

# CHAPTER IV

## DYSLIPIDAEMIA IN SOUTH AFRICA

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### INTRODUCTION

This epidemiological review will consist of three parts: (a) a historical account of work done in this field; (b) recommendations for further research; and (c) recommendations for combatting the problem in this country. The review will be as much concerned with coronary heart disease (CHD) as with dyslipidaemia because the latter is mainly a risk factor for coronary-related disease in particular rather than vascular disorders in general. Especially noteworthy in this regard is the lack of a relationship between dyslipidaemia and cerebrovascular disease and stroke.<sup>1</sup>

### History of lipid research in South Africa

Available information is not ideal. We do not have comprehensive lipid profiles in adequate numbers of males and females of all ages in all the population groups and performed simultaneously at regular intervals using standardised methodology. Groups have commonly not been stratified socio-economically and most studies have been done on urban rather than rural dwellers. There is a similar lack of information on CHD morbidity and mortality in this country.

The information is more or less in chronological order, beginning in 1946 after World War II. There appears to have been little work of note in this field before then.

We do not know when the CHD epidemic began in the white and Indian populations, but the disease was probably already common among them at the middle of this century. On the other hand, we can be certain that occlusive atherosclerosis of the coronary arteries and CHD were very rare among blacks at that time. Coloureds appeared to occupy an intermediate position. This pattern was based on evidence from clinical and hospital experience,<sup>2,3</sup> electrocardiographic studies,<sup>4</sup> and postmortem observations.<sup>5,6</sup>

It was this pattern which stimulated the first and landmark interracial survey of serum total cholesterol (TC) and diet in this country by Bronte-Stewart, Keys and Brock in Cape Town.<sup>7</sup> Their subjects were middle-aged men and they showed that blacks had a mean TC level of about 4 mmol/l, coloureds 5 mmol/l and whites 6 mmol/l. These levels were closely correlated with the intake of animal fat. Bronte-Stewart was also one of the first workers to demonstrate the adverse effect of cigarette smoking on serum lipids.<sup>8</sup> He showed that smoking depressed levels of  $\alpha$ -cholesterol and raised those of  $\beta$ -cholesterol. These electro-phoretically measured lipid fractions are the respective equivalents of high-density lipoprotein cholesterol (HDLC) and low-density lipoprotein

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cholesterol (LDLC) measured by current techniques.

At about the same time, studies were also under way in Johannesburg. Bersohn and Wayburne showed that mean serum TC levels were virtually identical in newborn black and white babies.<sup>9</sup> Hence differences in adult life were likely to be largely environmental. Walker and Arvidsson<sup>10</sup> found that mean serum TC values of Johannesburg black adults were between 4 and 4,5 mmol/l and that the rise with age was slight. Rural blacks had levels which were about 0,5 mmol/l lower, while in Johannesburg whites the values were 1 - 2 mmol/l higher and rose significantly with age. These variations were broadly correlated with fat intake. Antonis and Bersohn were the first to report triglyceride values.<sup>11</sup> Blacks had a mean level of about 1 mmol/l with no age trend. Whites under the age of 40 years also had a mean value of about 1 mmol/l, but in middle-aged subjects the mean rose to 2 mmol/l. Whites with CHD had a mean level of about 2,5 mmol/l. The fatty acid composition of the serum triglycerides was also analysed. Blacks had significantly greater proportions of dienoic, tetraenoic and hexaenoic fatty acids than whites. Antonis and Bersohn went on to demonstrate in a unique and major experimental study that the differences between blacks and whites with regard to serum triglyceride levels and triglyceride fatty acid composition were diet - and not race-related.<sup>12</sup>

In the 1960s Seftel and co-workers showed that CHD was rare also in aged and diabetic blacks. In a clinical and electrocardiographic survey of 296 blacks aged between 60 and 90 years, only one had evidence of myocardial infarction.<sup>13</sup> In a similar survey of 112 black diabetics, none had evidence of angina or infarction.<sup>14</sup> In both studies the rarity of CHD was associated with low TC levels.

