyle such as obesity, fat distribution, susceptibility to hypertension and hyperlipidaemia, and also in insulin resistance (Vague and Raccah, 1992; Liese *et al.*, 1998). Although genetics could probably partly explain the development of these risk factors, many can be explained by resistance to insulin-mediated processes.

Obesity is universally recognised as a factor to increase insulin resistance (Liese *et al.*, 1998). The association between obesity and insulin resistance is complicated by the importance of fat distribution with the accumulation of visceral fat having the strongest association with insulin resistance (Colagiuri and Brand Miller, 1997). Björntorp (1991) postulated that due to the fact that visceral fat is less sensitive to the lipolytic action of insulin, it delivers a large flux of free fatty acids (FFA) in the portal vein. This flux may increase hepatic gluconeogenesis and lipoprotein synthesis, diminish hepatic insulin clearance and through the Randle cycle may induce resistance to insulin-mediated glucose uptake in the liver and muscle tissue. Simultaneously, the stimulation of gluconeogenesis in the liver, will result in an increase in hepatic glucose output (Zimmet, 1993). Therefore, the loss of insulin's ability to maintain normal plasma FFA concentration is partly responsible for the development of fasting hyperglycaemia in NIDDM (Reaven, 1988; Flack and Sowers, 1991; Boden, 1997).

The characteristic lipid abnormalities seen as a result of insulin resistance include decreased HDL-C, increased VLDL triglyceride synthesis and an elevated serum triglyceride concentration (Zimmet, 1993). According to Tobey *et al.* (1991) hypertriglyceridaemia is mainly the consequence of an exaggerated hepatic synthesis of triglyceride under the influence of both high insulin impregnation and the presence of glucose and FFA fluxes. Low HDL-C levels are directly due to the excess of VLDL concentrations (Tobey *et al.*, 1991).

A secondary outcome of insulin resistance appears to be elevated PAI-1 levels (Vague and Raccah, 1992). Higher levels of PAI-1 are postulated to inhibit fibrinolysis and increase the risk of thrombogenesis and occlusion of coronary arteries (Potter van Loon *et al.*, 1993). Researchers have shown that an increase in insulin sensitivity through moderate weight loss and physical exercise improve PAI-1 levels (Winkler, 1997). Lindal *et al.* (1996) showed that subjects in the upper tertile of insulin resistance had a PAI-1 activity that was three times higher than men in the lower third and twice as high in women.

The role of insulin in the pathogenesis of hypertension is controversial. According to Meehan *et al.* (1993), however, insulin and blood pressure may be linked through shared functional or structural mechanisms of inherited or acquired nature. Hopkins *et al.*(1996) referred to hypertension, dislipidaemia and insulin resistance as "spokes on the wheel" rather than "links in a chain" with visceral obesity as the "postulated hub of the wheel". Swislocki (1990) mentioned that the sequella of insulin resistance in hypertension is multifactorial and includes an altered sodium balance, abnormal lipoprotein profile, reduced vasodilator activity, increased coagulation activity, increased local atherogenesis and increased sympathetic activity. There is evidence that the latter is achieved through significant increases in plasma catecholamine concentration associated with an increase in plasma insulin concentration, independent of any change in plasma glucose concentration (Reaven, 1988; Colagiuri and Brand Miller, 1997).

Experimental and epidemiologic data suggest that hyperinsulinaemia accelerates the development of atherosclerosis. These interrelationships between hyperinsulinaemia and atherosclerosis as well as between atherosclerosis and glucose intolerance, dyslipidaemia, hypertension and upper body obesity, are complicated because these conditions tend to cluster. Both direct and indirect mechanisms may be implicated (Zimmet, 1993).

2.2.4 Gender and population differences

Both similarities and differences among ethnic and gender groups have been documented

with respect to insulin levels, insulin resistance and the relation between insulin sensitivity and obesity.

