Public Health Classics

This section looks back to some ground-breaking contributions to public health, reproducing them in their original form and adding a commentary on their significance from a modern-day perspective. To complement the theme of this month's *Bulletin*, Michael Marmot comments on the 1985 paper by Geoffrey Rose on the study of the determinants of disease in individuals and in populations. The original paper is reproduced by permission of *The International Journal of Epidemiology*.

Economic and social determinants of disease

Michael Marmot[1]

Blessed, or burdened, with a traditional medical education, doctors are taught that the individual patient has priority. The ethical and just action is that which benefits the individual patient. What is, undoubtedly, a blessing for patients may be a burden for public health. Expanding the clinical role to embrace prevention commonly means focusing on the individual. This may include advice to pregnant women and young mothers, detection of risk factors, and counselling on behaviour change in middle age, or detection of early disease and decrements in functioning at older ages. These are all oriented to the detection and modification of individual risks.

The companion research strategy is the detection of individual risks — the understanding of what factors predict why one individual's risk of a particular disease should be greater than another's. The conceptual link with the individual focus of clinical medicine is seamless. The shift in focus is to prevention rather than treatment alone, but the focus on modifying individual risks is the same. Other disciplines, relevant to health, also have a primary focus on individual differences: genetics, psychology, microeconomics. How could a focus on the individual be misplaced? It is after all the individual who must be exposed to the environment, have a set of genetically determined susceptibilities, undergo pathological changes, sicken and, in the end, recover, continue with the condition, or die.

Those of us, from our various disciplines, trained in this way may lift our eyes from the individual in front of us, to observe that there are patterns of disease in the population: some countries or parts of countries have higher rates of disease than others; there are social, ethnic and gender differences in rates of disease occurrence. Might this not lead to evidence that factors outside the individual, in the environment, are related to risk?

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Armed with an individual difference approach to disease one might argue that a population characterized by a high rate of disease must have a high prevalence of high-risk individuals; and conversely for a low-risk population. Someone arguing the environmental case might cite the high rate of childhood illness in an area without a clean water supply as evidence against this individual focus. Such loose thinking would not convince the scientist with the individual focus who could point out that infected water would not be a cause of illness if individuals did not drink it or make up milk formula for infants with it. Further, there are surely individual differences in genetic susceptibility that determine why one exposed individual is more likely to succumb than another.

Into this longstanding debate came Geoffrey Rose (*1*). His argument was at once profoundly simple and simply profound. His thesis is that the causes of incidence rates may be different from the causes of individual cases within a population. This flows from the fact that the determinants of individual differences of characteristics within a population may be different from the determinants of differences between populations. There are important implications both for understanding causes and for strategies of prevention and public health.

At first glance the argument may be taken as a challenge to the fundamental notion that, in the end, it is the individual who must be exposed, sicken and die. It is not of course. For convenience, let us consider two levels of argument. At the simplest level, Rose's argument has to do only with range of exposures. In the population where every individual has smoked the same number of pack years of cigarettes, smoking would not be identified as a cause of lung cancer. Indeed, it would have no role in determining why one individual succumbed to lung cancer and another did not. To detect a relation between smoking and lung cancer one might compare this smoking population with another with low rates of smoking. Traditionally, such comparisons are treated with suspicion as subject to the ecological fallacy. It may not be the smokers in the

population that get lung cancer. Unless we could find a population in which there was variation of exposure to tobacco, such ecological analyses would be the main strategy open to us. We would probably accept it with reluctance as what we really wanted to know was whether an individual's smoking history was related to the individual's risk of lung cancer. This would come from a study of individual risks.

What if we were dealing with unclean water? Would the best study be one of individual risks? Not necessarily. If villages with clean water had a lower rate of childhood illness than villages without, would we argue that the best study was one of why one individual within a village became ill and another did not? This might provide very useful complementary information if, for example, children in families that boiled their water had lower rates of illness. But the main question might still be why one village had a higher rate of illness than another, and what could be done about it.