In 1963 Seftel, Keeley and Walker provided the first detailed description of a series of black patients with proven myocardial infarction.<sup>15</sup> The series consisted of 30 patients collected over a period of 11 years (1951 - 1961) at Baragwanath Hospital where the annual number of admissions over this period ranged from 26 000 to 48 000. These early sufferers were considerably westernised and this included habituation to a diet relatively high in animal fat and also raised serum TC and triglyceride levels. In 1970 Seftel, Kew and Bersohn reported on 24 black patients with myocardial infarction admitted to the Johannesburg Non-European Hospital (as it was called at that time).<sup>16</sup> Again they were westernised with raised serum lipid levels, but these 24 patients were seen over the much shorter period of 1965 to 1968 in a much smaller hospital where annual admissions over this period were only about 4000. Taken together these two reports suggested that, not only had CHD emerged in urban blacks, but that it was on the increase. Most clinicians working in large black hospitals today would agree that CHD is being seen with increasing frequency among blacks. However, the urban black population has also increased very considerably in recent decades and unless we know the size of the population at risk we cannot be sure that the incidence is increasing. If it is, the evidence points to dyslipidaemia associated with Western lifestyle as an important causal factor.

In 1967 Du Plessis and co-workers measured TC levels in 808 white and 585 black children aged 7 - 15 years living in the Pretoria area.<sup>17</sup> Mean levels in the blacks were about 4 mmol/l and in the whites between 5 and 5,5 mmol/l.

About a decade later the results of a survey of TC levels in free-living Johannesburg blacks were published.<sup>18</sup> The sample consisted of 499 males and 503 females whose ages ranged from 16 to 59. Mean TC values varied from about 3,5 mmol/l in the younger age groups to 5 mmol/l in the middle-aged group. Levels in a comparable group of USA whites ranged from 4 to 6 mmol/l.

The 1970s were also the decade of the discovery of the high prevalence of familial hypercholesterolaemia (FH) in South Africa. Credit for the discovery must go to Evan Stein who, as a young house physician at the Transvaal Memorial Hospital for Children, observed and documented the characteristics of a large series of FH patients.<sup>19</sup> The condition has since been extensively studied historically, epidemiologically, genetically, clinically, biochemically and

therapeutically. Much of this information has been recently reviewed.<sup>20</sup>

In South Africa FH is not a genetic curiosity, it is an important public health problem. In Afrikaners<sup>21</sup> and Jews<sup>22</sup> the prevalence of FH heterozygotes is about 1 in 70, which is about seven times greater than that in the peoples of Europe and America. The prevalence may be similarly high in South African Indians (H.C. Seftel, unpublished data). Since most FH sufferers die prematurely from CHD these high FH prevalences could help to explain the high CHD mortality in South African whites (60% of whom are Afrikaners) and Indians, especially in the younger age groups, and also why in these age groups Afrikaners have higher CHD death rates than English-speaking whites.<sup>23</sup> Clinically FH was found in as many as 10% of Afrikaners aged under 55 years with myocardial infarction.<sup>24</sup>

In the late 1970s Cyril Wyndham pioneered a new generation of epidemiological studies by carefully and imaginatively analysing death certificate data. In essence he found that the CHD mortality rates for South African whites and Indians were among the highest in the world, that the rates in Indians were even higher than those of whites, that rates for blacks were very low and that rates in coloureds were intermediate between those of whites and blacks.<sup>25-27</sup>

These studies by Wyndham set the stage for the systematic investigation of dyslipidaemia and other CHD risk factors in Cape white rural Afrikaners (CORIS),<sup>28</sup> coloureds in the Cape Peninsula (CRISIC),<sup>29</sup> blacks in the Cape Peninsula (BRISK)<sup>30</sup> and blacks,<sup>31</sup> whites<sup>32</sup> and Indians<sup>33</sup> in Durban. Methodology including population sampling, analysis and presentation of findings were standardised. In summary, important results were as follows:

