Coronary Artery Disease in South Asians
Second Meeting of the International Working Group
16 March 1997, Anaheim, California

Enas A Enas, Salim Yusuf, Satyavan Sharma
Coronary Artery Disease in Asian Indians (CAD) Research Foundation, Woodridge, IL, USA;
McMaster University, Hamilton, Ontario, Canada, and; the Cardiological Society of India

Introduction

The second meeting of the International Working Group (IWG) on Coronary Artery Disease (CAD) in South Asians (SA) was held at Anaheim, California, USA on 16 March 1997. Twenty-four clinical scientists from India, United Kingdom, United States, Canada, and Singapore participated in the discussions. The participants included: Arun Chockalingam, Viswanath Date, Prakash C Deedwania, Enas A Enas, Kenneth Hughes, Moti Kashyap, Arthur Klatsky, JL Mehta, Freny Vaghaiwalla Mody, Vikram Kamdar, S Padmavati, Narendra M Pai, Ramdas G Pai, Manotosh Panja, Dev B Pahlajani, Thomas Pearson, Vivian Rambihar, Mohammed F Saad, Kamal Sethi, PK Shah, Satyavan Sharma, N Shaukat, GC Sutton, Salim Yusuf. The first meeting of the IWG on CAD in SA held in Orlando Florida, USA in March 1996 concluded that CAD is a major problem among SA and special efforts may be required to prevent an imminent epidemic. It called for developing appropriate preventive strategies for younger populations due to the aggressive nature of early onset of CAD in SA. The goals of this meeting were to:

1. Reassess the magnitude of CAD in SA in various countries
2. Provide a forum for scientists working in this field to present their ideas, data, and future plans
3. Prioritise and coordinate future research
4. Plan future international conferences on this topic
5. Compile a list of ongoing major scientific studies in SA in various countries.

'South Asian' (SA) is the preferred term in the UK and Canada, whereas 'Asian Indian' (AI) is preferred in the US. The term 'Indian' is used in India and Singapore. Therefore, the terms Indian, Asian Indian, and South Asians are used interchangeably in this document.

CAD Among South Asians: International Data

New scientific information, which emerged from various countries after the first meeting, was reviewed in this meet.

Singapore's Data. Prof. Kenneth Hughes presented revealing data from Singapore, which has a population of 3.3 million. About 76 percent of the population are of Chinese origin, 14 percent Malays, seven percent Indians, and three percent are of other ethnic origins. About 80 percent of the Indians in Singapore have their origins in the South Indian states of Tamil Nadu and Kerala, with the remainder from Sri Lanka. A sevenfold higher rate of CAD in Indians than Chinese was first reported in Singapore more than 40 years ago based on an autopsy study of 10 thousand subjects. Subsequent clinical studies showed a fourfold higher rate of myocardial infarction (MI) in Indians. As a result of rapid industrialisation and affluence, CAD rates in this city-state more than doubled in the past 30 years, yet the fourfold higher rate of CAD in Indians persisted. Previous studies found that the increased susceptibility of Indians to CAD could not be explained by the conventional risk factors such as cigarette smoking, hypertension, diabetes, and high low-density lipoprotein cholesterol (LDL-C).

Dr. Hughes presented the results of the National University of Singapore Heart Study, a population-based study of cardiovascular risk factors. The key findings of this study (Table I), which have since been published, are:

1. Indians in Singapore have a higher rate of CAD than Chinese and Malays, but not higher rates of cerebrovascular disease (CBVD). These rates are similar to those of Canadian data but contrast with those from the United Kingdom, where SA have higher rates of both CAD and CBVD.
2. Malays had the highest body mass index (BMI), but Indians had the highest waist-hip ratio, indicating greater central obesity in the latter.

3. Indians had several features of the metabolic syndrome, including higher rates of glucose intolerance and higher fasting levels of insulin, than did Chinese and Malays.

4. Serum high-density lipoprotein (HDL-C) levels in Indians were significantly lower than in Chinese but similar to those in Malays.

5. Serum triglyceride levels were similar among the three ethnic groups.

6. Serum total cholesterol and LDL-C levels were similar, but Apo B levels were higher in Indians than in Chinese.

7. The rates of hypertension and cigarette smoking were similar in all the three groups.

8. The serum levels of plasminogen activating inhibitor (PAI-1), and tissue plasminogen activator (tPA) antigen were higher in Indians. These factors could reduce the rate of fibrinolysis and increase the risk of thrombosis in Indians. However, Indians did not have higher levels of plasma fibrinogen, factor VIIc, and prothrombin F1+2 levels.

