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Social Determinants of Health

Edited by

Michael Marmot

and Richard G. Wilkinson

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International Centre for Health and Society, University College London, UK

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Foreword

The health of populations is related to features of society and its social and economic organization. This crucial fact provides the basis for effective policy making to improve population health. While there is, understandably, much concern with appropriate provision and financing of health services and with ensuring that the nature of the services provided should be based on the best evidence of effectiveness, health is a matter that goes beyond the provision of health services. Policies pursued by many branches of government and by the private sector, both nationally and locally, exert a powerful influence on health – and this book shows the direction in which we should be going. Just as decisions about health services should be based on the best evidence available, so should policies related to the social determinants of health.

Researchers associated with the International Centre for Health and Society at University College London have accumulated a wealth of knowledge on the social determinants of health. The World Health Organization Regional Office for Europe's Centre for Urban Health was concerned to package that knowledge in a way that is useful to policy-makers. The result was *Social Determinants of Health – The Solid Facts* (Wilkinson and Marmot 1998). This accumulation of evidence was also fundamental to the *Independent Inquiry into Inequalities in Health* which I was commissioned to chair by the Government in Britain (Acheson 1998). Indeed, many of the authors of this book were closely involved in the presentation of evidence that underpinned the formulation of recommendations for policy development that resulted from that Inquiry.

This book results from the welcome efforts of members of the International Centre for Health and Society and their collaborators to summarize their research evidence around themes useful to policy-makers. Policy making will always involve a multiplicity of influences. The research summarized here shows that important among those influences must be the evidence on the social determinants of health.

Sir Donald Acheson
Chairman
International Centre for Health & Society
University College London

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1 Introduction

Michael Marmot

1.1 Introduction

The distinction between pure and applied research is, appropriately, blurred. Research that increases knowledge and understanding is of social value whether or not its practical implications are followed through in the short term. Curiosity-driven research might turn out to have greater application than research directed at an immediate practical problem. Knowledge and understanding might well have been the main social justification that most of the authors of this book would have given for their research. Those of us involved in research on social inequalities in health feel particularly vulnerable on the 'so what?' question. Time and again, we have been confronted by the question of whether research on social inequalities in health has any practical application. The hard form of this argument asserts that there are no societies without social inequalities, hence the research has little relevance.

Even an area with such obviously practical implications for public health as the research on smoking as a cause of premature mortality was initially greeted with some scepticism. If individuals will not change their behaviour, so the argument ran, what use is it to show that smoking increases risk of illness? The smoking example perhaps has some relevance. Indeed, it was the case that 'simply' showing the smoking disease link was insufficient to benefit the public health. There have been a number of important contributors to policies to reduce the burden of smoking-related diseases. Important among these have been summaries of the evidence in a form amenable to policy makers, and widespread public information about the links between smoking and health. Both of these have been important in developing policies which relate to taxation, advertising and sponsoring, health education, labelling, and restriction in public places. What concerns us here is not the details of smoking control policies but how to promote a discourse among policy makers and the public about relevant research findings. In this example we might note that we are interested not only in smoking as a cause of disease but in the determinants of smoking: the causes of the causes.

This seemed to be the right analogy when the Centre for Urban Health, WHO Regional Office for Europe, approached us at the International Centre

for Health and Society at University College, London to inquire if we could summarize work on the social determinants of health in 10 messages. The aim was that these messages should be relevant both to policy makers and the public. An important consideration was that each message should be supported by evidence. This book grows directly out of that process. Members of the International Centre for Health and Society and colleagues, represented in this book, developed 10 messages that were brought together in a booklet *Social determinants of health – the solid facts*, distributed widely by WHO to policy makers, researchers, and practitioners (Wilkinson and Marmot 1998). The ten messages form the topics for Chapters 2–11 of this book. Each of these chapters presents a summary of relevant research, giving the evidence underlying the message. A description of the WHO campaign, of which the Solid Facts is a part, and for which this book provides the evidence is given in the Epilogue.

Two key assumptions underlie the approach we took in producing messages for WHO and the chapters in this book. First, the impact of the social environment on health, as represented by social inequalities in health, is not a 'given'. By understanding how the social environment affects health, its specific features and pathways, it is potentially possibly to affect these with consequent impact on health. The second assumption follows from the first, namely that the social environment is not inchoate and amorphous, but that specific social determinants of health can be characterized and their separate effects on health studied.

1.2 Social and economic environment and health

1.2.1 Medical care?

For many commentators there is the untested assumption that inequalities in health arise from inequalities in health care. In one sense, it would be quite easy to see how this conflation of two disparate ideas could happen. In the industrialized world, countries spend between about 6 per cent and 14 per cent of gross domestic product on health care. It therefore looms large in health policy discussions. The logic might be characterized as follows: countries would not spend this much money on health care, actually medical care, if it were not effective; there are undoubted inequalities in access to medical care; therefore inequalities in health must result from inequalities in access to and delivery of medical care.