- The major CHD risk factors - dyslipidaemia, hypertension and smoking - were all very common among the white, coloured and Indian populations, an exception being smoking in black and Indian women.
- Cape Peninsula coloureds had a worse CHD risk factor profile than the Cape rural whites of the CORIS study. This could explain why Cape Peninsula coloureds had a CHD mortality rate in 1970 which was comparable with that of white inhabitants of the Peninsula. That the national CHD mortality rate for coloureds was lower than the Peninsular rate and intermediate between the national rates for whites and blacks presumably reflected the lower rates for coloureds living outside the Peninsula in rural areas and in small towns and villages.
- The bad risk factor profile of Indians was compounded by their very high prevalence of diabetes mellitus. Overall adult prevalence was between 10% and 15%, and in middle age as many as one third or more were diabetic.<sup>33,34</sup> This could explain why South African Indians have even higher CHD mortality rates than the white population.
- Blacks had the most favourable CHD risk factor status. In large measure this was due to their low prevalence of dyslipidaemia and high level of physical activity. Some serum lipid figures are instructive. Mean TC levels in white,<sup>28</sup> coloured,<sup>29</sup> Indian<sup>33</sup> and black<sup>30</sup> males aged 45 - 54 years were 6,39, 6,09, 6,28 and 4,2 mmol/l respectively. Corresponding values in females were 6,62, 6,30, 5,86 and 4,7 mmol/l. HDLC values tended to be higher in blacks and coloureds than in whites and Indians. More noteworthy, a HDLC/TC ratio protective against CHD (defined as HDLC/TC > 20%) was almost universal in blacks. For example, 96% of black males<sup>30</sup> had a protective ratio compared with about 75% of coloured males<sup>29</sup> and only 56% of Indian men.<sup>33</sup> While the CHD risk factor status of blacks was better than that of the other groups, it was by no means ideal. Cause for concern was the considerable prevalence of hypertension in both genders and the high prevalence of smoking in men.
- The CORIS investigators not only measured serum lipid levels in 7188 males and females aged 15 - 64 years but also took the opportunity of determining TC levels in 575 1- and 2-year-olds.<sup>35</sup> Based on these and other findings they defined desirable TC levels and criteria for the investigation of FH in males and females of all age groups ranging from 1 - 2 years to 55 - 64

years. In another subsample of 655 men and 731 women the CORIS workers analysed in detail the relationship between alcohol intake and serum lipids.<sup>36</sup> They showed that habitual alcohol intake was significantly related to higher levels of HDLC in both men and women. In men both HDL<sub>2</sub>C and HDL<sub>3</sub>C levels rose, but in women the rise was mostly in HDL<sub>2</sub>C.

- In a post-survey analysis the CRISIC investigators showed that only about 30% of the Cape Peninsula coloured population consumed a prudent diet.<sup>37</sup> In this population they also assessed the contribution of a number of variables to TC levels, including the saturated and polyunsaturated fat intakes, the polyunsaturated/saturated fat ratio, the cholesterol intake, the body mass index, age and socio-economic status.

In the 1990s the first survey of a variety of CHD risk factors was undertaken in 859 South African male scholars aged 15 - 20 years who were representative of the major population groups both ethnically and socio-economically.<sup>38</sup> The subjects comprised urban and rural blacks, Indians of higher and lower socio-economic status, coloureds of higher and lower socio-economic status, and middle-class whites. Both Indian groups, both coloured groups and the whites had a much greater prevalence and severity of CHD risk factors than the two black groups. This held for TC, LDLC, HDLC, the HDLC/LDL ratio, apolipoprotein B, apolipoprotein A-1, insulin, fibrinogen and body mass. In general, the CHD risk factor profile was worse in the higher socio-economic groups and it also tended to be worse in urban than in rural blacks.

In respect of one CHD risk factor, lipoprotein (a) [Lp(a)], the black scholars were distinctly worse off. Their Lp(a) levels were about 50% higher than those of whites, coloureds and Indians. The reason for this striking difference is probably genetic since Vermaak and co-workers in a study of neonatal cord blood samples showed that Lp(a) levels in blacks were 45% higher than those of whites.<sup>39</sup> This finding highlights the potential of blacks to develop CHD if their overall CHD risk factor profile deteriorates.