9. Indians had higher serum levels of lipoprotein (a) (Lp(a)). Since Lp(a) levels are largely genetically determined, this finding indicates genetic predisposition for CAD in Indians.

10. There were no ethnic differences in plasma levels of vitamins A and E. However Indians had lower plasma vitamin C levels than did Chinese, and lower serum selenium levels than Malays and Chinese. Lower levels of these antioxidants may render Indians more vulnerable to CAD. Indians also had lower serum ferritin levels.

These findings show an excess of several risk factors such as Lp(a), PAI-1, glucose intolerance, and central obesity among Indians in Singapore, compared to Chinese and Malays, which could possibly explain the higher prevalence of CAD in Indians.

**United States' Data.** Dr. Arthur Klatsky presented recent findings on the state of CAD hospitalisation among 207 SA in California, compared to 13,330 other Asian-Americans. Using whites as the reference and Cox proportional hazards models controlled for age, sex, BMI, education, marital status, smoking and alcohol, the relative risks (RR) of CAD hospitalisation by ethnic groups were: Chinese 0.6 (p=0.004), Filipino

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**TABLE 1**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AI</td>
<td>Chinese</td>
<td>p-Value</td>
<td>AI</td>
</tr>
<tr>
<td>Number</td>
<td>170</td>
<td>147</td>
<td>–</td>
<td>172</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.2</td>
<td>23.3</td>
<td>0.03</td>
<td>26.2</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.93</td>
<td>0.90</td>
<td>&lt;0.01</td>
<td>0.84</td>
</tr>
<tr>
<td>Abdominal diameter (cm)</td>
<td>22.7</td>
<td>21.0</td>
<td>&lt;0.01</td>
<td>22.4</td>
</tr>
<tr>
<td>Fasting serum insulin (mU/l)</td>
<td>8.6</td>
<td>6.5</td>
<td>&lt;0.01</td>
<td>9.1</td>
</tr>
<tr>
<td>Glucose intolerance (%)</td>
<td>27.8</td>
<td>11.1</td>
<td>&lt;0.01</td>
<td>20.3</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>130</td>
<td>129</td>
<td>0.35</td>
<td>130</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>82</td>
<td>82</td>
<td>0.55</td>
<td>79</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>20.7</td>
<td>18.0</td>
<td>0.49</td>
<td>19.6</td>
</tr>
<tr>
<td>Serum LDL cholesterol (mg/dl)</td>
<td>155</td>
<td>151</td>
<td>0.17</td>
<td>155</td>
</tr>
<tr>
<td>Serum HDL cholesterol (mg/dl)</td>
<td>28</td>
<td>34</td>
<td>&lt;0.01</td>
<td>34</td>
</tr>
<tr>
<td>Fasting serum triglyceride (mg/dl)</td>
<td>159</td>
<td>142</td>
<td>0.06</td>
<td>133</td>
</tr>
<tr>
<td>Serum apo lipoprotein B (mg/dl)</td>
<td>128</td>
<td>120</td>
<td>0.03</td>
<td>120</td>
</tr>
<tr>
<td>Serum lipoprotein A1 (mg/dl)</td>
<td>127</td>
<td>140</td>
<td>&lt;0.001</td>
<td>138</td>
</tr>
<tr>
<td>Serum lipoprotein (a) (mg/dl)</td>
<td>18.1</td>
<td>12.5</td>
<td>&lt;0.01</td>
<td>22.7</td>
</tr>
<tr>
<td>Plasma PAI-1 (ng/ml)</td>
<td>26.7</td>
<td>21.8</td>
<td>0.01</td>
<td>29.5</td>
</tr>
<tr>
<td>Plasma tPA antigen (ng/ml)</td>
<td>10.3</td>
<td>8.4</td>
<td>&lt;0.01</td>
<td>9.2</td>
</tr>
<tr>
<td>Plasma fibrinogen (gm/l)</td>
<td>2.7</td>
<td>2.6</td>
<td>0.32</td>
<td>3.3</td>
</tr>
<tr>
<td>Plasma factor VIIc (%)</td>
<td>126</td>
<td>128</td>
<td>0.68</td>
<td>139</td>
</tr>
<tr>
<td>Plasma prothrombin F1+2 (nmol/l)</td>
<td>1.5</td>
<td>1.4</td>
<td>0.60</td>
<td>1.7</td>
</tr>
</tbody>
</table>

