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Review

Nutrition and hemostasis: A focus on urbanization in South Africa

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South Africa is experiencing a rapid urbanization of its African population characterized by a demographic, nutrition, lifestyle, and health transition. The resultant high prevalence of high cardiovascular disease, in particular of stroke, is of concern. In this narrative review it is suggested that, together with hypertension, changes in the hemostatic system may be one of the major contributors to stroke in this population. It is further suggested that these changes are related to increased fat and animal protein intakes, decreased intakes of total carbohydrate and dietary fiber, as well as persistent suboptimal micronutrient intakes of Africans in transition. The effects of this nutrition transition on plasma fibrinogen, fibrin network structures, plasminogen activator inhibitor 1 activity levels and some other clotting and fibrinolytic factors are discussed. It is concluded that despite indications of present protective mechanisms against the development of coronary heart disease (CHD) in this population the observed changes in diet and hemostatic profiles may eventually lead to a high prevalence of both stroke and CHD in urban black South Africans. It is further suggested that timely nutritional interventions and research of effects thereof on the hemostatic system are urgently needed.

Keywords: Fibrinogen / Nutrition transition / PAI-1 / South Africa / Urbanization

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1 Introduction

South Africa is experiencing a process of rapid and continuous urbanization and modernization of Africans from rural communities. This process is characterized by a demographic and health transition that is marked by circumstances and behaviors leading to a double burden of disease: poverty and undernutrition-related infectious diseases as well as lifestyle and overnutrition-related non-communicable diseases (NCDs) [1]. The overall burden of cardiovascular disease (CVD) is predicted to rise by approximately 150% in developing countries in the next 20 years [2]. In Africa alone it is predicted to affect 1.3 million people yearly. It seems however, that stroke rather than ischemic heart disease, is a unique feature of the health transition associated with urbanization of black South Africans. Already in 1984 – 1986, mortality rates from CVD indicated that in urban black South Africans, stroke had the highest mortality rate (96.4 *per* 100 000) followed by hypertension, diabetes mellitus and then only ischemic heart disease (13.1 *per* 100 000) [1]. More recently, in 2000, Norman *et al*. [3] showed that the age-standardized mortality rates *per* 100 000 from stroke was double in the African population (145 for men and 160 for women) compared to the white population (72 for men and 84 for women).

Recognized NCD risk factors that have been shown to be affected by different stages of urbanization in the Transition and Health during Urbanization in South Africans (THUSA) study, include increases in hypertension, obesity, smoking habit, and hyperfibrinogenemia [1]. Despite the increasing presence of these risk factors, black South Africans have a favorable serum lipid profile with lower total cholesterol (TC) and higher HDL-cholesterol (HDL-C) levels than other ethnic groups in South Africa [1]. Serum TC levels, however increase in the most affluent (Westernized) Africans [1]. Black South Africans seem furthermore to have genetically determined low homocysteine levels [4]. Changes in dietary intakes during urbanization are considered to play a prominent role in the observed increase in NCD risk factors [5]. Results from the THUSA study indicated that with urbanization there was a reduction in intake of the carbohydrate rich staple food (maize porridge) and

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Abbreviations: CVD, cardiovascular disease; **NCD,** noncommunicable disease; **PAI,** plasminogen activator inhibitor; **TC,** total cholesterol

an increase in intake of animal-derived foods and added fats/oils [5]. Micronutrient status seemed to improve in the most affluent urban group, although optimal recommended intakes for calcium, iron, and ascorbic acid were not met, probably because the total fruit and vegetable intake was still below the recommended minimum level of 400 g/day [6].

Apart from the evidence of urbanization and dietary changes on fibrinogen [7], there is a scarcity of information regarding the effect of urbanization on any other hemostatic markers. In fact only a limited number of studies have investigated the hemostatic profile of black South Africans, let alone investigating the effect of urbanization. The focus of this review is to present the data available on the hemostatic profile (coagulation and fibrinolytic proteins) of black South Africans and to discuss this in the light of urbanization to show a possible link between dietary changes and the increased risk of CVD, especially stroke in Africans in transition.

2 Hemostatic profile of black South Africans

2.1 Fibrinogen

The most evidence by far exist for fibrinogen and plasminogen activator inhibitor-1 activity (PAI-1_{act}), both of which are considered to be recognized CVD risk markers [8]. Table 1 presents the fibrinogen and PAI-1_{act} levels of different groups of black South Africans obtained from different studies. The study subjects were divided into a rural group (deep rural areas and farm workers), a group in transition (who live in low-income areas surrounding cities) and an urban/Westernized group of mainly professionals, business people, and politicians.