So far, so simple and relatively uncontroversial. The choice of studying differences within populations or differences between populations relates mainly to the range of exposures. But there is another level to the argument. These different questions may have quite different policy implications. The implications of the studies of between-individual differences might be advice about boiling water. The implication of the between-village differences may be engineering to provide a clean water supply. Rose lays out clearly the implications of his understanding for two different approaches to the prevention of chronic disease: the high risk and the population approach.

This leads on to the problem of how we deal with risks that are socially and politically determined. The individual level of analysis may be appropriate for understanding how individuals may be affected but may miss the operation of social causes. Amartya Sen has argued that famines do not occur in countries with well functioning democracies (*2*). How would a study of why one starving child in a refugee camp died more slowly than another help with this insight? How would it be relevant to policy? It would not help and would not be relevant. The relevant level of analysis is social even though the outcomes are disease and death.

Political economy and individual differences in susceptibility span the range of Rose's distinction between the causes of cases and the causes of incidence rates. In between these extremes, this distinction has far-reaching implications. Regrettably, they are not widely remembered. Let us examine a further example from the field of inequalities in health.

In Britain, by tradition, the term health inequalities means differences between social groups (*2, 3*). An economist put it to me that the social gradient in health (*4*) explained only a small part of total inequalities in health. The first problem was linguistic. As an economist he used the term inequality to apply to the total variance in health in the population. His conclusion was that the social group to which an individual belonged made a small contribution to the total individual variation in health. He is, of course, correct. But that conclusion applies to most explanations of individual differences in health. From the first Whitehall study of British Civil Servants, we calculated that only 7% of the individual level variance in lung cancer mortality could be explained by age, smoking and employment level (*5*). Another way of saying that smoking accounts for little of the individual differences in the occurrence of lung cancer, is to observe that most smokers do not die of lung cancer. Yet, the group differences are dramatic: 95% of lung cancer deaths in this cohort occurred in smokers.

Similar conclusions apply to the question of social inequalities in health. The determinants of individual differences in risk may be different from the determinants of differences between social groups. This accounts for reluctance (*6–8*) to apply the term inequality, as economists do, to individual differences in health (*9*).

Rose developed the ideas in this classic paper into his brilliantly clear book, *Strategy of preventive medicine* (*10*). His conclusion was: "The primary determinants of disease are mainly economic and social, and therefore its remedies must also be economic and social". ■

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Sick Individuals and Sick Populations

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Aetiology confronts two distinct issues: the determinants of individual cases, and the determinants of incidence rate. If exposure to a necessary agent is homogeneous within a population, then case/control and cohort methods will fail to detect it: they will only identify markers of susceptibility. The corresponding strategies in control are the 'high-risk' approach, which seeks to protect susceptible individuals, and the population approach, which seeks to control the causes of incidence. The two approaches are not usually in competition, but the prior concern should always be to discover and control the causes of incidence.

THE DETERMINANTS OF INDIVIDUAL CASES

In teaching epidemiology to medical students, I have often encouraged them to consider a question which I first heard enunciated by Roy Acheson: 'Why did *this* patient get *this* disease at *this* time?'. It is an excellent starting-point, because students and doctors feel a natural concern for the problems of the individual. Indeed, the central ethos of medicine is seen as an acceptance of responsibility for sick individuals.

It is an integral part of good doctoring to ask not only, 'What is the diagnosis, and what is the treatment?' but also, 'Why did this happen, and could it have been prevented?'. Such thinking shapes the approach to nearly all clinical and laboratory research into the causes and mechanisms of illness. Hypertension research, for example, is almost wholly preoccupied with the characteristics which distinguish individuals at the hypertensive and normotensive ends of the blood pressure distribution. Research into diabetes looks for genetic, nutritional and metabolic reasons to explain why some people get diabetes and others do not. The constant aim in such work is to answer Acheson's question, 'Why did *this* patient get this disease at this time?'.

The same concern has continued to shape the thinking of all of us who came to epidemiology from a background in clinical practice. The whole basis of the case-control method is to discover how sick and healthy individuals differ. Equally the basis of many cohort studies is the search for 'risk factors', which identify certain individuals as being more susceptible to disease; and from this we proceed to test whether these risk factors are also causes, capable of explaining why some individuals get sick while others remain healthy, and applicable as a guide to prevention.