*Hughes K. J Epidemiol Comm Health 1997; 51: 394-399
Inclusion of total cholesterol, blood glucose, and systolic blood pressure to the percent energy from carbohydrates, 32 percent from fat and eight percent from saturated fat. Leisure-time physical activity averaged 136 minutes per week and correlated directly with HDL-C level. The high rate of CAD in the presence of a low level of risk factors in these highly educated professionals suggests the possible role of a genetic risk factor uninfluenced by even maximum modification of lifestyle. Lp(a) is such a risk factor and was indeed found in a subgroup of these physicians. Lp(a) levels are genetically determined and not influenced by diet or exercise. Its levels are significantly elevated in SA, which indicates a genetic predisposition to CAD in this population.

Although the subjects in the CADI study were not representative of AIs in general, the results suggest that conventional approaches to prevention and treatment of CAD may be insufficient in AIs. The documented excess of CAD, despite maximum modification of lifestyle, underscores the need for a more aggressive approach to prevention and treatment, including pharmacological therapy, in selected cases.

National mortality data for AI in US are not yet available. Mortality for CAD and stroke for six ethnic groups in the state of California from 1985 to 1990 was recently reported7 (data not presented but included in this report due to their relevance). The standardised mortality rate (SMR) for all causes was significantly lower among AI men and women than in Whites. With 100 as the standard for Whites, the SMR for all-cause mortality was 56 for AI men and 48 for AI women; the stroke mortality was also low in AI with an SMR of 53 in men and 90 in women. The overall SMR for CAD in AI was 92 for men and 79 for women. However, young AI men in age range 25-44 had a significantly higher SMR and proportionate mortality (PMR) for CAD (SMR of 120, and PMR of 350), indicating a high degree of prematurity. Though AI women had a low SMR and PMR for CAD in the age range 25-44, AI women in the age range 45-64 had an SMR of 130, and PMR of 210 (Table 2).

Thus, AI in the US have a higher incidence, prevalence and mortality than Whites. The limited CAD mortality data available in the US indicates that premature CAD is responsible for the higher magnitude of CAD, as has been well documented in other countries. The CAD rates among other Asian-Americans are similar or lower, with Chinese-Americans having significantly lower rates of CAD than Whites.

**Canadian Data.** Prof. Yusuf presented data from the Canadian National Mortality Database which demonstrates higher rate of cardiovascular disease (CVD) mortality and lower rate of cancer mortality among SA than in Chinese. Compared with Chinese, the CAD mortality rates were threefold higher in SA men and fourfold higher in SA women. However, mortality from lung cancer and colorectal cancer in SA was less than one-third of the Chinese. The Chinese in the US also have high cancer mortality and low CAD mortality.

Prof. Yusuf also reviewed the trends over the past 16 years, which demonstrate the largest reductions in CAD mortality among SA Canadians followed by Chinese Canadians, with the smallest reductions in CAD mortality occurring in White Canadians. As a result, by 1992 the CAD mortality rates in SA were similar to Whites. However, SA had lower cancer mortality rates (all sites) - about one-third of Whites in
TABLE 2
Standardised Mortality Ratios (SMR)* and Proportionate Mortality Ratios (PMR)* per 100,000 for CAD and Stroke in Asian Indians Compared with Whites and Chinese in California, USA - 1993

<table>
<thead>
<tr>
<th></th>
<th>Age-Range (Years)</th>
<th>Men</th>
<th></th>
<th></th>
<th></th>
<th>Women</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>White</td>
<td>Asian Indian</td>
<td>Chinese</td>
<td></td>
<td>White</td>
<td>Asian Indian</td>
<td>Chinese</td>
</tr>
<tr>
<td>SMR-All Causes</td>
<td>25-84</td>
<td>103</td>
<td>56</td>
<td>64</td>
<td>104</td>
<td>48</td>
<td>64</td>
<td>104</td>
<td>48</td>
</tr>
<tr>
<td>SMR-Stroke</td>
<td>25-84</td>
<td>97</td>
<td>53</td>
<td>100</td>
<td>98</td>
<td>79</td>
<td>91</td>
<td>79</td>
<td>53</td>
</tr>
<tr>
<td>SMR-CAD</td>
<td>25-84</td>
<td>108</td>
<td>92</td>
<td>55</td>
<td>103</td>
<td>130</td>
<td>40</td>
<td>130</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>25-44</td>
<td>100</td>
<td>120</td>
<td>25</td>
<td>100</td>
<td>90</td>
<td>40</td>
<td>90</td>
<td>40</td>
</tr>
<tr>
<td>PMR-CAD</td>
<td>25-44</td>
<td>100</td>
<td>95</td>
<td>45</td>
<td>100</td>
<td>210</td>
<td>60</td>
<td>210</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>45-64</td>
<td>100</td>
<td>180</td>
<td>80</td>
<td>100</td>
<td>210</td>
<td>60</td>
<td>210</td>
<td>60</td>
</tr>
</tbody>
</table>