The table shows that there is an increase in fibrinogen concentration with urbanization, to levels higher than the level of 2.8 – 3.0 g/L, thought to be already associated with an increased CVD risk (Table 1) [1]. The women in all levels of urbanization have higher fibrinogen values than the men. Mean values for both men and women in all groups were above 2.5 g/L, the value usually regarded as the concentration associated with a low risk of CVD [9], indicating relatively high levels of fibrinogen for black South Africans. It is clear that these higher levels are already present at an early age as both boys and girls (average age of 15 years) already presented with these higher levels (Table 1). Similar higher fibrinogen levels were also found in the ARIC study which indicated that African Americans had higher fibrinogen levels than Caucasians [10].

2.2 PAI-1

Very low PAI-1_{act} levels was found in a rural group of Vendas, one of the African tribes in South Africa [11] compared to the group in transition or the urbanized group. Unfortunately there is no other data available on rural black South Africans to support these findings. Despite increases in PAI-1_{act} levels with urbanization, the levels for the urbanized group are still within the normal reference range. The relatively high PAI-1_{act} levels that is reported for the group in transition [12], was measured in a much older population with an average BMI over 30 making direct comparisons with the other studies difficult. As can be seen from the urbanized group, the obese subdivision (BMI > 30) also had higher PAI-1_{act} levels than the normal weight group, indicating a possible association with obesity. In comparison with Caucasian women, the PAI-1_{act} levels of both the obese and diagnosed metabolic syndrome African women were much lower and still within the normal range, indicating a possible ethnic genetic influence [13]. The PAI-1_{act} levels of teenage black South Africans were low for both boys and girls but a clear gender difference were observed, with girls having PAI-1_{act} levels five times higher than those of the boys.

2.3 Other hemostatic factors

Much less information is available for the other hemostatic factors. Adelstein *et al*. [14] compared the hemostatic profile of black and Caucasian diabetic patients with nondiabetic subjects. The female Caucasian diabetic patients had significantly inhibited antithrombin III function and raised factor VII and factor V levels compared to the black diabetic women. In contrast, black diabetic patients had higher functional antithrombin III levels than the black non-diabetic subjects. Vermaak *et al*. [15] compared black and Caucasian subjects who had been exposed to the same environment and western diet for at least 2 years and found that factor VII was 26.6% lower in adult black Africans compared to the Caucasians. Van Wyk *et al*. [16] determined the hemostatic profile of San (Bushmen) who were relocated from Namibia to South Africa. They determined activated partial thromboplastin time, prothrombin time, thrombin time, fibrinogen (Table 1), and coagulation factors V, VII, VIII, IX, X, XI, and XII. They found that almost all the hemostatic variables were statistically significantly lower than those of a Western population reference group, except for fibrinogen. Vorster *et al*. [17] reported fibrinogen, prothrombin, prothrombin time, partial thromboplastin time, thrombin time, factor V, VII, VIII, IX, X, XI, and XII, antithrombin III and plasminogen of a group of black farm workers following a traditional low-fat, low-cholesterol diet, and reported that the hemostatic factors were within normal ranges. Nienaber [18] subdivided a group of 117 black girls and 78 boys, in transition, into subdivisions for gender, physical activity, fat percentage and height for age (indication of stunting). She found significant gender differences for PAI-1_{act} levels (Table 1) despite adjustment for fat percentage and physical activity. Fibrinogen was increased in both the stunted group (indication of long-

Table 1. Fibrinogen and PAI-1_{act} levels, from different studies, for black South Africans, divided demographically into rural, in-transition, and urban