#### **Practical implications and consequences of the information collected on dyslipidaemia and CHD in South Africa**

1. These problems are epidemic not only among whites and Indians but also among the metropolitan coloured population. It would also be wise to assume that they have emerged and are increasing among urban blacks.
2. Based on both local and international data, measures to prevent or correct dyslipidaemia have been instituted by a number of agencies. Important in this regard are the consensus guidelines on measuring and managing hypercholesterolaemia drawn up for the medical profession in 1988<sup>40</sup> (the 'Cholesterol Consensus') and the dissemination of this and much other practical advice to both health professionals and lay persons by the Heart Foundation of Southern Africa.
3. Most importantly, all epidemiological studies have stressed the frequency with which dyslipidaemia coexists with other CHD risk factors which therefore mandates a comprehensive approach to prevention in both populations and individuals. Especially noteworthy in this regard is the pioneering and landmark comprehensive intervention study by the CORIS investigators.<sup>41</sup> They demonstrated that CHD risk factors including dyslipidaemia could be reduced in the rural Afrikaner communities studied using a cost-effective media-based health education programme.
4. Investigators have appreciated the need to standardise the laboratory investigation of dyslipidaemia at all three relevant levels, namely pre-analytical (procurement of valid samples for measurement),<sup>42</sup> analytical (accurate and reproducible methods of serum lipid measurement),<sup>43</sup> and post-analytical (interpretation of serum lipid levels including the definition of reference ranges and guidelines for action).<sup>42</sup>

5. Finally, during the last two decades CHD mortality rates have fallen by about 50% in whites, 40% in Indians and 30% in coloureds.<sup>44</sup> This is probably due to a combination of primary prevention, better treatment and secondary prevention of CHD. The relative contributions of these three components in South Africa is unknown but it is likely, as in other countries where CHD mortality has fallen, that preventive measures have played an important role. This must, in part at least, be a consequence of the work and efforts outlined in the review but the problem of CHD, both actual and potential, remains formidable and there is no place for complacency. Thus, CHD mortality rates for Asians are still probably the highest in the world and those for whites remain among the highest.<sup>44</sup>

### **Recommendations for further research on dyslipidaemia in South Africa**

In the context of combatting CHD, the major chronic disease of lifestyle associated with dyslipidaemia, some would argue that little further research is necessary. They would say that with our current knowledge of the prevalence and severity of dyslipidaemia in South Africa taken together with what we already know about other CHD risk factors - hypertension, smoking, diabetes, obesity, physical inactivity and heredity - we can largely explain the prevalence of CHD in our different populations and take the necessary preventive measures. For example, most if not all the risk factors are common in the populations with high CHD prevalence (namely whites, Indians and metropolitan coloureds), and that the probable reason the disorder is commonest in Indians is their very high frequency of diabetes. The latter problem in Indians taken together with an unduly high prevalence of FH in Afrikaners, Jews and Indians could also help to explain the high frequency of CHD in relatively young whites and Indians. On the other hand, CHD is uncommon in blacks because, despite their high prevalence of hypertension, smoking, obesity and perhaps diabetes, they are protected by their favourable lipid profile and a relatively high degree of physical activity.

However, others would argue that our knowledge of dyslipidaemia in the different populations is still fragmentary - in time, space, numbers and demography. More data are needed on the current situation in regard not only to dyslipidaemia but also to other CHD risk factors in order to determine priorities for which segments of the population to target for intervention programmes and also to establish baselines to measure the effectiveness of such programmes.

In our view these two standpoints are complementary rather than mutually exclusive and have been overtaken by events. The CHD epidemic remains serious and urgent action to prevent its emergence in developing populations is essential. Intervention programmes of varying scope and degree have been operating for a number of years and what is needed now is action to intensify them and make them more effective. We cannot delay while further research is undertaken. Nor is this necessary considering the respective time scales of intervention and research. Intervention must proceed based on present, albeit incomplete, knowledge and will require decades to impact significantly on our populations. However, research must also proceed and its results should emerge over the shorter time scale of years to influence and refine the longer-term preventive strategies. Just as we need intervention priorities, so we need research priorities in keeping with available resources.

### **Research recommendations**

- We need more surveys of lipid and other CHD risk factors in urban and rural communities, not only among blacks but also among other ethnic groups. As noted in the preceding section, CHD mortality rates appear to be substantially higher among metropolitan coloureds than among their rural counterparts. Among whites the converse may be the case.
- Future surveys should ideally involve not only rural and city dwellers but also intermediate communities in regional towns, small towns and villages and the informal or squatter areas whose inhabitants are currently estimated to number about 7 million.