There is, of course, a gap in this logic. Because there are inequalities in access, it does not follow that these are the causes of inequalities in health. On the contrary, there are inequalities in the onset of new disease, which is not a medical care issue, and there are inequalities in mortality from diseases not amenable to medical intervention (Mackenbach et al. 1989).

The purpose of this book, however, is not to examine the effectiveness and limits of medical care. Universal access to high-quality and effective medical care (if it were not effective it could not be high quality) should be part of an

advanced civilized society. Lack of access to effective medical care is likely to lead to unnecessary morbidity and suffering. For the purposes of this book we take this as unproblematic and not requiring further elaboration. Medical care is only relevant to this book's discussions of the social determinants of health if we have somehow got it wrong. In other words, are we mistaken in concluding that childhood environment, the work environment, unemployment, patterns of social relationships, social exclusion, food, addictive behaviour, and transport are related to causation of ill health when, in fact, these apparent relationships could all be accounted for by lack of access to good-quality medical care? Clearly, we judge that these relationships are causal and are determinants of differences in disease rates within and between societies. They create problems with which the medical care system must cope. Defects in the medical care system are not the cause of the problems.

1.2.2 Constitution or individual risk?

There is much interest in the genetic basis of human disease. Researchers in this tradition look for the interaction of genetic predisposition with individual exposures to account for individual differences in disease. Thus, for example, smoking causes lung cancer; most smokers do not die of lung cancer; there must therefore be some genetic or other factor determining which smokers succumb and which do not. We do not question such a formulation, but point out that it is only part of the picture. It is important to ask whether it can account for differences in risk of disease between *populations.*

Two of the clearest types of evidence demonstrating the importance of the environment come from migrant studies and time trends. When people change environment their patterns of disease risk changes. In my earliest work on epidemiology, I was part of a collaborative group studying heart disease and stroke in men of Japanese ancestry living in Japan, Hawaii, and California (Marmot et al. 1975; Syme et al. 1975; Worth et al. 1975; Winkelstein et al. 1975; Nichaman et al. 1975). The further the Japanese migrated across the Pacific, the higher their incidence of coronary heart disease and the lower the rate of stroke. One might be tempted to argue that this is not a demonstration of the importance of the environment in changing risk of disease, but that the Japanese who were genetically more likely to develop heart disease were more likely to leave Japan. If there were such selective migration, this genetic predisposition would have to determine not only the fact of leaving Japan but the distance travelled. Japanese in Hawaii have rates of heart disease intermediate between those in Japan and those in California. A simpler interpretation of the facts is that environment and life style affected disease rates. In California, we had evidence that the rate of heart disease went up with degree of acculturation (Marmot and Syme 1976). Whatever the importance of genetic predisposition, the environment in which these people lived played an important role in determining their disease risk.

Over short periods of time, genetic predisposition to disease of individuals and populations cannot change materially but disease rates can change markedly. Figure 1.1 shows the changing pattern of suicide mortality by socio-economic status (Registrar General's Social Class) in England and Wales. Over the 20 year period, the social gradient increased dramatically in a way that could not be accounted for by a shift of predisposed individuals between social classes (Drever et al. 1996).

It is also worth making a distinction between individual risk factors and environmental causes of disease. Syme has pointed to two limitations of the individual risk-factor approach. First, individual risk factors explain only a part of variations in the occurrence of disease. Secondly, it has proved difficult to modify individual risk factors by trying to persuade individuals to change their behaviour (Syme 1996). There has been success in modifying individual risk in people at especially high risk, such as drug treatment of high cholesterol and high blood pressure. As Rose has pointed out, while this has benefit for the individuals concerned, it makes a limited contribution to reducing disease rates in the whole population (Rose 1992). Rose goes further and suggests that the causes of individual differences in disease may be different from the causes of differences between populations. It is these population determinants that are the focus of this book.

1.2.3 Social and economic environment – non-infectious disease

The overall relation between economic fortunes and health is shown in Fig. 1.2, taken from the World Development Report (World Bank 1993). It