* SMR and PMR for the total population of California are taken as 100. Wild SH, et al. Ann Epidemiol1995; 5: 432-439

SA men and about two-third of Whites in SA women. The mortality from CBVD in Canada (which has the lowest stroke rate in the world) were surprisingly similar among men and women in all the three ethnic groups. These data from Canada indicate that the high rates of CVD mortality among SA reported in several countries can be decreased substantially.

United Kingdom Data. Recent data from UK (data not presented but included due to relevance) seem to parallel the Canadian pattern. All-cause mortality in SA in the UK is similar to those born in England and Wales. With 100 as the standard, the SMR for CAD in SA men is 146 at all ages, increasing to 158 between the ages of 45-49 years and 169 between the ages of 20-44 years. In SA women, the corresponding rates of SMR for CAD were 151, 153 and 118 respectively (Table 3). From 1971 to 1991, the national average SMR for CAD fell by 29 percent in men and 17 percent in women. Among the various immigrants, SA had the smallest decline of 20 percent in men and seven percent in women whereas Caribbeans showed the steepest decline of 38 percent in men and 40 percent in women.

Unlike in Canada, where the CBVD rates among SA are similar to Whites, SA in the UK have a higher rate of stroke death. With 100 as the standard for those born in England and Wales, the SMR for CBVD in SA is 155 for men and 141 for women. Only Afro-Caribbeans had higher SMR for stroke (men 168, women 157) than SA. However, the pattern of cancer mortality rates was low and similar to that of Canada, with SA having an SMR of 45 in men and 33 in women for lung cancer and 59 for breast cancer.

Dr. Shaukat reported the results of a study of 238 pairs of patients, admitted during 1987-93 and matched for age, sex, date of admission, type of infarction, site of infarction, and the incidence of angina, reinfarction or death during a follow-up of one to seven years. Patients of the Indian subcontinent origin had a higher prevalence of diabetes (35% vs 9%) and lower prevalence of smoking (39% vs 63%). During a mean follow-up of 39 months, mortality was twofold higher among patients of Indian subcontinent origin compared to patients of European origin, even after adjustment for smoking, diabetes, and the use of thrombolytic therapy. Coronary angiography was performed with similar frequency in the two groups. Triple-vessel disease was the commonest finding in patients of Indian subcontinent origin, whereas single-vessel disease was the commonest in Europeans. This study clearly demonstrates significantly greater severity, morbidity, and mortality from CAD among Asian Indians in the UK, unexplained by smoking, diabetes and hypertension.

The results of a prospective study of the relation between CAD mortality and risk factors in 1,515 Europeans and 1,420 SA men 40-49 years of age were recently reported (data not presented but included due to their relevance). There were 34 CAD deaths among SA and 20 deaths among Europeans during a median follow-up of 6.8 years. Apart from age and smoking, the strongest predictors of CAD mortality in SA men were glucose intolerance, raised serum cholesterol and low HDL-C. The age-adjusted RR for CAD death for SA was 2.0, which increased to 3.1 after adjusting for smoking and cholesterol (p<0.001). Adjusting for glucose intolerance reduced the RR to 2.4. Further adjustments for insulin level, waist-hip ratio, body mass index, hypertension, fasting triglycerides and HDL failed to reduce the RR any further. Thus, all the conventional and measured risk factors failed to explain
### TABLE 3

Standardised Mortality Ratios for Coronary Artery Disease and Cerebrovascular Disease in England and Wales by Country of Birth, 1989-92