- All age groups should be studied with stress on youth. Among other reasons, information on young people is needed to plan and motivate proper health education curricula in our schools.
- Perhaps most importantly, we must survey populations stratified socio-economically, e.g. manual labourers, artisans, clerical workers, managers, executives and professionals in both the private and public sectors. We know that socio-economic status influences CHD and its risk factors considerably, and is also highly relevant in planning intervention programmes. In Western countries CHD mortality and CHD risk factors are worse in the lower than in the higher socio-economic strata of the population, but in South Africa the converse may hold.<sup>38</sup> A particular priority for research is our black middle class who appear to be the main potential victims of CHD in the black community.
- With regard to dyslipidaemia it would be desirable to measure not only the standard lipids - TC, LDLC and HDLC - but also other lipoproteins which may be related to the development of CHD such as Lp(a), apo E phenotypes, LDL subfractions and oxidised LDL.
- Practically, with a view to comprehensive and meaningful intervention, surveys of dyslipidaemia must be co-ordinated and integrated with those of the other CHD risk factors which so commonly coexist with dyslipidaemia. This will demonstrate how substantially the impact of dyslipidaemia on CHD is modulated by coexisting risk factors. It will stress the principle that when dyslipidaemia coexists with other risk factors the risk of CHD rises geometrically or multiplicatively rather than additively. Conversely, correction of multiple risk factors may confer benefit which is multiplicative rather than additive. Most CHD occurs in people with multiple mild or moderate risk factors and reduction of overall risk is the best tactic for preventing the disorder.

In brief, the objectives of further research must be to consolidate and refine existing knowledge and thereby enhance the effectiveness and efficiency of intervention strategies in our different populations.

### **Combatting dyslipidaemia in South Africa**

If the foregoing review premises and recommendations are accepted, our immediate task is to devise and implement better preventive programmes along the lines suggested below. This will involve assembling teams consisting of many agents and agencies. In particular we need an update of the 1988 'Cholesterol Consensus'. But this must also be expanded since the 'Cholesterol Consensus' was largely directed at doctors and patients rather than at populations. The advantage of doing this now is that we can make use of the extensive experience of intervention programmes in other countries. These have been comprehensively reviewed in two recent publications from Europe<sup>45</sup> and the USA<sup>46</sup>.

### **Strategies for combatting dyslipidaemia**

These must be pursued within a comprehensive framework directed at combatting all CHD risk factors. This involves three levels of prevention: *primordial* prevention aimed at preventing the emergence of dyslipidaemia, especially by actions taken in childhood, and particularly relevant to developing populations in whom CHD is still uncommon; *primary* prevention aimed at reducing the present load of dyslipidaemia in order to reduce the incidence of first clinical events; and *secondary* prevention aimed at reducing dyslipidaemia and hence CHD recurrences after the first event. In accordance with conventional practice all three forms of prevention are directed at both populations and individuals.

## Population strategies

It is now generally agreed that the population approach is by far the most cost-effective, and this certainly applies to South Africa where resources are limited and there are so many other lifestyle-related and environmental disorders.

The basis of population strategies is that dyslipidaemia is pandemic and that most CHD occurs in the many people who have mildly or moderately disturbed lipid levels rather than in the few with marked abnormalities. Population strategies need effect only small changes in lipid levels ('a small step to the left' of the distribution curve) to produce a large reduction in CHD. Thus, in developed populations Law, Wald and Thompson have recently estimated from an extensive meta-analysis that a 10% (0,6 mmol/l) reduction in TC can produce a reduction in CHD of 50% at age 40, 40% at age 50, 30% at age 60 and 20% at age 70.<sup>47</sup> They state that the benefit can be realised within 5 years, and that the 10% TC reduction is achievable with a realistic dietary change of reducing total dietary fat from about 42% to 35% of total calories or reducing saturated fat from 20% to 13%.

Comprehensive population strategies have two components. First is a general one aimed at improving the bad psychosocial, economic and political environment which is not only the main generator of risk factors and vulnerable victims, but which also inhibits corrective action by all health agencies. Second are the specific lifestyle measures capable of reducing the prevalence and severity of dyslipidaemia and other CHD risk factors, such as a diet appropriate in energy and nutrient composition, moderate alcohol consumption for those who wish to drink, no smoking - active or passive, stress management and moderate regular aerobic isotonic exercise. These lifestyle measures can be attractively and succinctly presented as the 'Cardiovascular Health Charter' and widely and continuously disseminated to all our population groups. Stress must be placed on the principle of multiplicative risk and benefit.