Results from the Bogalusa Heart Study showed that females tended to be fatter than males and whites fatter than blacks during childhood and adolescence. In later age black females were more overweight than whites. In both sexes of the white population and in black women this obesity influenced lipoprotein adversely (Wattigney *et al.*, 1991). Results from the Charleston Heart Study indicated that the risk for all-cause mortality was predicted by BMI in white females but not in black females although the BMI of black females was greater (Stevens *et al.*, 1992). Walker *et al.* (1991) also reported "healthy" obesity among black South African women, with low CHD risk factors despite the presence of obesity.

Results from both the Bogalusa Heart Study (Wattigney *et al.*, 1991) and the National Heart, Lung, and Blood Institute Growth and Health Study (NGHS) in the USA (NGHS research group, 1992) indicated that black women were more at risk for high blood pressure than their white counterparts.

Results from the Insulin Resistance and Atherosclerosis Study (IRAS)(Haffner *et al.*, 1996) indicated that African-Americans and Hispanics seemed to be more insulin resistant when compared with non-Hispanic whites. Insulin sensitivity was found to be inversely associated with waist-to-hip ratio, independent of BMI in both genders and all ethnic groups in the IRAS (Karter *et al.*, 1996).

Higher insulin levels were reported in European-American men, compared to women. These differences could only be partly explained by BMI and waist-to-hip ratio (Ferrara *et al.*, 1995).

2.2.5 Influences of lifestyle

In an overview, Zimmet (1997), noticed that although NIDDM is mainly associated with

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Pima Indians in the USA, whites and urban Aborigines, a steady stream of reports continue to highlight the explosion of NIDDM in many societies associated with lifestyle changes. The same tendency was reported locally by Levitt *et al.* (1993) in their study on the prevalence and identification of risk factors for NIDDM in urban black South Africans in Cape Town.

Numerous reviews have emphasised the rarity of CHD in Africa (Walker, 1999). Seedat and Mayet (1999) also reported that black South Africans have a minimal rate in the occurrence of CHD. However, Mollentze *et al.* (1995) reported that all elements for a potential epidemic of atherosclerotic cardiovascular disease were present in both rural and urban South African blacks from the Free State, although the urban population had the worst risk profile. The importance of these findings is the observation of the researchers that the processes associated with urbanisation were no longer occurring only in urban populations, but also in rural settings.

Known environmental factors that are risk determinants in the development of the metabolic syndrome will be discussed very briefly. Some of the factors will be addressed in more detail in the discussion of the results of the study in Chapters 4 and 5.

- **Age:** It is believed that insulin resistance increases with age. Reports from the Bogalusa Heart Study (Wattigney *et al.*, 1991) indicated an inverse association between serum lipoprotein and age in white males as well as between obesity and age in black women. It is also generally accepted that glucose tolerance deteriorates with advancing age (Ratzmann *et al.*, 1992). Combined analysis of data from the ARIC and Cardiovascular Health Study (CHS) cohorts suggested a greater impact of the smoking habit and HDL-C for elderly whites and a decreased impact of HDL-C for elderly black women in the development of atherosclerosis (Howard *et al.*, 1997). However, in a review on the effect of aging on insulin resistance, Kohrt (2000) stated that age-related increases of insulin resistance were rather due to increases of adiposity and decreases of physical activity and that aging *per se* has little effect on insulin action.

- **Physical inactivity:** It was recognised in ancient times that physical exercise may

be beneficial in the treatment of DM (Horton, 1988). Exercise appears to improve insulin sensitivity through weight loss and fat distribution (Zimmet *et al.*, 1997) and assumes great importance due to the beneficial effects also on lipoprotein levels and hypertension (Zimmet, 1993).