Reference	Subject characteristics	Age (years)	Rural	Transition	Urban
Fibrinogen (2.43–3.23 g/L)[a]		mean (std)	mean (std)	mean (std)	mean (std)
[7]	Female (n = 201)	35–44.9	3.38 (0.87)	3.69 (1.25)	3.97 (0.81)
	Male (n = 111)	35–44.9	2.91(0.93)	3.7 (1.23)	3.64 (1.03)
[13]	Female (n = 95)	30.5 (8.17)			3.86 (1.1))
[78]	Male and female – diabetic subjects (n = 20)	53.0 (8.29)		4.25 (0.80)	
	Male and female – nondiabetic subjects (n = 18)	52.9 (7.13)		4.02 (0.86)	
[17]	Male (n = 25)	28.1 (7.0)	2.79 (0.53)		
[11]	Male (n = 17)	19.3 (1.31)	2.55 (0.38)		
[79]	Male (n = 45)	45–54		2.72 (1.04)	
	Female (n = 54)	45–54		3.13 (0.89)	
[18]	Boys (n = 77)	15.9 (1.38)		2.59 (0.47)	
	Girls (n = 116)	15.5 (1.32)		2.80 (0.49)	
[80]	Rural blacks (n = 156)	19.4 (2.2);	3.12 (0.65)		
	Urban blacks (n = 102)	18.6 (1.9)			3.26 (0.81)
[16]	San male and female (n = 95)	30 (12)		4.2 (1.4)	
[14]	Black diabetic subjects (n = 33)	40–65		3.34 (1.03)	
	Nondiabetic subjects (n = 19)	17–33		3.15 (0.76)	
PAI-1_{act} (2.6–13.2 U/mL)		mean (std)	median (25th; 75th percentiles)		
[13]	Female (n = 95)	30.5 (8.17)			5.2 (2.3; 7.9)
	Female (BMI > 30 kg/m^2; n = 33)	33.15 (8.15)			6.67 (4.63; 9.84)
	Female (BMI < 25 kg/m^2; n = 39)	28.5 (7.50)			4.73 (1.36; 6.88)
	Female (diagnosed metabolic syndrome, n = 15)	33.1 (7.15)			6.77(5.42; 13.8)
	Female (without any markers for Metabolic syndrome, n = 19)	27.0 (6.23)			4.14 (1.36; 7.81)
[12]	Male and female – diabetic subjects (n = 20)	53.0 (8.29)		16.4 (9.34–19.6)	
	Male and female – nondiabetic subjects (n = 18)	52.9 (7.13)		14.6 (13.6–20.1)	
[11]	Male (n = 17)	19.3 (1.31)	0.80 (0.00–5.4)		
[18]	Boys (n = 77)	15.9 (1.38)		0.68 (0.00; 3.03)	
	Girls (n = 116)	15.5 (1.32)		3.45 (0.98; 5.65)	

a) Reference values given for a healthy population by the manufacturers of the test procedure.

term, chronic undernutrition) as well as in the overfat group (body fat percentage of >20% for boys and >25% for girls). Thrombin–antithrombin complex was significantly higher in girls than in boys, but after separate adjustment for physical activity and fat percentage the difference disappeared. Factor VIIIc showed no differences for any of the subdivisions. Her results indicated that these hemostatic factors are likely to be modifiable through behavioral changes and optimal nutrition status throughout early life.

2.4 Fibrin network structure

Apart from investigating hemostatic protein concentration and activity levels, our group has also been interested in the structure of the fibrin network that forms when fibrinogen is activated. Fibrin network structure can vary, and specific structure types are considered to contribute to increased CVD risk. In general, fibrin clots with thinner fibers, more branch points, and smaller intrinsic pores are more dense and resistant to lysis, and are associated with atherothrombotic risk [19]. Malan [20] compared the fibrin network structures of gynoid and android obese black South African women with those of normal weight black South African women. There were differences in the fibrin network structures between the normal weight and the obese women, despite there being no differences in the fibrinogen concentration, one of the most important factors influencing fibrin network structure. Fibrin network clots of the normal weight women were more permeable than those of the obese women, significantly so for the gynoid obese group. In agreement with this, the fibrin fibers of the normal weight women were thicker than those of the obese women. Clots made of thicker fibers generally have larger pore sizes making the clots more permeable. Pieters *et al*. [12] compared the fibrin network structure of black South African diabetic patients with a black nondiabetic reference group

and found no differences in permeability, compaction, or kinetics of clot formation. Other groups, however, found in general that clots formed from diabetic patients were denser, with thinner fibers and less porous than those formed from healthy individuals [21 – 23]. This discrepancy in findings may be explained by the fact that both the diabetic and nondiabetic group in the study of Pieters *et al*. [12] had high fibrinogen concentrations (4.25 d/L ± 0.80 and 4.02 d/L ± 0.86) which possibly overshadowed the effect of diabetes and the resultant glycation of fibrinogen. The clots of the diabetic subjects were, however, lysed by tissue plasminogen activator at a significantly slower rate than those of the nondiabetic subjects (unpublished results).