To confine attention in this way to within-population comparisons has caused much confusion (particularly in the clinical world) in the definition of normality. Laboratory 'ranges of normal' are based on what is common within the local population. Individuals with 'normal blood pressure' are those who do not stand out from their local contemporaries; and so on. What is common is all right, we presume.

Applied to aetiology, the individual-centred approach leads to the use of relative risk as the basic representation of aetiological force: that is, 'the risk in exposed individuals relative to risk in non-exposed individuals'. Indeed, the concept of relative risk has almost excluded any other approach to quantifying causal importance. It may generally be the best measure of aetiological force, but it is no measure at all of aetiological outome or of public health importance.

Unfortunately this approach to the search for causes, and the measuring of their potency, has to assume a heterogeneity of exposure within the study population. If everyone smoked 20 cigarettes a day, then clinical, case-control and cohort studies alike would lead us to conclude that lung cancer was a genetic disease; and in one sense that would be true, since if everyone is exposed to the necessary agent, then the distribution of cases is wholly determined by individual susceptibility.

Within Scotland and other mountainous parts of Britain (Figure 1, left section)[1] there is no discernible relation between local cardiovascular death rates and the softness of the public water supply. The reason is apparent if one extends the enquiry to the whole of the

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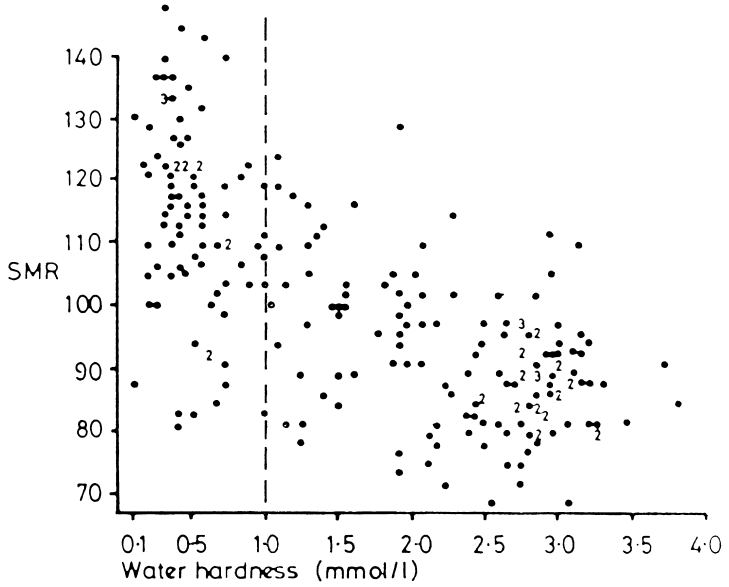

FIGURE 1 *Relation between water quality and cardiovascular mortality in towns of the UK.*[1]

UK. In Scotland, everyone's water is soft; and the possibly adverse effect becomes recognizable only when study is extended to other regions which have a much wider range of exposure ($r = -0.67$). Even more clearly, a case-control study of this question within Scotland would have been futile. Everyone is exposed, and other factors operate to determine the varying risk.

Epidemiology is often defined in terms of study of the determinants of the distribution of the disease; but we should not forget that the more widespread is a particular cause, the less it explains the distribution of cases. The hardest cause to identify is the one that is universally present, for then it has no influence on the distribution of disease.

THE DETERMINANTS OF POPULATION INCIDENCE RATE

I find it increasingly helpful to distinguish two kinds of aetiological question. The first seeks the causes of cases, and the second seeks the causes of incidence. 'Why do some individuals have hypertension?' is a quite different question from 'Why do some populations have much hypertension, whilst in others it is rare?'. The questions require different kinds of study, and they have different answers.

