

Monitoring of Trends and Determinants in Cardiovascular Disease; mostly developed countries),⁹ INTER-SALT,¹⁰ INTER-HEART,¹¹ and the Prospective Urban and Rural Epidemiologic Study (PURE)—the last two involving low-, middle-, and high-income countries. These studies will complement the more traditional cohort studies generally conducted within relatively homogenous populations.

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Commentary: Geoffrey Rose's thinking about coronary artery disease

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Two decades ago, Geoffrey Rose was clear about the essentials of atherosclerotic coronary disease. It is insidious, treatable, the source of endless puzzlement and, most importantly, eradicable.

In 1982 he related measurements of cholesterol and blood pressure which had been made in 40- to 59-year-old men in the Seven Countries Study (Finland, Greece, Holland, Italy, Japan, the USA, and Yugoslavia) to rates of death from coronary heart disease 5, 10 and 15 years later in the corresponding but much larger age cohorts identifiable from national mortality statistics.¹ He showed persuasively that the closeness of the correlation about the regression line increased with time so that measurements of cholesterol in particular, made in the late 1950s predicted almost perfectly international differences in mortality from coronary heart disease in the mid-1970s. He argued, therefore, that the data were consistent with a delay of

10 years or more between exposure to hypercholesterolaemia or hypertension and the maximum effect of these risk factors on coronary death rates. In passing, he noted that a delay of this magnitude was not inconsistent with a rapidly appearing benefit of reduction of cholesterol or blood pressure.

This understanding of the time course of coronary artery disease, based on epidemiological data, accords well with pathology and data from clinical studies. A myriad complexities notwithstanding, atherosclerosis can be ascribed to gradual (over decades) deposition in the artery wall of cholesterol from the low-density lipoproteins (LDLs) of plasma, and lowering of LDL cholesterol by diet, drugs, or surgery is rapidly followed (in months) by a reduced risk of myocardial infarction.

In contemporary cardiology we still seem to be puzzled by the dual concept of the rapid salutary effects of removal of a slowly working agent of disease. For example, the rapid reduction in risk demonstrated in clinical trials of lowering LDL cholesterol with statins was thought to require an explanation in addition

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to that involving lipoproteins, and numerous reports were quickly published about the pleiotropic effects of these drugs (i.e. the pharmacological effects of statins other than the lowering of plasma LDL levels).² As might be expected from experience with betablockers and ACE inhibitors, scientific and commercial interests were mixed in exploring and exploiting the alleged advantages of the pleiotropic properties of competing statins. Bristol-Myers Squibb even co-sponsored a clinical trial to compare the ability of its own, weaker statin with that of a competitor's more powerful statin to lower rates of death or a major cardiovascular event in survivors of a recent acute coronary syndrome. The company appeared to expect that the putative beneficial pleiotropic (anti-inflammatory) effects of pravastatin would at least negate the greater reduction of LDL levels by atorvastatin. As it turned out, however, the results demonstrated the rapidly emerging superiority of the drug lowering LDL levels the most,³ consistent with Geoffrey Rose's more straightforward understanding of the disease.

In his 1982 article, Rose also cited Framingham data showing that high plasma cholesterol did not predict coronary disease as well in older as in younger persons, and he wrote, 'Possibly the determination of individual risk has a different basis from the determination of rates in populations.' This concept was fully developed in a later article, 'Sick individuals and sick populations'.⁴ Rose believed that a high consumption of dietary fat is what makes coronary artery disease common in populations, but individual differences in intake of dietary fat, like individual differences in concentrations of plasma cholesterol or in blood pressure, do not identify high-risk individuals very well. 'The determinants of incidence are not necessarily the same as the causes of cases.' When a risk factor is present throughout a population, the disease afflicts those who are susceptible to it, typically by genetic disposition, and risk can be lowered in the susceptible by individual lifestyle changes or by drugs. The disease can only be eradicated (in the population), however, by a population strategy.

Geoffrey Rose came to epidemiology from clinical medicine, and he appreciated 'the enormous difficulty for medical personnel to see health as a population issue and not merely as a problem for individuals'. He was nevertheless quite clear in writing that it was the population approach, not that based on the identification and treatment of high-risk individuals, which could enable us to eradicate the disease or make it less common. 'Once a social norm of behaviour has become accepted and (as

in the case of diet) once the supply industries have adapted themselves to the new pattern, then the maintenance of that situation no longer requires effort from individuals.'

The identification of societal factors such as industry is crucial, since Rose believed, and I agree,⁵ that the major determinants of common diseases such as coronary artery disease are economic, industrial, and political. Decisions to implement remedies are therefore mainly political, but it is depressingly easy to identify players with conflicting political interests in preventing or inadvertently promoting the disease. Recent studies in both the United States⁶ and Europe⁷ have shown that government policy, as well as the interests of the food industry, continues to promote the disease. Efforts truly to control coronary artery disease are not very complicated, but they are politically daunting in a way that prevention, diagnosis, and treatment, directed at individuals, are not. As demonstrated by the North Karelia project, however, an effective population approach is feasible,⁸ and, as argued by Geoffrey Rose, it behoves politicians to take public health into account when formulating policies for education, urban planning, the economy, and industry.⁹

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