3 Discussion

3.1 Dietary changes

Urbanization is associated with an increased risk for NCDs, which is in part attributed to dietary changes [5]. These changes include increases in fat, animal protein, and some micronutrient intakes and decreases in intakes of plant protein, total carbohydrate, and dietary fiber from cereals and grains [6]. The effect of these dietary changes on the hemostatic profile is, however, not clear. This review aims to discuss possible links between the changing diet and the hemostatic profile of black South Africans during urbanization.

3.2 Fibrinogen

Fibrinogen levels seem to increase with urbanization. Fibrinogen concentration is determined by many demographic, environmental, dietary as well as genetic factors [9, 24]. It is suggested that 30 – 50% of the plasma fibrinogen level is genetically determined [24]; this is also evident from the high fibrinogen concentrations observed in almost all the studies reported on black South Africans (Table 1) despite differences in demographic location. Fibrinogen is also affected by several drugs (such as fibrates, statins, anti-inflammatory drugs, aspirin, and vasodilators), age, smoking, alcohol consumption, body mass, gender, physical activity, and season [25]. Although dietary components have been shown to affect fibrinogen concentration, the effect seems to be modest. The relationships of dietary fat content and type with hemostatic factors have received more attention than those of other nutrients. Some studies have also investigated energy intake, fiber content, vitamins, tea, extruded dry beans, onions, fish oil, garlic, parsley, vegetarian diet, and eggs [9, 17, 24, 26 – 33]. Results from the THUSA study indicated that lower plasma fibrinogen levels were associated with dietary intakes compatible with prudent dietary guidelines (low intakes of animal protein; *trans* fatty acids and higher intakes of plant protein, dietary fiber, vitamin E, and iron and a high dietary polyunsaturated to saturated fatty acid ratio). In conjunction with this, both under and overnutrition were found to be associated with high plasma fibrinogen [7]. The results of Nienaber [18] are in agreement with these findings, reporting increased fibrinogen levels for both stunted (undernourished) and overfat black South African teenagers. The relationship between increased fibrinogen and undernutrition in fetal life, infancy, and early childhood is not new and is thought to be caused by impaired liver development during critical early periods of life [34]. On the other hand the relationship with overnutrition and fibrinogen can be seen in the associations of increased fibrinogen with NCDs such as obesity, metabolic syndrome, diabetes, and CVD. Fibrinogen is an established risk marker for CVD [35]. Fibrinogen levels have been shown to be increased in diabetes [36], and an independent association between insulin and fibrinogen has been established [37]. Fibrinogen levels are furthermore considered to be determined by obesity *per se* [38]. Previous work from our laboratory indicated that in patients diagnosed with the metabolic syndrome, fibrinogen clustered with body mass markers (waist circumference and BMI) and other acute phase proteins such as C-reactive protein (CRP) [39]. This relationship may be explained in that excess body fat may result in the development of an inflammatory state as a consequence of excessive cytokine secretion such as, IL-1 and -6 and tumor necrosis factor α and β, by adipose tissue. These cytokines act as primary stimulators of the production of acute phase proteins (including fibrinogen) by the liver [40].

It seems therefore that while the direct effects of the diet on fibrinogen concentration may be modest, dietary changes resulting in the development of NCDs such as obesity, insulin resistance and diabetes may have a more pronounced effect. This explains, in part, the increased fibrinogen levels observed in black South Africans during urbanization.

3.3 Fibrin network structure

Due to the central role fibrinogen plays in the hemostatic system, the structure of the fibrin network has also received attention and is now considered to have the potential to increase CVD risk when abnormal. Altered fibrin network architecture has been observed in patients with premature coronary artery disease [41], myocardial infarction [42], and diabetes mellitus [22, 23, 43] as well as in obesity [20]. The effect of diet on the fibrin network structure is not clear as only a few studies have investigated this. Pectin, a dietary fiber found in some fruit and vegetables, was shown to increase the permeability and lysability of the fibrin network and to decrease tensile strength of the fibrin fibers [28, 44]. Palm oil, red palm oil, and sunflower oil had no independent effect on fibrin network structure [27]. A vitamin C supplement was found to increase fibrin network compaction, the latter being an indication of clot rigidity. Clot rigidity is mainly determined by fiber size, the amount

of crosslinking and branch points that form between different fibrin fibers within the network [45].

A study comparing the changes in fibrin network structure between fit and unfit Caucasian men following a physical activity intervention (to exhaustion), found that the fit men formed fibrin network structures that were less resistant to lysis; the unfit men formed fibrin networks that were less permeable and more resistant to lysis, after completion of the exercise intervention [46].

