Community intervention to control plasma lipids

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A necessary part of the strategy of modification of hypercholesterolaemia to prevent coronary heart disease (CHD) is the detection and treatment, by diet or by drugs, of high risk individuals. There are several drawbacks to this approach: (i) the cost of screening to find individuals at risk and of monitoring by physicians of their therapy; (ii) the problem of labelling asymptomatic people as 'sick' and advising them on special diets; (iii) difficulties in compliance. If the community norm is to eat a diet high in fat, it is difficult for individuals to change, both because it marks them as 'odd' within the culture and because foods low in saturated fat may be difficult to obtain and are expensive.

A further limitation is that only those individuals at highest risk may benefit. In a country with a high rate of CHD the problem is that the mean is high. The aim therefore should be to reduce the population mean and shift the whole distribution to the left. This suggests a policy of health education and of policies that remove the barriers against choosing a healthy diet. Even were such policies to be implemented successfully these alone would not abolish social and regional differences in CHD mortality.

It sometimes seems that for every article, review, or committee report that says that a diet rich in saturated fats is a cause of coronary heart disease (CHD) there is a letter, counter-article or broadsheet from industry sources disputing the fact. This is not only a scientific debate about the establishment of proof of causation but a crucially important public health debate about whether community recommendations on changing diet for the prevention of CHD are justified.

The thrust of this paper is that: (i) CHD mortality rates can change rapidly and this is strong evidence that CHD is, in principle, preventable; (ii) if diet is importantly involved in the aetiology of CHD — and evidence supplied by others in this symposium argue strongly that it is — then only an approach to the whole community is likely to have any appreciable impact on CHD incidence and mortality rates; (iii) this approach must be multifactorial; but (iv) social and regional inequalities in the occurrence of CHD, are unlikely to be abolished by such approaches, at least in the short term.

The symposium is entitled Lipoproteins and Atherosclerosis, but the epidemiological and much of the clinical work in this area has been directed at clinical disease or death. This is not a criticism. Admittedly, the relation between atherosclerosis and clinical disease may not be a simple 1 : 1 ratio. Thrombosis, as well as playing a part in atherosclerosis, may also precipitate an acute event. Other factors — coronary spasm, myocardial, electrical — may also be important. Nevertheless it remains true that clinical CHD is not common unless atherosclerosis is common and although atherosclerosis may not be a sufficient determinant of CHD, it is probably a necessary one. We study CHD because it is easier to study epidemiologically, but more importantly, it is the clinical disease we seek to prevent.

Changing CHD mortality rates of the community

Figure 1 charts trends in CHD mortality rates in selected countries. The dramatic decline in the U.S.A. and, to a lesser extent, Finland, France, Japan and, latterly, England & Wales and Scotland have excited much attention. The extent to which this represents a decline in case-fatality or a decline in incidence is not known precisely. This uncertainty underlies the setting-up by WHO of MONICA — monitoring trends in cardiovascular disease and its risk factors — in many countries.

In the meantime a judgement that there has been
a decline in CHD incidence rates seems reasonable as: (a) WHO figures based on myocardial infarction registers show a high correlation internationally between incidence and mortality rates; and (b) data from the U.S.A. show that among some employed groups, Californian physicians' and employees of the Dupont corporation, there has been a decline in CHD incidence.

If this is the case, it shows that CHD rates of a community can change very rapidly — by more than 30% in a dozen years in the U.S.A. This gives confidence that preventive efforts have the potential of showing results, at least in the 5–10 year span. The exact role of dietary change in these trends is far from clear. In the U.S.A., dietary consumption surveys indicate a decrease in many sources of saturated fat, particularly dairy products, eggs and visible fats, whereas national food disappearance data do not. Both sources show an increase in polyunsaturated fat consumption and an increase in the polyunsaturated to saturated fatty acid (P:S) ratio.

The point is that, whether or not dietary change has been principally responsible, CHD rates can change.