Population strategies are cost-effective but not cheap. They require considerable, sustained and imaginative efforts by many agencies including central and local health authorities, all health professionals and their organisations, voluntary and welfare bodies, the media and, above all, schools and training institutions which must teach a compulsory, examination subject called the 'Science of Living'. A major priority must be devising a meaningful curriculum for such a subject. All agencies must deliver the same message in forms appropriate to our different populations. Legislation is essential to ensure the implementation of comprehensive population strategies and includes regulating the activities and behaviour of the tobacco, liquor and food industries. This includes laws on taxation, advertising, labelling of contents, and, in the case of smoking, banning it in public places.

Population strategies do *not* include mass screening for dyslipidaemia, which is markedly cost-ineffective. This is now generally accepted in affluent Western populations<sup>48-50</sup> and certainly applies in this country.

## Individual strategies

Essential for their success is a system in which all cardiovascular risk factors are not only properly assessed and scored (e.g. using a risk-disk<sup>51</sup>) but also in which intervention and sustained follow-up is provided. In general, the most practicable and cost-effective way of doing this is by selective casefinding or opportunistic screening by health workers such as doctors and nurses who have regular contact with substantial numbers of individuals at risk in the population and who are then able to intervene and follow-up, i.e. "the health worker who screens is the health worker who treats". In this way compliance is maximized and by spreading the strategy over time the impact on clinical work load as well as on laboratory resources and costs is minimized. Management of risk is first and forever by lifestyle modification. If medicines are used lifestyle measures must continue.

While the principles of individual intervention are plain, the important and difficult question must be asked of how we implement them in this country. This applies to risk factor management generally but is especially problematic with regard to dyslipidaemia. In particular who should be screened for dyslipidaemia, which lipid fractions should be measured and how should it be managed? The issues are many, diverse and controversial even if we confine ourselves largely to TC, the lipid fraction which is most relevant clinically to CHD and about which we have most information:

- As already stressed, raised or undesirable TC levels are pandemic with up to 80% of the adults in our developed populations affected.<sup>40</sup>
- There is variation in the accuracy and reproducibility of TC assays<sup>43</sup> and this is more marked for other lipid measurements.
- As a screening test for CHD, TC lacks both sensitivity and specificity - 38% and 75% respectively according to Framingham data.<sup>48</sup>
- Cholesterol testing generates many problems including anxiety, complacency in screenees with apparently normal results, high costs and much inconvenience. These stem from the initial cholesterol tests, repeat cholesterol tests and lipograms, especially those which include clinically irrelevant or meaningless lipid measurements, other tests of liver, kidney and thyroid function to exclude secondary causes of hypercholesterolaemia, the creation of patients for life, referral of patients for expensive cardiological investigations, and prescription of costly medications with long-term follow-up and monitoring.
- As indicated at the beginning, TC is a risk factor for CHD but for not much else. By contrast, smoking is bad for cardiac, cerebral and peripheral arteries and also for the aorta.
- We must also again stress that the impact of TC as a risk factor for CHD is overwhelmingly modulated by the other risk factors with which it commonly coexists. The extent of this modulation in the UK has been graphically described by Tunstall-Pedoe and Smith<sup>52</sup>. Considering TC, hypertension and smoking for CHD risk ranking, use of a "dummy cholesterol reading, instead of the actual reading, leads to only a third of men or women moving more than one decile of risk from where they would have been had the reading been available." In South Africa we know that both FH heterozygotes and homozygotes with very high TC levels can live for long periods if they do not have other risk factors such as smoking or hypertension (H.C. Seftel - unpublished observations).
- While selective casefinding or opportunistic screening and management is the most cost-effective strategy for individuals it, like the population approach, is not cheap. If properly done it requires a considerable investment in time, effort, expertise and resources on the part of both interventionist and patient. This applies even if only lifestyle intervention is undertaken.
- As far as intervention with expensive cholesterol-lowering drugs is concerned, it is now generally agreed that these are not cost-effective except in high-risk patients. Various meta-analyses of randomised controlled trials have indicated that while cholesterol-lowering drugs reduce coronary mortality this may be offset by increased mortality, from other causes so that there is no overall effect on total mortality.<sup>49</sup> In fact the reduction in coronary mortality observed in these trials is small. Yudkin has calculated that in non-diabetic men a 10-year mortality from CHD of 14,4 per 1000 would be reduced by a mean of only 0,82 per 1000 by cholesterol-lowering drugs.<sup>53</sup> By contrast, low-dose aspirin and stopping smoking would be far more effective, reducing CHD mortality by 2,64 and 2,74 per 1000 respectively. Even in high-risk patients the benefit of cholesterol-lowering drugs is not large.<sup>49</sup> This is because the term 'high-risk' is a *relative* description. The *absolute* risk even for middle-aged westernised men with a combination of risk factors is low. For example, in the UK a man of 45 with both hypercholesterolaemia and diabetes has an 83,5% chance of surviving for the next 10 years, and a 92,5% chance of not