Pieters *et al*. [12] investigated the effect of glycaemic control in uncontrolled type 2 diabetic black South African subjects on the fibrin network architecture. Due to the presence of continuous high blood glucose in the uncontrolled diabetic patients, the fibrinogen molecules in the diabetic patients became significantly glycated compared to those in nondiabetic patients. Achievement of glycaemic control resulted in a significant reduction in fibrinogen glycation. When investigating fibrin network architecture in a plasma model, no differences in architecture were observed with glycaemic control, despite the reduction in fibrinogen glycation. However, when fibrinogen was purified from the plasma of the diabetic patients and a purified fibrinogen model was used to investigate fibrin network architecture, it was found that fibrin network formation kinetics were altered, resulting in clots with increased permeability and faster lysis rates. All of these changes correlated strongly with markers of glycaemic control (unpublished results). The results of these two models illustrate the important point that in most studies, model systems are used to investigate a research question and that different conclusions can be reached, depending on the model that is used. The results obtained by using any model system, might therefore also not be a true representation of actual *in vivo* situations, suggesting that conclusions should always be drawn with great care.

The fibrin network structure of black South Africans, the factors that influence it and the role of urbanization on these structures are complex. Dietary components may have direct effects on fibrin network structure, but dietary changes that result in decreased fibrinogen concentration may have a more pronounced effect as fibrinogen concentration is one of the main kinetic factors affecting fibrin network structure. Furthermore, prevalence of NCDs such as obesity and diabetes (which increases with urbanization) are associated with a more atherogenic fibrin network structure. But altered fibrin network architecture is also associated with coronary artery disease, which is a condition that is rarely seen in black South Africans despite the increase in other NCDs. Therefore, the factors that protect black South Africans at present from the development of coronary artery disease may also have a favorable effect on the fibrin network structure. One such a factor is homocysteine. Hyperhomocysteinemia has been demonstrated to be an independent risk marker for occlusive vascular disease [47]. Homocysteine has also been indicated to have direct effects on fibrin network structure. When fibrin networks were formed from plasma that was incubated with homocysteine, the fibrin network became more compact and more resistant to lysis [48, 49]. Black South Africans have been shown to be protected by genetically low levels of homocysteine due its effective metabolism [4]. Clearly, much more research is needed before conclusions can be drawn regarding the role of fibrin networks in CVD in Africans.

3.4 PAI-1

PAI-1 is one of the main inhibitors of the fibrinolytic process and is therefore considered to be a potential risk factor for CVD. It is also involved in other processes like cell migration and tissue remodeling as well as being a strong acute-phase reactant [50]. PAI-1_{act} levels in black South Africans are low in general but with a tendency to increase with urbanization. Table 1 shows that within the urbanized group there is a further distinction to be made with increased PAI-1_{act} levels in obese and diagnosed metabolic syndrome patients compared to normal weight individuals and subjects without any markers for the metabolic syndrome. Despite these differences, PAI-1_{act} levels were still within the suggested normal range. Elevated PAI-1 concentrations are well established as a core feature of the metabolic syndrome in Caucasians [13, 51 – 54] but it may play a less prominent role in black Africans and African Americans as PAI-1_{act} levels were found to have a much weaker association with metabolic syndrome markers compared to what was seen in Caucasians [13, 55]. Previous studies have also shown lower levels for black South Africans and African Americans compared to Caucasians [13, 56, 57]. In order to explain these differences, the association of PAI-1 with individual components of the metabolic syndrome will be discussed.

3.5 PAI-1 and obesity

PAI-1 is associated with several components including obesity and the abnormal lipid profile [58]. While PAI-1 has consistently been associated with obesity, especially central adiposity, several *in vitro* studies have shown that visceral adipose tissue produces more PAI-1 than subcutaneous adipose tissue [59 – 61]. This might be explained by the larger number of stromal cells in visceral fat. African-American women tend to have less visceral adipose tissue than Caucasian women, despite similar waist circumferences [62], which might explain the lower overall PAI-1_{act} levels, as well as the much weaker association between PAI-1 and measures of obesity. Similar data for black South Africans are not available. PAI-1 is furthermore consistently associated with blood lipids [58, 63] and black South Africans have, in general, a favorable lipid profile with low TC and

high HDL-C [5]. This may further contribute to the low PAI-1_{act} levels observed.