The scale of the problem

Any plan of action to combat the high rates of CHD must take into account the scale of the problem. Figure 2 reproduces data from the British Regional Heart Study. The prevalence of CHD by ECG criteria reaches nearly 20% by age 55–59, and by ECG or questionnaire the prevalence rate is an alarming 30%. Any approach to prevention that concentrates only on the 5–10% at the top end of the risk distribution curve is destined to miss the majority of cases that occur. A disease that is so
widespread demands a major community change for its amelioration.

I hasten to add that proponents of prevention are not aiming to achieve immortality for the population, but postponement of premature disease and death—an avoidance of a 27–30% prevalence at ages 50–59, or 20% at ages 45–49.

What is true of CHD prevalence is true also of plasma cholesterol levels. Current recommendations are that the mean plasma cholesterol of a population should, ideally, not exceed 200 mg dl⁻¹ (5.16 mmol l⁻¹). In the U.K., mean cholesterol levels are closer to 230–240 mg dl⁻¹ (5.9–6.2 mmol l⁻¹). The problem in a high rate population is not, therefore, only that of a high proportion at increased risk, but that the majority of individuals are at increased risk.

**Approaches to prevention**

There appears to be a consensus, even among strong critics of a dietary approach to prevention, that abolition of smoking is a necessary part of prevention of CHD. To stop there, however, would still leave a major problem. Data from the Whitehall study (Table 1) show that the major cause of death in non-smokers is still CHD. In fact, because lung cancer is such an uncommon cause of death in non-smokers, proportionately, CHD is marginally more common. These data do not argue for lack of benefit in giving up smoking. They argue that there are powerful causes of CHD operating among non-smokers and smokers. Smoking further increases the risk. This is illustrated in Fig. 3, in data taken from the baseline screening of the American Multiple Risk Factor Intervention Trial (MRFIT). Among smokers, and among non-smokers, blood pressure and serum cholesterol are strongly and independently related to CHD mortality. Whatever

**Table 1** Per cent of all deaths due to a particular cause. Whitehall men 40–64

<table>
<thead>
<tr>
<th>Cause</th>
<th>Non-smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>44</td>
<td>42</td>
</tr>
<tr>
<td>Stroke</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Other cancer</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>Other</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Figure 2 Prevalence of coronary heart disease in men in the British Regional Heart study according to London School of Hygiene Cardiovascular Questionnaire and ECG criteria of probable ischaemia.

Figure 3 Coronary heart disease mortality per 1000 in five years in white males aged 35–57 screened at the baseline of the American Multiple Risk Factor Intervention Trial.
the level of these two other risk factors, smoking further increases the risk.

This level of association between risk factors and mortality is sufficiently strong to argue strongly for a causal association — relative risk between highest and lowest risk categories is 7·1 (17·49 vs 2·4). This has also been interpreted as a relatively imprecise level of prediction\[8\], as the majority of people in the highest risk category do not develop CHD in the short to medium term, six years (although, undoubtedly they will in the longer term). Both assertions are reasonable and are compatible. It is likely that serum cholesterol, elevated blood pressure and smoking are implicated in the aetiology of CHD, but the level of prediction is such that there is substantial misclassification involved in classifying individuals: false positives as described above and, of great importance, false negatives, i.e. those who will go on to develop CHD but are not in the high risk category.

Another way of saying this is that the relative risk is high but not the population attributable risk. This is illustrated in Fig. 4, put together by Rose\[8\] from Framingham data. The dotted line shows a smoothed curve of the relation between CHD mortality and serum cholesterol — a not-quite doubling of risk between those with a cholesterol of >340 mg dl\(^{-1}\) (8·8 mmol l\(^{-1}\)) and those with values <190 mg dl\(^{-1}\) (4·9 mmol l\(^{-1}\)). The histograms show the distribution of serum cholesterol levels in the population. The numbers above the histograms are related to the population attributable risk. They represent the number of excess CHD deaths at each cholesterol level attributable to having a serum cholesterol greater than that of the lowest category, <190 mg dl\(^{-1}\). These calculations are based on the assumption that the cholesterol-CHD association is causal. Of 34 'attributable' deaths in this notional population, only 10 (29%) come from the approximately 10% of the population with a serum cholesterol \(\geq 280\) mg dl\(^{-1}\) (7·2 mmol l\(^{-1}\)). The majority of CHD deaths, and even the majority of deaths attributable to raised plasma cholesterol occur in the large group of the population at moderately increased risk. For example, nearly half of the attributable CHD deaths occur among people whose serum cholesterol levels were in the range 190–249 mg dl\(^{-1}\) (4·9–6·4 mmol l\(^{-1}\)) — not 'high risk' under any usual definition of the term.