<table>
<thead>
<tr>
<th>Country/Region of Birth</th>
<th>CAD</th>
<th>CBVD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Total population</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>(age 20-69 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scotland</td>
<td>120</td>
<td>130</td>
</tr>
<tr>
<td>Ireland</td>
<td>124</td>
<td>120</td>
</tr>
<tr>
<td>East Africa</td>
<td>131</td>
<td>105</td>
</tr>
<tr>
<td>West Africa</td>
<td>56</td>
<td>62</td>
</tr>
<tr>
<td>Caribbean</td>
<td>46</td>
<td>71</td>
</tr>
<tr>
<td>South Asia</td>
<td>146</td>
<td>151</td>
</tr>
<tr>
<td>Age 20-44 years</td>
<td>169</td>
<td>118</td>
</tr>
<tr>
<td>Age 45-59 years</td>
<td>158</td>
<td>153</td>
</tr>
<tr>
<td>Age 60-69 years</td>
<td>135</td>
<td>152</td>
</tr>
</tbody>
</table>

Wild S, McKiegue P. BMJ 1997; 314: 705-710

the excess mortality in SA. Lp(a) levels were reportedly not measured.

Dr. G.C. Sutton described the problem in establishing the prevalence of CAD in SA by using conventional epidemiological methods such as the Minnesota Code for ECG analysis. These methods, validated in male Caucasians, may not be quite applicable to SA, particularly to women. Rather than assessing prevalence, which depends on the incidence and case fatality, it would be better to examine the incidence. This has been done in a fixed population of 150,000 people in West London, which contains about 90 percent Whites and about 10 percent SA. All cases of sudden coronary death, acute MI, stable angina and unstable angina were identified in this community. The cases of sudden death were established from the Coroner's mortuary, the acute ischaemic cardiac syndromes from the hospital serving this population (Hillingdon Hospital) and the cases of stable angina by running a "dedicated rapid-access chest pain clinic" for this population. In a 19-month period, 250 such cases were enrolled from the population of 150,000. Caucasian/SA comparisons showed significantly higher incidence rates of CAD in SA. Thus, the results of this study further confirm the higher incidence of CAD in SA in UK and complement the findings of McKiegue et al.¹⁰

**Indian Data.** Dr. S. Padmavati was skeptical as to whether CAD rates are really high in India and wondered if hospital statistics are biased due to greater availability and use of diagnostic facilities in recent years. She cautioned against extrapolating the data from overseas Indians. She felt that among coronary risk factors (CRF), hypertension, cigarette smoking and glucose intolerance are applicable to India. She was of the opinion that raised serum cholesterol levels are not an important risk factor for Indians.

Prof. Yusuf also reviewed the data from an Indian case-control study which demonstrated the importance of conventional CRF, in particular the marked dose-response associated with cigarette and beedi smoking. There was also a continuous relationship between glucose levels and MI risk even among non-diabetics, indicating the importance of small increases in glucose within the range considered to be normal for the Western population. The odds ratio for MI was 2.6 for diabetes and 6.7 for smoking more than 10 cigarettes per day with diabetic smokers having an odds ratio of 10.6.

### Mechanism of CAD

Dr. Sanjay Kaul presented the data on platelet-dependent thrombosis (PDT) and platelet activation in hypercholesterolemia. HDL-C correlated inversely with thrombus formation with enhanced PDT evident at low HDL-C and vice versa. His study indicates that increased susceptibility to thrombosis in patients with low HDL-C may, in part, explains the inverse relationship between HDL-C and the incidence of coronary artery disease. This may be especially important in Indians who have low HDL-C.

Prof. P.K. Shah discussed how modifying HDL-C could become a future therapeutic strategy. He discussed the exciting possibility in raising the HDL-C by genetic engineering as a further way to reduce atherosclerosis. The failure of the conventional risk factors to explain the higher prevalence of CAD and the excess of non-conventional risk factors like elevated levels of Lp(a) and PAI-1 in Indians calls for an intensified research for these and other emerging risk factors like homocysteine.

### Report from the President, Cardiological Society of India (CSI)

Dr. Satyavan Sharma gave an overview of realities and challenges in developing the preventive strategies for CAD in India. The globalisation of India and the aspirations of the middle class are bound to increase the threat of CAD to the epidemic proportions in the coming years. The middle class is undergoing tremendous changes in lifestyle and socioeconomic factors, such as acquiring cars and consuming increasing amounts of alcohol and tobacco. The dining patterns are also changing rapidly with greater use of
fast foods, meats, and fats. The number of fast food restaurants, including Pizza Huts and McDonalds is increasing rapidly. All these changes are leading to sedentary habits, decreased physical activity, and increased consumption of unhealthy foods.