3.6 Genetics of PAI-1

Another possible reason for the general low PAI-1_{act} levels, is the presence of the 4G/5G polymorphism. This is a common single bp insertion/deletion polymorphism in the promoter region of the PAI-1 gene that affects gene transcription [64]. The nature of this polymorphism can be described as a response polymorphism, which implies that the difference in PAI-1 levels between 4G and 5G becomes more obvious in the presence of disease and/or environmental factors [58]. The 4G/5G polymorphism has been shown to be associated with plasma PAI-1 levels. In general, the highest PAI-1 levels are observed for the 4G-allele [64, 65], although the influence of this polymorphism on plasma PAI-1 levels is considered to be only moderate. In African Americans, the 4G-allele is less common than in Caucasians; African Americans have a higher prevalence of the 5G-allele [57, 66, 67]. The only evidence form Africans is from a small case-control study performed in South African Zulu women in which the prevalence of the 5G-allele was even higher than generally observed in African Americans [68]. The likelihood of the higher prevalence of the 5G-allele might therefore be another explanation for the observed low PAI-1_{act} levels. Furthermore, prospective studies have indicated that the 4G allele has a protective effect against stroke [69 – 71], although the evidence from case-control studies, is not conclusive [72]. This may in part explain the high prevalence of stroke, rather than coronary artery disease, observed in the black South African population. A large prospective epidemiological study (PURE – Prospective Urban and Rural Epidemiological Study) is currently underway in which the prevalence of the 4G/5G genotype and PAI-1_{act} levels will be investigated in a large number of urban and rural black South African volunteers in order to provide data on Africans.

3.7 Diet and PAI-1

Apart from the above-mentioned associations of PAI-1 with metabolic markers, dietary factors have also been shown to influence PAI-1_{act} levels. Nutrients that have received the most attention are n-3 fatty acids and alcohol. The effect of n-3 fatty acids on PAI-1_{act} levels is not clear as intervention trials produced conflicting results. In general it seems as if n-3 fatty acids may increase PAI-1 but the effects are modest and depend on the type of fat [58]. Epidemiological studies seem to indicate that light to moderate drinking is associated with favorable coagulation and fibrinolytic profiles and that heavy or binge drinking is associated with lower fibrinolytic capacity with increases in PAI-1 [73]. Experimental studies seem to indicate however, that the short-term ingestion of alcohol leads to the temporary inhibition of the fibrinolytic system through a rise in circulating PAI-1 levels [73]. As PAI-1 is an acute phase protein, antioxidants may reduce PAI-1 through attenuation of the response to infection. Cross-sectional data on vitamin C and PAI-1 indicated an inverse association between serum ascorbate and PAI-1 [74] but an intervention trial showed no changes in PAI-1_{act} levels following an 8 wk ingestion of 500 mg vitamin C [26]. Other studies included the effect of tea which found no effect on PAI-1_{act} levels [75]. While red palm oil, palm oil, and sunflower oil also had no effects on PAI-1_{act} levels [27], both fish oil and olive oil were found to increase PAI-1_{act} levels [76] and extruded dry beans significantly decreased PAI-1_{act} levels [31].

Urbanization and the accompanying increase in NCDs seem to result in a modest increase in PAI-1_{act} levels although not nearly to the same extent as observed in Caucasians. Dietary changes that result in worsening of the lipid profile, as observed in the urbanized black South Africans, may contribute to this increase. It is speculated that PAI-1 levels in black South Africans are strongly regulated by genetic factors, although this remains to be proven.

4 Conclusion

In conclusion it seems that the dietary changes associated with urbanization, and the resultant increase in NCDs, may have a negative effect on the hemostatic profile of black South Africans. These negative effects can already be seen at a young age. If addressed in time, it is possibly modifiable through behavior changes. It is also evident that other factors, apart from the diet, such as genetic composition, play an important role in the determination of hemostatic protein concentration and activity. In addition, the black South African population also has protective mechanisms that could have a beneficial effect on the hemostatic profile, such as a favorable lipid profile and low homocysteine levels. It could however, be that with more urban black South Africans exposed to affluence and Western lifestyles over longer periods, dyslipidemia, and obesity may increase to such an extent that these protective mechanisms are no longer effective. This phenomenon of a shift in CVD during transition from stroke to CHD has already been observed in the INTERHEART Study [77] which reported an increasing prevalence of myocardial infarction in urban black South Africans.

The authors have declared no conflict of interest.

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