- **Nutritional factors:** Both under- and overnutrition occur in lower income developing countries, reflecting the trend in which an increasing proportion of people consume the types of diets associated with a number of chronic diseases (Popkin, 1994). Under-/malnutrition is generally higher in rural areas than in urban ones (von Braun *et al.*, 1993). Overnutrition normally presents in obesity. Although obesity occurs in both rural and urban populations, obesity is an increasingly widespread problem in urban populations (Gross and Monteiro, 1989). Results from the Brisk Study indicated that the diet of urbanised black South Africans represents a phase towards a progressively atherogenic Western diet (Bourne *et al.*, 1993). The composition of a diet, independent of weight loss, also plays an important role in the development of insulin resistance. According to Wolever (2000) the reduction of post-prandial glucose and insulin responses may be a way to interrupt the deterioration of β-cell function due to excess insulin secretion. However, although fructose produces much lower glucose and insulin responses, large amounts of fructose fed to humans reproduce the features of the metabolic syndrome (Wolever and Brand Miller, 1995). Thus, although the composition of a diet plays a role in the development of insulin resistance, further work needs to be done to investigate the optimal amount and type of dietary carbohydrate in the prevention and treatment of the metabolic syndrome (Wolever, 2000).

- **Urbanisation:** This will be discussed in paragraph 2.4 of this chapter.

- **Low birth weight and "Thrifty Phenotype":** Low birth weight has been proposed as a new risk factor for the development of IGT/NIDDM and the metabolic syndrome by Hales and Barker (1992). Low birth weight is a reflection of nutritional deficiency in utero. It is hypothesised that in the long-term it results in impaired development of the endocrine pancreas (Hales and Barker, 1992). Hales and Barker (1992) proposed the "Thrifty Phenotype" hypothesis suggesting
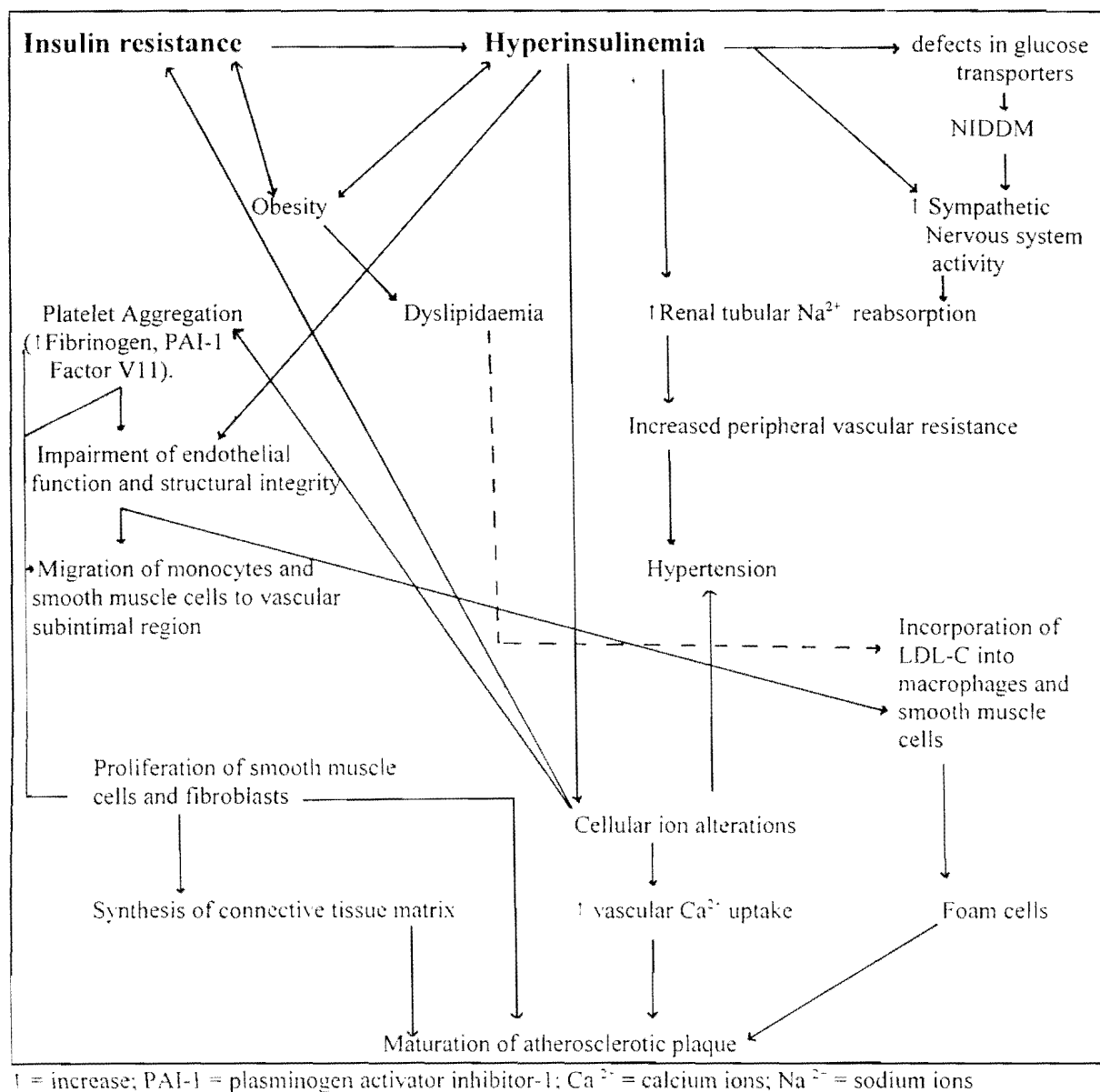
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that the development of IGT/NIDDM and eventually the metabolic syndrome mainly results from environmental determinants and that genetic factors play a minimal or no role. However, according to Simmons (1995) these hypotheses are not consistent. Data from Pima Indians showed an "U" shaped curve between birth weight and the risk to develop NIDDM. It also fails to explain why populations with high birth weights (eg. Pima Indians and Polynesians) can have a high prevalence of NIDDM (Simmons, 1995).