Figure 2 shows the systolic blood pressure distributions of middle-aged men in two populations—Kenyan nomads[2] and London civil servants.[3] The familiar question, 'Why do some individuals have higher blood

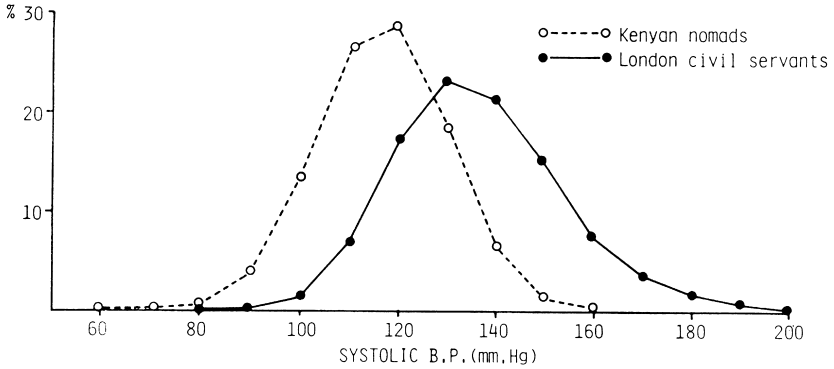

FIGURE 2 *Distributions of systolic blood pressure in middle-aged men in two populations.*[2,3]

pressure than others?' could be equally well asked in either of these settings, since in each the individual blood pressures vary (proportionately) to about the same extent; and the answers might well be much the same in each instance (that is, mainly genetic variation, with a lesser component from environmental and behavioural differences). We might achieve a complete understanding of why individuals vary, and yet quite miss the most important public health question, namely, 'Why is hypertension absent in the Kenyans and common in London?'. The answer to that question has to do with the determinants of the population mean; for what distinguishes the two groups is nothing to do with the characteristics of individuals, it is rather a shift of the whole distribution—a mass influence acting on the population as a whole. To find the determinants of prevalence and incidence rates, we need to study characteristics of populations, not characteristics of individuals.

A more extreme example is provided by the population distributions of serum cholesterol levels[4] in East Finland, where coronary heart disease is very common, and Japan, where the incidence rate is low: the two distributions barely overlap. Each country has men with relative hypercholesterolaemia (although their definitions of the range of 'normal' would no doubt disagree), and one could research into the genetic and other causes of these unusual individuals; but if we want to discover why Finland has such a high incidence of coronary heart disease we need to look for those characteristics of the national diet which have so elevated the whole cholesterol distribution. Within populations it has proved almost impossible to demonstrate any relation between an individual's diet and his serum cholesterol level; and the same applies to the relation of individual diet to blood pressure and to overweight. But at the level of populations it is a different story: it has proved easy to show strong associations between population mean values for saturated fat intake *versus* serum cholesterol level and coronary heart disease incidence, sodium intake *versus* blood pressure, or energy intake *versus* overweight. The determinants of incidence are not necessarily the same as the causes of cases.

HOW DO THE CAUSES OF CASES RELATE TO THE CAUSES OF INCIDENCE?

This is largely a matter of whether exposure varies similarly within a population and between populations (or over a period of time within the same population). Softness of water supply may be a determinant of cardiovascular mortality, but it is unlikely to be identifiable as a risk factor for individuals, because exposure tends to be locally uniform. Dietary fat is, I believe, the main determinant of a population's incidence rate for coronary heart disease; but it quite fails to identify high-risk individuals.

In the case of cigarettes and lung cancer it so happened that the study populations contained about equal numbers of smokers and non-smokers, and in such a situation case/control and cohort studies were able to identify what was also the main determinant of population differences and time trends.

There is a broad tendency for genetic factors to dominate individual susceptibility, but to explain rather little of population differences in incidence. Genetic heterogeneity, it seems, is mostly much greater within than between populations. This is the contrary situation to that seen for environmental factors. Thus migrants, whatever the colour of their skin, tend to acquire the disease rates of their country of adoption.

Most non-infectious diseases are still of largely unknown cause. If you take a textbook of medicine and look at the list of contents you will still find, despite all our aetiological research, that most are still of basically unknown aetiology. We know quite a lot about the personal characteristics of individuals who are susceptible to them; but for a remarkably large number of our major non-infectious diseases we still do not know the determinants of the incidence rate.

Over a period of time we find that most diseases are in a state of flux. For example, duodenal ulcer in Britain at the turn of the century was an uncommon condition affecting mainly young women. During the first half of the century the incidence rate rose steadily and it became very common, but now the disease seems to be disappearing; and yet we have no clues to the determinants of these striking changes in incidence rates. One could repeat that story for many conditions.