Assessment of the Real Magnitude of the Problem. Many studies have shown a prevalence of CAD of 10 percent among urban Indians, which is 3 to 4-fold higher than contemporary rates in the North America and Europe. The available epidemiological data have provided us with some useful information; however, the data collected over a wide range of years has several limitations. There is a need for reliable data on incidence, prevalence, and mortality from CAD in rural and urban India.

There are various paradoxes reported from angiographic and clinical studies in rural and urban areas of north and south India. Some of these paradoxes include higher rates of CAD in urban areas where smoking rates are low and equally high rates in women and men, though smoking rates are negligible among Indian women. These paradoxes need to be analysed more carefully to reach meaningful conclusions. It is possible that this may stem from poor case-definitions due to non-specific ECG criteria such as ST-T changes in epidemiological studies.

A study of 3,000 apparently healthy individuals in the age group, 30-40 years in an executive health check-up scheme for a leading hospital in Bombay, revealed that at least one CRF was present in 60 percent of individuals, two CRF in 29 percent and three in 10 percent. This observation underscores the need to assess the real magnitude of the risk factors for the entire country so as to effectively plan national preventive strategies.

Importance of Lifestyle Factors. The impact of lifestyle and environmental factors is clearly demonstrated by the rise and fall of CAD in the middle and latter part of the 20th century in the Western industrialised societies. No major alterations in the genetic pool could explain this phenomenon. Conversely, the reduction in cigarette smoking and the lowering of elevated blood pressure and elevated cholesterol has played a crucial role in the decline of CAD. More than 50 percent of this decline of CAD in the US has been attributed to a modest reduction in the cholesterol level of population (mainly through reduced intake of saturated fat) and a significant reduction in cigarette smoking. Treatment of hypertension is responsible for substantial reduction in stroke and a small reduction in CAD mortality. The prevention of CRF can be approached in two ways: Individual-based strategies which seek to help those with the highest risk, and the population-based strategies which seek to reach the entire population.

Individual-Based Strategy. This approach aims at identifying individuals with markedly elevated risk factors and targeting them for interventions to reduce their risk of CVD. This begins with lifestyle modifications such as low intake of saturated fat in diet, regular exercise, tobacco abstinence, and maintenance of ideal body weight and minimising waist circumference. Individual physicians and national societies are best suited to provide guidance for individual-based strategies. If successful, the benefits to the individual are large, since the degree of risk prior to intervention was also substantial. Although both physicians and patients are generally motivated to act in high-risk patients, an individual with high blood cholesterol may not be very successful in following a low-saturated fat diet if the remainder of the family continues to indulge in a high-fat diet. Reducing the serum cholesterol level from 300 mg/dl to 250 mg/dl reduces the risk of CAD by 50 percent but the individual is still at double the risk of CAD compared to one with a serum cholesterol of 200 mg/dl, and threefold higher risk than one with a cholesterol of 150 mg/dl. Since the number of persons in the high-risk category is proportionately much smaller than those in the moderate risk group, the overall benefits to the society from treating the high-risk individuals are limited in terms of avoiding death and disability. However, the benefit can be greatly enhanced by a broader approach.

Treatment of High-Risk Individuals. Regular check-ups for the control of blood glucose, blood pressure, blood cholesterol, and other risk factors are needed in high-risk individuals. Those with persistent abnormalities, despite maximum lifestyle modification, may require pharmacotherapy for dyslipidemias, hypertension, and insulin resistance syndrome. Other therapeutic agents include antiplatelet drugs, antioxidants and estrogen replacement therapy in selected cases. There is a need for randomised clinical trials in selected Indian populations at reputed centres in collaboration with international institutions to ascertain the benefit and risks of various therapeutic interventions and their applicability to those of Indian origin.