- **Others:** It is also hypothesised that stress influences the development of insulin resistance (Surwit *et al.*, 1992). This factor was not examined in the present study. Factors that include lifestyle habits and consequences such as HIV-status and alcohol intake are discussed in Chapters 4 and 5 of this thesis.

2.3   Characteristics of the metabolic syndrome

It is no easy task defining the metabolic syndrome. There are diversities in expressions associated with it. As indicated previously, it has been suggested that insulin resistance and hyperinsulinaemia are involved in the etiology of three chronic diseases of lifestyle namely NIDDM, hypertension and CHD/CAD. For the purpose of this thesis the metabolic syndrome can be described as the clustering of related risk factors of these three chronic diseases in certain individuals with insulin resistance as underlying common factor (Reaven, 1988). The role of insulin resistance in this regard is summarised in Figure 2.4.

According to the review by Liese *et al.* (1998) on the development of the metabolic syndrome, the overall prevalence of metabolic abnormalities varies across populations. However, evaluations of clustering in the middle-aged Mexican-American and non-Hispanic white population of the San Antonio Heart Study and the slightly older African-American ARIC cohort and other populations have shown striking similarities. Many analytical studies have documented the metabolic syndrome and its components. However, only a few prospective epidemiologic studies have focussed on the clustering characteristics of the metabolic syndrome. Some of the studies which documented the clustering of the risk factors which relate to insulin resistance, and/or the influence of insulin resistance on clustering of risk factors, and therefore described the metabolic syndrome as defined in this thesis, are summarised in Table 2.2.

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Insulin resistance ⟶ Hyperinsulinemia ⟶ defects in glucose transporters

↓

NIDDM

↓

↑ Sympathetic Nervous system activity

↓

Obesity

Dyslipidaemia

↑ Renal tubular Na²⁺ reabsorption

Platelet Aggregation (↑Fibrinogen, PAI-1 Factor V11).