There is hardly a disease whose incidence rate does not vary widely, either over time or between populations at the same time. This means that these causes of incidence rate, unknown though they are, are not inevitable. It is possible to live without them, and if we knew what they were it might be possible to control them. But to identify the causal agent by the traditional case-control and cohort methods will be unsuccessful if there are not sufficient differences in exposure within the study population at the time of the study. In those circumstances all that these traditional methods do is to find markers of individual susceptibility. The clues must be sought from differences between populations or from changes within populations over time.

PREVENTION

These two approaches to aetiology—the individual and

the population-based—have their counterparts in prevention. In the first, preventive strategy seeks to identify high-risk susceptible individuals and to offer them some individual protection. In contrast, the 'population strategy' seeks to control the determinants of incidence in the population as a whole.

The 'High-Risk' Strategy

This is the traditional and natural medical approach to prevention. If a doctor accepts that he is responsible for an individual who is sick today, then it is a short step to accept responsibility also for the individual who may well be sick tomorrow. Thus screening is used to detect certain individuals who hitherto thought they were well but who must now understand that they are in effect patients. This is the process, for example, in the detection and treatment of symptomless hypertension, the transition from healthy subject to patient being ratified by the giving and receiving of tablets. (Anyone who takes medicines is by definition a patient.)

What the 'high-risk' strategy seeks to achieve is something like a truncation of the risk distribution. This general concept applies to all special preventive action in high-risk individuals—in at-risk pregnancies, in small babies, or in any other particularly susceptible group. It is a strategy with some clear and important advantages (Table 1).

TABLE 1 *Prevention by the 'high-risk strategy': advantages.*

1. Intervention appropriate to individual
2. Subject motivation
3. Physician motivation
4. Cost-effective use of resources
5. Benefit:risk ratio favourable

Its first advantage is that it leads to intervention which is appropriate to the individual. A smoker who has a cough or who is found to have impaired ventilatory function has a special reason for stopping smoking. The doctor will see it as making sense to advise salt restriction in a hypertensive. In such instances the intervention makes sense because that individual already has a problem which that particular measure may possibly ameliorate. If we consider screening a population to discover those with high serum cholesterol levels and advising them on dietary change, then that intervention is appropriate to those controlled trial of smoking cessation in London civil servants we first screened some 20000 men and from them selected about 1500 who were smokers with, in addition, markers of specially high risk for cardio-respiratory disease. They were recalled and a random half received anti-smoking counselling. The results, in terms of smoking cessation, were excellent because those men knew they had a special reason to stop. They had been picked out from others in their offices because, although everyone knows that smoking is a bad thing, they had a special reason why it was particularly unwise for them.

There is, of course, another and less reputable reason why screening enhances subject motivation, and that is the mystique of a scientific investigation. A ventilatory function test is a powerful enhancer of motivation to stop smoking: an instrument which the subject does not quite understand, that looks rather impressive, has produced evidence that he is a special person with a special problem. The electrocardiogram is an even more powerful motivator, if you are unscrupulous enough to use it in prevention. A man may feel entirely well, but if those little squiggles on the paper tell the doctor that he has got trouble, then he must accept that he has now become a patient. That is a powerful persuader. (I suspect it is also a powerful cause of lying awake in the night and thinking about it.)

For rather similar reasons the 'high-risk' approach also motivates physicians. Doctors, quite rightly, are uncomfortable about intervening in a situation where their help was not asked for. Before imposing advice on somebody who was getting on all right without them, they like to feel that there is a proper and special justification in that particular case.

The 'high-risk' approach offers a more cost-effective use of limited resources. One of the things we have learned in health education at the individual level is that once-only advice is a waste of time. To get results we may need a considerable investment of counselling time and follow-up. It is costly in use of time and effort and resources, and therefore it is more effective to concentrate limited medical services and time where the need—and therefore also the benefit—is likely to be greatest.

A final advantage of the 'high-risk' approach is that it offers a more favourable ratio of benefits to risks. If intervention must carry some adverse effects or costs