Population-Based Strategy. The population-based approach aims to lower risk factors in the population through both government and community action. Since there is a continuum of risk associated with most CRF, more people making small changes will result in large benefits to the society, as opposed to large changes in a small number of high-risk patients. This phenomenon
is termed as "prevention paradox" by Prof. Geoffrey Rose. The population-based strategy emphasises the importance of exercise, consumption of healthy foods and the danger of tobacco, and aims to lower the blood cholesterol and blood pressure levels of the entire population. A 10 percent reduction in the average level of serum cholesterol of the US population has been estimated to reduce the risk of CAD by 20 to 30 percent. If every American had a diastolic blood pressure value a mere 2 mm Hg lower than his or her present value, the number of heart attacks that could be prevented would exceed those that could be avoided by effectively treating every American with a diastolic blood pressure of 95 mm Hg or higher. A decrease in diastolic blood pressure of 6 mm Hg for the entire American population could reduce the incidence of stroke by 42 percent. Such changes in blood pressure and blood cholesterol levels can be easily achieved and sustained through modest reductions in weight, salt and fat intake and a programme of regular exercise. There is no reason to doubt that the magnitude of benefit is likely to be any lower among Indians compared to other populations.

If the entire population adopts a healthy eating pattern with low intake of saturated fat and high intake of fresh fruits and vegetables rich in antioxidant vitamins, high-risk individuals will also have a greater success in pursuing such diets. If the next generation of Indians grow up in such an environment, the population level of blood cholesterol and BP will remain low. Further, progress in tobacco control will gradually decrease the risks of MI and numerous cancers associated with this habit.

Both the government and the community should be involved in the population-based prevention and control of CRF. The population-based strategy should eventually lead to a set of recommendations designed to help all Indians to lower their blood cholesterol and blood pressure levels and other risk factors, and thereby reduce their likelihood of developing CAD, by changes in eating patterns and physical activity.

Reduction in Established and Emerging CRF through Combined Strategy. It is important to recognise that the population-based strategy and the high-risk strategy are not mutually exclusive, but synergistic. The population-based, lifestyle-linked, risk reduction approaches are particularly relevant in the Indian context to protect the low-risk groups from augmenting their CAD risk. Two such groups are children and rural populations. This strategy may also help avoid drug therapy in moderate risk groups in urban areas, with its attendant economic and biologic costs. Both these approaches have been successfully combined in many countries. In the US, age-adjusted death from CAD has declined by over 50 percent and stroke over 60 percent in the past 30 years. Reductions in serum cholesterol, cigarette smoking and treatment of hypertension have been largely responsible for this decline. Even greater reductions in CAD morbidity and mortality have been demonstrated in Finland.

Tobacco Industry. In India, tobacco is consumed in several forms such as cigarettes, beedies, zarda, gutka, hukka, and betel leaves and in tooth pastes. The tobacco industry is now a multicrore rupee (multi million dollar) industry and the menace of tobacco consumption needs to be tackled by public education, statutory warning, legislation, and higher taxation. The government has a greater role to play in tobacco control, as the increase in cigarette tax has been found to significantly reduce the consumption of cigarettes in several countries. Now that cigarette consumption is decreasing in the West, the cigarette manufacturers are concentrating their marketing efforts in the developing regions of the world.

Agricultural Practice and Food Industry. There is a need for greater production and easier availability of edible oils, fruits and vegetables, which are low in saturated fats and rich in antioxidants and fibre, at affordable prices. There is also an urgent need to pass government legislation for product labelling of the ingredients and additives in all food products. The packaged products should clearly display the amount and percentage of total fat, saturated fat, salt and calories. No such practice currently exists in India.

Standardisation of Lipid Laboratories. There is total lack of standardisation of methods of cholesterol and triglyceride estimation across the country and the results vary widely (as high as 100 mg/dl) between the laboratories. Most laboratories do not determine lipoprotein fractions.

Indian Guidelines. The National Cholesterol Education Programme (NCEP) guidelines may not be totally appropriate for the Indian population, many of whom have greater abnormalities of triglycerides, HDL-C and Lp(a). There is a need to develop specific guidelines for the Indian population by the CSI in conjunction with relevant international research, publish them in the Indian Heart Journal, and be subsequently reproduced in other journals. Likewise, the NCEP Report of the Expert Panel on Population Strategies for Blood Cholesterol Reduction can be adopted after appropriate modification for the Indian population. Consideration should also be given for Indian guidelines for the control of hypertension and other risk factors.
The poor infrastructure prevailing in most organisations in India poses a mammoth task. The CSI, its various local branches, the Government of India, and State Governments need to collaborate constructively with voluntary agencies like CADI Research Foundation, Chicago and the Population Health Programme in Cardiovascular Diseases at McMaster University, Hamilton, Canada in developing practical preventive strategies applicable to India.