Increased peripheral vascular resistance

Impairment of endothelial function and structural integrity

→Migration of monocytes and smooth muscle cells to vascular subintimal region

Hypertension

Incorporation of LDL-C into macrophages and smooth muscle cells

Proliferation of smooth muscle cells and fibroblasts

Cellular ion alterations

Synthesis of connective tissue matrix

↑ vascular Ca²⁺ uptake

Foam cells

Maturation of atherosclerotic plaque

↑ = increase; PAI-1 = plasminogen activator inhibitor-1; Ca²⁺ = calcium ions; Na²⁺ = sodium ions

Figure 2.4 **The role of insulin resistance in the clustering of risk factors** [Compiled from Flack and Sowers (1991); Resnick (1993); Winkler (1997)].

This summary of studies in which risk factors for the metabolic syndrome (associated with insulin resistance) cluster, illustrates that no information on possible clustering of risk factors (related to insulin resistance) in South African blacks is available.

Table 2.2   **A summary of some epidemiological studies on the clustering characteristics of the metabolic syndrome with insulin resistance as common underlying factor**

Reference	Measured metabolic disorders	Study	Design	Sample size, age and gender	Subject characteristics	Results: clusters or associations
Fontbonne and Eschwége, 1991.	Blood glucose, insulin, TG, TC, HDL, BP, BMI, fibrinolytic activity, VLDL-TG	Paris Prospective Study	Cohort	n=7 038; 43-54 years male	Paris civil services	↑ TG; ↑ Glucose
Ferrannini et al., 1992	Diabetes, obesity, dislipidaemia and hypertension	The San Antonio Heart Study	Cross-sectional	n=2 930; 25 - 64 years male/female	Mexican-American non-Hispanic White	↑ TG; ↑ Glucose
Haffner et al., 1992 a&b	Fasting serum insulin and glucose, TG, LDL, HDL, BP	San Antonio Heart Study	Cohort	n=1 125; 25 -64 years male/female	Non-Hispanic White, Mexican-American	↑ TG; ↓HDL-C; ↑ BP, ↑BMI, less favourable body fat distribution
Mitchell et al., 1992	Insulin, HDL, BP, TG, BMI, WHR, Triceps, subscapular skinfolds	San Antonio Family Heart Study	Family study (analytical)	n=5149; 25-64 years	Mexican-Americans and Hispanic whites	↑ TG; ↓HDL-C; ↑ BP stronger in Mexican-Americans than whites
Lindahl et al., 1993	Fasting glucose, insulin, TC, TG, HDL, BP, BMI, WHR,	MONICA	Cross-sectional	n=758; 25 - 64 years male/female	Northern Sweden	↑ TG; ↓HDL-C; ↑ BP; BMI; WHR
Selby et al., 1993	Insulin, HDL, Hypertension, WHR LDL subclass phenotype	Kaiser Permanente Women Twins Study	Twin study	n=341 pairs; mean=51 years; women	White	↑ VLDL
Zimmet et al., 1994	Fasting glucose, insulin, lipids, BP, anthropometry	Mauritius	Cross-sectional	n=5 080; 25 - 74 years male/female	Indian, Creole, Chinese, Mauritians	associated with upperbody obesity, NIDDM and ↑ TG
Carmelli et al., 1994.	NIDDM, Hypertention, obesity	NAS NRC	Twin study	n=2 508 pairs; 56-68 years, male	Whites	clusters influenced by 59% genetic and 41% environmental factors
Rodriguez and Sharp, 1996	Fasting glucose, insulin, TG, TC, HDL, Fib, BP, BMI, WHR	Honolulu Heart Program	Cross-sectional;Cohort	n=3 741; 71 - 93 years , male	Japanese-American; Hawaii	↑ TG; ↓HDL-C; ↑ BP; BMI; WHR

Table 2.2 (Continue)