A strategy aimed solely at high risk individuals, therefore, has the twin defects of type 1 and type 2 error — it labels individuals as 'high risk' who will not develop CHD in the medium term; and it misses the large number of individuals at moderately increased risk from whom came the majority of subsequent CHD cases. It is also costly, as it entails screening of the population to find those individuals with high lipid levels.

Rose\[8\] continues this argument by pointing out that we should be thinking not of high-risk individuals but of high risk populations. The point is made for blood pressure (Fig. 5). Comparing a 'high blood pressure population' (London civil servants) with a 'low blood pressure population' (Kenyan nomads), what is striking is not only that there is a lower prevalence of 'hypertension', however defined, among the Kenyans but that the whole distribution is shifted to the left. This changes the view of the public health task — not only to reduce the prevalence of people with high values, but to change the distribution of the whole population. A similar argument applies to plasma cholesterol levels.

Does a community approach to prevention work?

This question can be divided into two parts which I shall take in reverse order: (1) does change in plasma lipid levels lead to change in CHD incidence and mortality and (2) are strategies aimed at modifying plasma lipid levels in the community effective in doing so?

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**Figure 4** Prevalence distribution (histogram) of serum cholesterol concentrations related to coronary heart disease (CHD) mortality (interrupted line) of men aged 55–64. The number above each column represents an estimate of attributable deaths per 1000 population per 10 year period (from Rose\[8\]).
(1) LOWERING LIPIDS TO LOWER CHD RISK

It should be possible to make a causal judgement on the first question without appeal to clinical trial data. To take an analogy: we would feel fairly confident in asserting that giving up smoking leads to reduction in CHD, without the support of a trial of primary prevention — the only such trial did show modest support for the proposition11. Our confidence would derive from the strong epidemiological, clinical and pathological data supporting the smoking-CHD link. The data on ex-smokers suggests that, within 5 years, the excess CHD risk is reversible.

We should be able to make a similar judgement on the relation between plasma cholesterol and CHD: it is likely that someone whose plasma cholesterol is low through life will have a lower CHD risk than someone whose plasma cholesterol is high. It is also likely that a diet low in total fat, with a P:S ratio of 0.5 or above will help maintain plasma cholesterol at a low level. The epidemiological data do not tell us very precisely if the risks are reversible and over what period of time. The trial data are useful here. As summarized by Peto, earlier in this symposium, the diet and drug trials of lipid lowering point strongly to reversibility of risk. The reduction in CHD achieved by lipid lowering is broadly consistent with the predictions made from the epidemiological data.

It should be noted that for a high risk approach to prevention, the question of reversibility is crucial, because the aim is to reduce lipid levels that are already high. This is more akin to an intermediate prevention rather than true primary prevention. For a community approach to prevention the aim is broader and longer-term: it is to prevent high lipid levels from occurring — primary prevention — as well as to lower lipid levels that are already high.

For some commentators, the trials of reversibility are persuasive but they have, largely, been conducted in high risk individuals. May the results be extrapolated to the bulk of people at moderately increased risk? The consistency with epidemiological observations suggests that they can. In addition, the largest set of data linking serum cholesterol to mortality — that from the screening data on 348,874 men in the American MRFIT study — show (Fig. 6) that the relation of serum cholesterol to CHD is continuous, and fairly linear for the bottom four deciles of serum cholesterol.