**Role of Cardiological Society of India in Achieving the Goals.** The CSI will be 50 years old in 1998. However, it has not been able to have a major impact on public policy nor has it developed a coordinated link with the government. This has been due to poor infrastructure, varying academic interests of the office bearers, and limited financial resources. The areas where the CSI can contribute are:

(a) education of cardiologists and other professionals in the importance of primary and secondary prevention strategies
(b) organising major symposia on preventive cardiology during future annual CSI conferences
(c) establishment of specific guidelines for Indian patients in collaboration with the international working group or other professional organisations
(d) media interaction for creating awareness and promoting prevention
(e) publishing booklets for public awareness and education
(f) interaction with the government in influencing and developing government policies especially targeted at tobacco control and food product labelling
(h) publishing periodic summaries of emerging information in the *Indian Heart Journal.*

**Potential Role of CADI Research Foundation in India.** In order to effectively implement its strategies, the CADI Foundation should develop its own infrastructure in India with the following main goals:

1. Developing a forum of interested experts with organisational skills in various parts of India
2. Facilitating preventive strategies in concert with CSI, Indian College of Cardiology, media and government
3. Holding a major conference once in two years in a metropolitan Indian city.

Dr. Sharma expressed optimism that CADI Foundation, CSI and other interested agencies would work together towards our common goal of fighting the malignant CAD in young Indians with its enormous morbidity and mortality.

**Recommendations to Governments.** Any population-based strategy requires full participation of the government at national and state levels. The United States Department of Agriculture (USDA) and Department of Health and Human Services (DHHS) and the NCEP have jointly published Guidelines for all Americans. These guidelines are:

1. Eat a variety of foods
2. Avoid too much fat, saturated fat and cholesterol
3. Eat foods with adequate starch and fibre
4. Avoid too much sugar
5. If you drink alcoholic beverages, do so in moderation
6. Maintain desirable weight
7. Be physically active.

Other agencies have strongly recommended that every American stop smoking if he/she is already a smoker and to exercise for 30 to 60 minutes 3 or 4 times a week. These guidelines can be modified to the Indian setting and go into a national policy document that can be presented to the government for formulating preventive strategies. Since conventional risk factors do not explain the higher prevalence of CAD in Indians, a more aggressive approach to prevention and treatment of all risk factors may be necessary.

**Public Education.** To implement the above community-based strategies, there is a greater need for public education. The CSI during its various conferences should provide necessary public education on prevention. There should be documents and release of information to electronic and print media from the CSI and CADI Research Foundation from time to time, about the importance of lifestyle modification in the prevention and control of CRF and CAD.

**Consensus**

There was a general agreement among the participants that South Asians indeed have a high rate of CAD both in India and overseas and preventive strategies should be taken at an earlier age than in other populations. Although conventional risk factors do not explain the excess of CAD in Indians, tobacco abuse, hypertension, diabetes, and abdominal obesity are important CRFs in Indians as in other populations. Among the lipid risk factors, total cholesterol, LDL-C, HDL-C, triglycerides, and Lp(a) are also important. Waist-to-hip ratio may be a better marker of obesity than body mass index, both of which should be lower in Indians than the reference standard in the western populations. Indians appear to have a genetic predisposition to CAD, possibly mediated through
elevated Lp(a), levels of which are largely genetically determined. More research is needed to define its role and other emerging risk factors in the excess burden of CAD in Indians. Since the individual's genetic makeup cannot be changed, greater attention should be focussed on modifying environmental factors. Increasing physical activity and decreasing caloric consumption are fundamental in preventing and correcting the metabolic abnormalities among Indians. In men, the avoidance of cigarette smoking and the consumption of tobacco products, however, may have the most immediate and profound impact in reducing the risk of CAD.

The IWG is compiling a list of ongoing studies on South Asians worldwide. A compendium of such major studies will be published periodically. Those who are conducting any such studies are requested to send a one-page summary to Prof. Salim Yusuf, Director of Cardiology, HGH McMaster Clinic, Hamilton General Hospital, 237 Barton St East, Hamilton ON Canada, L8L2X2; Tel: 905-527-7327; Fax: 905-521-1116. E mail: Yusufs@fhs.csu.mcmaster.ca.

The next meeting is scheduled for 29 March 1998 in Atlanta, immediately preceding the Annual Scientific Sessions of the American College of Cardiology. Those who wish to be invited for this meeting should kindly contact Dr. Enas (Fax 630-960-1863).

References