Reference	Measured metabolic disorders	Study	Design	Sample size, age and gender	Subject characteristics	Results : clusters or associations
Mykkänen et al., 1996	Fasting glucose, insulin, TG, HDL, BP, BMI, WHR	Finland	Analytical	n=153; 53 - 61 years male/female	non-DM, Finland	↑ TG; ↓HDL-C; ↑ BP;
Ekoé et al., 1996	Insulin, glucose, TG, TC, LDL, HDL, BP, BMI, WHR, Uric acid	Algonquin Indian communities	Cross-sectional	n=352; mean=35 years male/female	Algonquin Indians	↑ TG; ↓HDL-C; ↑ TC; BMI; subscapular skinfolds
Schmidt et al., 1996	NIDDM, TG, HDL, Hypertension, Uric acid	ARIC study	Cross-sectional	n=14 481; 45-64 years male/female	African-American; Whites	↑ TG; ↑ glucose; BMI; WHR
Liese et al., 1997	NIDDM, TG, HDL, BP, BMI, WHR	ARIC study	Cohort	n=6 113; 45 - 65 years male/female	African-American, Whites	↑ Insulin predicted 95% of two and more clusters of MMS components
Gaillard et al., 1997	Socioeconomic status, family history for CHD and DM, physical activity, insulin, BMI, WHR, BP, TC, TG, LDL-C, HDL-C, VLDL, C-peptide, Glucose.	Relative study	Analitical	42 men; 1158 women; 25-65 years.	African-American	independent of socioeconomic factors: ↑ TG; ↓HDL-C; ↑ TC; ↑ BMI; ↑WHR , ↑VLDL clusters with ↑ Insulin
Bonora et al., 1998	Insulin, glucose, BP, HDL-C, LDL-C, TG, TC, apoproteins, fibrinogen, antithrombin 111, BMI, alcohol intake, cigarette smoking, activity level,	The Bruneck Study	Cross-sectional	500 men; 500 women; 40-79 years.	Non-diabetics from Bruneck, Italy	High and low insulinaemia clusters with several risk factors for atherosclerosis such as hyperglycemia, dislipodaemia, hypertension

↑ = increased; ↓ = declined

For explanation of abbreviations: referred to LIST OF ABBREVIATIONS

2.4   Urbanisation of South African blacks

2.4.1   Introduction

South Africa is presently experiencing a rapid process of urbanisation, especially of Africans leaving underdeveloped rural areas to seek a better life in urban environments. In 1993, 48.3% of the total South African population was urbanised, compared to 53.7% in 1996 (Anon, 1998). During this period the percentage urbanised Africans increased from 35.8% to 43.3%, while only small increases in the coloured and Indian populations, and a slight decrease in the white population occurred (Anon, 1998).

Urbanisation results in a demographic transition. Globally, it has also been associated with a health and epidemiological transition, during which both detrimental and beneficial effects on health have been described (Murray and Lopez, 1990; Yach *et al.*, 1995; Shetty and McPherson, 1997). Although the epidemiological transition in developing countries is characterised by a decrease in infant mortality, fertility and most infectious diseases (Murray and Lopez, 1990; Shetty and McPherson, 1997), it is not necessarily accompanied by industrialisation and improved economic circumstances (Yach *et al.*, 1995). According to Gross and Monteiro (1989), urbanisation could also lead to urban poverty and situations where behaviours which increase risk of chronic diseases of lifestyle co-exist with high risks of infectious diseases, resulting in a "double burden of disease".

In this study, the possible influence of urbanisation on the development of the metabolic syndrome in Africans of the Northwest province has been examined. Therefore, in this section, this population will be briefly described. The terms urbanisation, urban and rural will be defined in context of the study, and the expected changes during urbanisation will be delineated, using the review by MacIntyre (1998) as basis.

2.4.2   The African population of the Northwest province of South Africa

Central Statistics (1997) gives the present population for the Northwest province as three million. This comprises approximately 63% Setswana, 14% isiXhosa and 8% Sesotho

speakers (Janse van Rensburg, 1995).