For a community approach to prevention, it is somewhat artificial to ask if lipid-lowering, in isolation, lowers CHD risk. Multifactorial prevention is recommended, on the basis of observational data.
Table 2: Predicted reduction in CHD — based on plasma cholesterol, cigarettes, weight and systolic blood pressure (WHO-factory trial)

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.K.</td>
<td>-3.9</td>
<td>-11.2</td>
</tr>
<tr>
<td>Belgium</td>
<td>-15.8</td>
<td>-20.0</td>
</tr>
<tr>
<td>Italy</td>
<td>-28.2</td>
<td>-22.3</td>
</tr>
<tr>
<td>Cracow</td>
<td>-4.2</td>
<td>-41.3</td>
</tr>
<tr>
<td>All</td>
<td>-11.1</td>
<td>-19.4</td>
</tr>
</tbody>
</table>

There is some trial evidence to support it. The WHO factory trial\(^1\) showed that the greater risk factor reduction in Belgium and Italy, than in the U.K. (Table 2), corresponded with a reduction in CHD in Belgium (statistically significant) and Italy, but not the U.K. (Fig. 7).

(2) DOES INTERVENTION LEAD TO MODIFICATION OF RISK FACTORS?

It is the view of the investigators that the greater success in reducing risk factors (Table 2) in the Belgian and Italian arms of the WHO trial reflected their greater efforts at health education. Behind the disappointing U.K. results there may be a message. They were more successful at reducing smoking than other risk factors. Why? One explanation is that in the U.K., there has been a national shift in public opinion about smoking. There has been much publicity, some successful advertising, near-total commitment to anti-smoking by the medical profession. Smoking has shifted from a majority to a minority habit. Against this background, health education against smoking may be effective.

By contrast, until the last two or three years, there had been almost no public activity aimed at dietary change. The level of public ignorance is high, there has been difficulty of access to low fat foods in canteens, cafes, cafeteria and supermarkets, little attempt at health education, and the divisions within the medical profession have been given wide publicity. Against this background, there was little success in the U.K. trial in dietary change. A reasonable inference is that dietary education aimed at selected individuals has more chance of success if there are accompanying changes in the population and community at large. In the U.S.A. where dietary change appears to be fairly widespread, both the intervention and control groups in the MRFIT study reduced their diets — to the extent that there was a net difference in serum cholesterol of only 2% between the groups.

Other attempts at changing smoking and diet on a community scale, most notably in North Karelia\(^1\) and Stanford\(^1\) have had some success. In both cases, the approaches involved more than individually targeted health education.

Social class differences

Initiatives in health education/behaviour change are not equally successful in all social groups. For example, Table 3 shows data on smoking by social class in Great Britain.\(^1\) Between 1972 and 1982 smoking prevalence declined at a slightly faster rate in non-manual than manual classes, so that the higher prevalence in the manual classes remained undiminished.

The problem is more general than this. As Fig. 8 shows\(^1\), the improvement in CHD mortality and other cause of mortality, in England and Wales, over the decade 1971–1981 is not shared equally by all social groups. There has been a decline in CHD mortality in non-manual men and women, and increase in the manual. Similarly, regional differences

Table 3: Prevalence of cigarette smoking in Great Britain among men and women aged 16 and over\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>1972</th>
<th>1982</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>43</td>
<td>58</td>
</tr>
<tr>
<td>Women</td>
<td>38</td>
<td>45</td>
</tr>
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Figure 8  Standardized mortality ratios (SMR)* for select causes of death in Great Britain 1970–72 and 1979–83 for manual (○—○) and non-manual (■—■) groups. *For each cause the SMR in 1979–83 is 100 for each sex. (a) Men aged 20–64. (b) Married women aged 20–54 classified by husband’s occupation.

persist. We cannot be complacent. We do not understand completely the causes of CHD. A community intervention based on diet and smoking is likely to be beneficial. In the short term, at least, it is unlikely to reduce social inequalities in CHD mortality rates and these require urgent attention.

References