Commentary: AG Shaper and KW Jones, ‘Serum-cholesterol, diet and coronary heart-disease in Africans and Asians in Uganda’

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The central importance of the control of blood cholesterol concentrations for prevention of coronary heart disease in individuals and in populations is now so widely accepted that it is hard to imagine the extraordinary controversy over the role of high blood cholesterol in the aetiology of coronary heart disease, only a few decades ago. Leading British cardiologists such as Sir John McMichael in the 1970s and Sir Michael Oliver in the 1980s were vociferous in their opposition to the lipid hypothesis, and it was not till the publication of the Lipid Research Clinics Coronary Primary Prevention Trial in 1984 and then the Scandinavian Simvastatin Survival Study in 1994 showing that lowering low density lipoprotein cholesterol reduced coronary mortality that clinical opinion eventually reversed. It may have taken many decades and randomized trials to persuade cardiologists of the relevance of blood lipids to atherosclerosis, but what is notable is that early epidemiological studies in the 1950s led by pioneers such as Ancel Keys and Jeremiah Stamler generated many of the hypotheses that still hold today. In this study published in 1959, Shaper and Jones made several observations and postulated explanations for differences in coronary heart disease rates in different communities that continue to have relevance.

Shaper started with the observation as a clinician in the 1950s that coronary heart disease in the African population in Uganda was almost non-existent, and this appeared to be confirmed by necropsy studies. On the other hand, coronary heart disease appeared to be a major problem in the Asian community in Uganda with a high proportion of deaths attributed to coronary heart disease. Shaper and Jones noted that although the significance of a high serum cholesterol level in the pathogenesis of coronary atherosclerosis could not yet be taken as proven, it was supported by indirect evidence. In view of the radically different rates of coronary heart disease observed in the two communities in Kampala, they conducted a study to compare serum cholesterol concentrations in 317 African and 354 Asian males in Kampala at three age levels, 12 years, 20 years and >40 years with about a hundred individuals in each age and ethnic group. The main findings were that the African males had substantially lower mean serum cholesterols (4.4, 4.3 and 3.8 mmol/l in the three age groups, 12 years, 20 years and >40 years, respectively) than in the Asian males (5.4, 5.7 and 6.5 mmol/l, respectively). They additionally observed that mean cholesterol levels did not appear to increase in the older age groups in African males, whereas in the Asian males, mean levels showed a steep increase with age.

Though Shaper and Jones did not appear to collect detailed dietary data from individuals in the study apart from identifying vegetarians and non-vegetarians in the Asian group, they presented descriptions of dietary patterns then prevalent in African and Asian communities around Kampala. They cited reports from other studies indicating relatively low meat and fat intakes (~16–20 g a day) in the African communities, with possibly up to 40 g fat a day in more well-to-do families. With estimated intake of 2000 calories per day, this would be ~10–20% of total caloric intake. In contrast, though Asian communities comprised Hindus who were largely lacto-ovo-vegetarians, and Muslims who had meat, fish and poultry in their diets, it was estimated that fat and oils provided a large proportion, ~30–40%, of total caloric intake in the Asian community, whatever the religious or dietary group. A subgroup analysis of vegetarians and non-vegetarian Asians
showed no major differences in the mean cholesterol levels, suggesting these differences were unlikely to be explained by differences in meat intake.

Much of the discussion focused on the factors responsible for the considerable differences in the mean serum cholesterol levels of Africans and Asians. The authors argued that the factors responsible for these differences must be present at all three ages and may be those responsible for the differing susceptibility to coronary heart disease in Africans and Asians. They cited a study from South Africa indicating that African and European babies at birth have similar serum cholesterol concentrations, despite significant differences in such concentrations in the African and European mothers, which suggested that for each community with its own specific nutritional background, the characteristic serum cholesterol levels are reached in early life, possibly because of the change over to adult types of food. They indicated that their own findings agreed with this. Related to this was the observation that the rise of serum cholesterol with age was not a necessary concomitant of ageing, and the implications of their findings taken with other studies were that increases in cholesterol levels run strikingly parallel to increases in consumption of animal fats and a rise in income. They speculated it might be that with increasing age, or decline in physical activity, physiological mechanisms are less able to deal with a heavy intake of fat.

They concluded that the observations on serum cholesterol levels in different parts of the world were consistent with the hypothesis that the level of blood lipids is artificially raised in modern civilizations, and that this appears to be an essential condition for coronary heart disease to become endemic among people. They also suggested that differences in levels of blood cholesterol corresponded to their different consumption of fat.

There are of course many limitations to this study, which the authors themselves acknowledged. They recognized the heterogeneous religious and sectarian backgrounds of the Asian groups, the different African tribal groupings and the rapidly changing social and economic patterns of a developing society, making it almost impossible to select what might be considered representative groups for the measurement of blood cholesterol levels; their sampling was from schools in Kampala for the 12-year-olds, new students at a college who came from all parts of East Africa for the African 20-year-olds and people attending their general practitioners for >40-year-old Asians and people attending outpatients for >40-year-old Africans. Their assessment of usual diets in Africans and Asians were not conducted in the individuals who were seen but based on descriptions from other studies, and the differences in coronary heart disease rates in the two groups were also based on clinical reports and observations. This was essentially an ecological study, which compares average dietary patterns, blood cholesterol concentrations and coronary heart disease rates in two groups.

Nevertheless, it was studies such as these generating the early evidence that cumulatively contributed towards the large prospective studies and eventually the randomized trials that established the central role of lipids in coronary heart disease. Shaper went on to lead other landmark research including establishing the prospective British Regional Heart Study, which continues to today, and to be a major advocate of cardiovascular disease prevention. In these days of ever-larger genome-wide association studies involving hundreds of thousands of participants looking for minute effect sizes, and a somewhat rigid hierarchical approach to study designs with randomized trials at the top and ecological studies at the bottom of the list in terms of scientific inference, it is encouraging to be reminded that often it is the initial clinical and ecological observations that generate the original hypotheses. Cardiovascular disease is a success story in terms of the identification of major physiological risk factors, such as blood lipids and blood pressure, which have been amenable to pharmacologic interventions and randomized clinical trials and risk reduction in individuals. However, this study also reminds us of the challenges that still remain: to understand and to influence the major environmental and lifestyle factors such as diet, smoking and physical activity that determine a community’s propensity for chronic diseases. The continuing huge geographical, socio-economic and secular differences in health indicate that the major determinants are environmental. As Shaper and Jones remarked, differences between communities may also give us clues as to possible factors responsible. The questions that epidemiological research continues to address are to identify what these are and what we can do about them.

Conflict of interest: None declared.

References