The Sotho and Tswana people originated from the bed of reeds at Ntswana-tstatsi, which means 'where the sun rises' (Lye, 1980). The initial migrations took place in the thirteenth to fourteenth centuries or earlier (van der Wateren and Immelmann, 1988). The present day Sotho-Tswana people migrated from the north over a period of time and dispossessed the earlier San inhabitants of the area (van Warmelo, 1974).

At the beginning of the 19th century the Sotho-Tswana was a well established population with developed social and political institutions (Cornwell, 1988). Despite frequent quarrels and splitting, the people appeared to have prospered and spread over the Northwest provinces. The Southern Sotho occupied the land south and east of the Vaal river and the Tswana the larger area in the northwest (Lye, 1980). The beginning of the 19th century was also characterised by warriors of the powerful Zulu nation from Natal, attacking and dispersing all tribes in their path. This period of unrest and war became known as the "Difaqane", a Sotho word meaning "the scattering" and lasted from approximately 1812 to 1837 (Maylam, 1986; Lye, 1980; van der Wateren and Immelmann, 1988; Cornwell, 1988). The "Difaqane" possibly marked the first changes to the 'traditional' Sotho-Tswana lifestyle that would increase in momentum with contact with Europeans and urbanisation (Maylam, 1986).

The Sotho-Tswana came in contact with Europeans from the London Missionary Society for the first time in 1816. Between 1820 and 1846 mission stations were established among several tribes (Schapera and Comaroff, 1991). The Sotho-Tswana also came into contact with the Voortrekkers who had trekked from the Cape and settled in the Transvaal. In the beginning of the 19th century first contact with white explorers were made (Schapera and Comaroff, 1991). As the 19th century progressed, the Sotho-Tswana came more and more into contact with whites as well as being caught up in the political and economic movement of the time. The presence of the white farmers put further pressure on the Sotho-Tswana by reducing the amount of land available for agriculture and hunting (Schapera and Comaroff, 1991). The combined effects of the "Difaqane" and the presence of white settlers were to scatter the Sotho-Tswana people throughout

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Southern Africa. However, the ancestral lands which survived the "Difaqane" and white settlements, have been maintained (Setiloane, 1976). Although the Sotho-Tswana culture has been influenced by the white culture, much of the core culture has remained (Comaroff and Comaroff, 1991).

2.4.3 Urbanisation

As mentioned earlier, urbanisation is a process which takes place in many developing countries. To understand the effects of urbanisation, it is important to clarify the meanings of the terms usually associated therewith.

2.4.3.1 Rural

The term 'rural' usually refers to an area of countryside where the inhabitants depend primarily on agriculture for their livelihood and which does not fall into a metropolitan area (Gelderblom and Kok, 1994).

2.4.3.2 Urban

Definitions of the term 'urban' are based on criteria such as population density, type of administration, economic base and access to services (Yach *et al.*, 1995).

2.4.3.3 Migration

In South Africa, a large proportion of the economy utilises migrant labour, particularly the mining industry. According to Moodie (1991) a migrant worker is one who is recruited in his home area and contracted to work, often miles away from his home, only returning home occasionally. Migration can be permanent or circular. Permanent migration is the once-off transfer of a person from a rural to an urban environment (Gelderblom and Kok, 1994). Circular migration is when the migrant returns to his place of origin on retirement (Gelderblom and Kok, 1994).

2.4.3.4 Acculturation

McLeod and Hanks (1985) defined the term 'culture' as the " total of the inherited ideas, beliefs, values and knowledge, which constitute the shared base of social action". Acculturation therefore occurs when two groups with different cultures come into

prolonged contact resulting in change (usually rapid) in the original behaviour and traits of either or both groups (Palinkas and Pickwell, 1995).