dying of CHD in those 10 years.<sup>53</sup>

- Apart from TC and its close correlate LDLC, many other serum lipids have been associated with CHD both genetically and environmentally. However, their clinical or therapeutic relevance is unclear, debatable or negative. The latter applies, for example, to apoproteins A, B and Lp(a), which have little or no place in individual intervention strategies but have appeared on lipogram reports at considerable cost and with questionable accuracy. The case for HDLC is better because apart from being apparently cardioprotective its elevation may occasionally explain a raised TC and also because low levels can be raised by lifestyle measures such as weight reduction, smoking cessation and exercise. On the other hand, it must be stressed that there is no evidence from a specifically designed trial to show that treating initially low levels of HDLC will reduce the risk of CHD. Similar considerations apply to serum triglyceride levels except that hypertriglyceridaemia has not been established as an independent risk factor for CHD. It seems rather to be a marker for the constellation of abnormalities described as the metabolic syndrome and which can also be managed by lifestyle modification.
- Females, who constitute the majority of humanity, are at lesser risk of CHD and the foregoing caveats apply especially strongly to them. Some have proposed that only women at very high risk of CHD should be screened and treated for hypercholesterolaemia.<sup>54</sup> In menopausal women many would give priority to oestrogen replacement therapy which has a variety of beneficial effects including a favourable influence on the serum lipid profile and CHD incidence.

In short, while there is no question that dyslipidaemia is a risk factor for CHD it is only one of many such factors and its cost-effective detection and management in individuals is highly problematic, especially in this country. This is a major reason why we need an update of the 'Cholesterol Consensus'. We cannot simply follow the recent European and American guidelines which involve the screening of large numbers of individuals, the frequent performance of lipograms and prescription of cholesterol-lowering drugs, and the setting of new and lower TC levels for the initiation and goals of treatment.

The central point at issue is the definition of high-risk individuals. Thus, in the European guidelines<sup>45</sup> a high-risk individual is someone who has:

- (a) CHD or peripheral vascular disease (in South Africa about 12 000 individuals die annually from CHD events but about three times as many survive); or
- (b) a single severe risk factor (in South Africa up to 20% of westernised adults have TC levels which put them at high risk<sup>40</sup>); or
- (c) two or more risk factors with *each* of the following being regarded as a risk factor, namely high TC (generally > 5,2 mmol/l), low HDLC (< 1 mmol/l), hypertension, cigarette smoking, diabetes, obesity, high plasma fibrinogen, family history of CHD or peripheral vascular disease, male gender, postmenopausal status in women, and age (> 60 years in men and women).

This definition means that the majority of middle-aged white, coloured and Indian individuals in South Africa would be potential candidates for extensive investigation, treatment and follow-up of dyslipidaemia by health professionals - an obviously impractical and unaffordable situation. We must therefore devise our own guidelines in keeping with available resources and health priorities generally. The details of these should be the task of the 'Cholesterol Consensus' update. Our own general recommendations in the light of this review would stress the need for a meaningful definition of high-risk individuals, restrict initial testing to TC, emphasize the reduction of overall risk by lifestyle measures, and reserve drug therapy at this time for individuals at very high risk.

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