2.4.3.5 The urbanisation process

Urbanisation is thus the increase in population in an urban area, due to the migration of people from rural areas (Gelderblom and Kok, 1994). However, in reality, the process of urbanisation is complex and many settlement areas do not clearly meet the criteria of 'urban' or 'rural' but have characteristics of both (Gelderblom and Kok, 1994). This 'contamination' between rural and urban populations was also found in African communities in the Free State Province of South Africa by Mollentze *et al.* (1995).

In the past, the urbanisation process in South Africa, followed the so called 'push-pull' dynamic (May, 1989). Factors such as loss of agricultural land, few cash generating opportunities and poverty acted to 'push' migrants from the rural to the urban areas. Other factors such as the need for family unity and obligations in the rural areas, served to 'pull' the migrants back to their rural home. More recently, increasing poverty and deterioration in rural areas have weakened the 'pull' while decreased living costs in urban and peri-urban has strengthened the 'push'. This has resulted in a change in the urbanisation process in South Africa, from that of circular migration to a more permanent migration towards urban and peri-urban settlements (May, 1989).

2.4.4 Expected health impact of urbanisation

The most negative effects of urbanisation are seen in the informal settlement areas where shacks are constructed of almost any usable material. There are no or limited electricity, running water, sanitation and sewage or refuse removal (von Schirnding and Yach, 1992). Overcrowding is common and associated with increased danger of infectious diseases such as gastroenteritis, respiratory tract infections and tuberculosis (Bradshaw and Buthelezi, 1996).

The expected health outcomes of urbanisation in South Africa with its possible effects on health status, are given in Figure 2.5. In this figure possible determinants, indicators and risk markers or factors are also shown. This model was used to design the THUSA

study and will be discussed in the next chapter.

| CHANGES EXPECTED DURING URBANISATION (TRANSITIONS) | POSSIBLE EFFECTS ON HEALTH STATUS | POSSIBLE DETERMINANTS INDICATORS, MARKERS, RISK FACTORS AND HEALTH OUTCOMES TO MEASURE |

Demographic 1
- Movement from rural to urban; (population density ↑)
- Industrialisation
- Environmental pollution ↑
- Economic growth
- Improved education
- Better housing
- Access to medical services/information
- Access to water, electricity/sanitation
- Communication (technotronics) and diversity of information

Cultural and lifestyle
- Acculturation: from mono- to multicultural
- Globalisation/westernisation/"modernisation"
- Societal changes:
- family support networks, values, etc.
- Individual behavioural changes
  Stress exposures
  Smoking, drinking
  Coping mechanisms
  Activity patterns
  Dietary patterns/food sources

Demographic 2
Urban poverty ↑
Crime, violence ↑

- Mortality/morbidity ↓
- Infectious diseases ↓
- Fertility and number of children ↓
- Population ages

Chronic diseases of lifestyle ^

Risk factors for chronic diseases ^

Psychological ill-health

Malnutrition (over & under)

Coexistence of infectious and chronic diseases

"Double burden" of diseases

Demographic profiles
- population (literature:sensus)
- subjects: questionnaires on age, housing, h/h food security, water/electricity/sanitation, h/h composition, income, ownership, education, etc.
Behaviours
- smoking/snuff-taking
- drinking
- HIV-status
- reproductive (questionnaire)
Psychosocio-profiles (questionnaires)
- Symptoms of psychopathology
- Indications of psychological strengths
- Coping strategies
- Perceived stress/social support
- Acculturation
- Individualism - collectivism
Health profile
- Medical history, clinical examination
- Blood, serum, plasma, urine: biochemical analyses
- GTT
- Blood pressure
- Anthropometry
- Dietary intakes
- Activity patterns
- Stress-tests, etc.
- Cardiovascular reactivity

Figure 2.5   Expected health outcomes of urbanisation [Adapted from Vorster et al (2000)]. GTT = glucose tolerance test; h/h = household; ↑ = increase; ↓ = decline

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