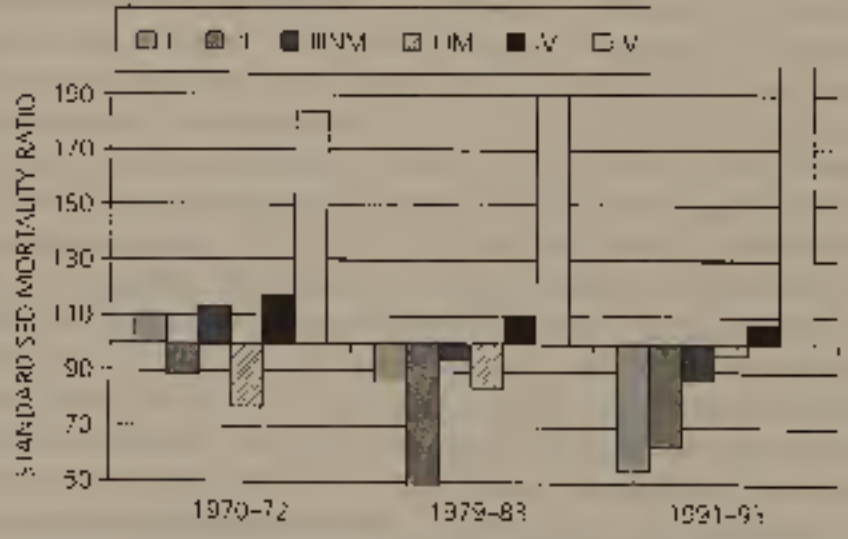

Fig. 1.1 Suicide by social class in England and Wales, males, 1970–93. 1970–72 does not include undetermined injury. Professional, II, employers and managers, IIINM, intermediate and junior non-manual, IIIM, skilled manual and non-professional, IV, semi-skilled manual and personal service, V, unskilled manual. (From Drever et al. 1996.)

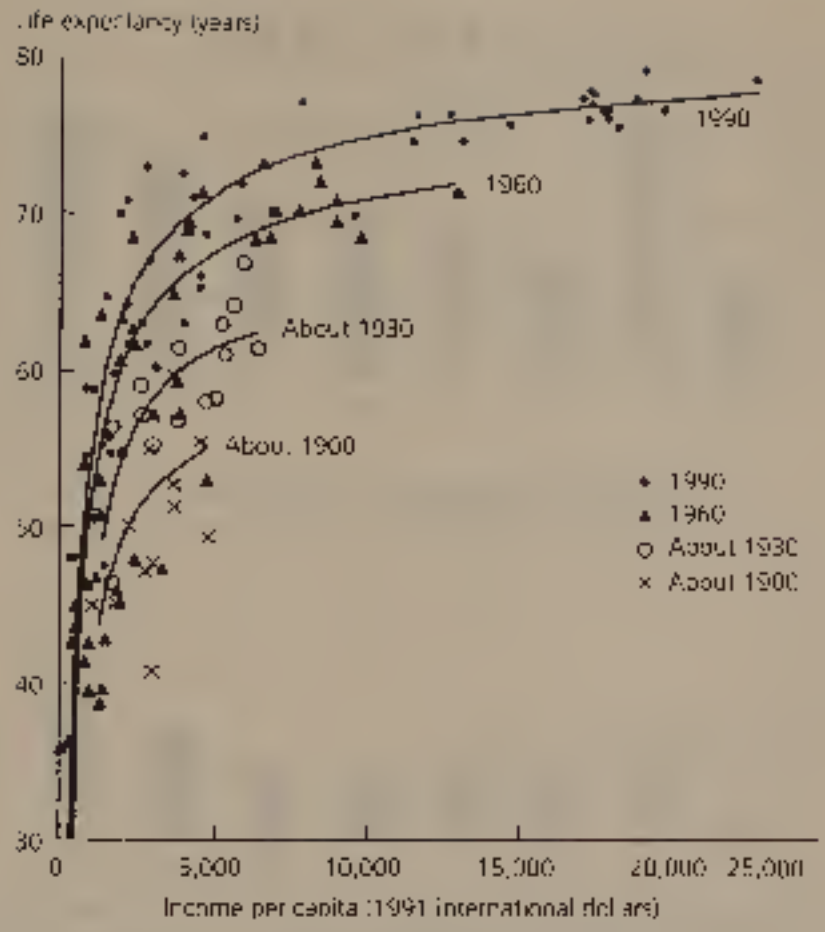

Fig. 1.2 Life expectancy and income for selected countries and periods (World Bank 1993)

shows that, for the poor countries of the world there is a clear relation between gross national product (GNP) per capita and life expectancy. At the lower end of the range of GNP, the relationship is quite steep: small increases in per capita GNP are related to relatively large increases in life expectancy. This causes little surprise. Malnutrition and infectious diseases that result in a high burden of maternal, infant, and childhood deaths are related to poverty. Improvement in living conditions that goes along with increases in GNP in poor countries will result in improvements in life expectancy. This is well understood.

What is perhaps less well understood is that the major causes of morbidity and mortality in developed countries, non-infectious diseases and external causes of death, are also related to the social environment. Increasingly, these are also the major health problems for the developing world. Figure 1.3 (a and b) is taken from the WHO Global Burden of Disease study (Murray and Lopez 1996). By looking at probability of death between 15 and 60 years of age, it removes the contribution of deaths in infancy, childhood, and old age. It shows that by 2020, for every region of the world, chronic diseases, including cardiovascular disease, cancer, and respiratory disease will be more important causes of death

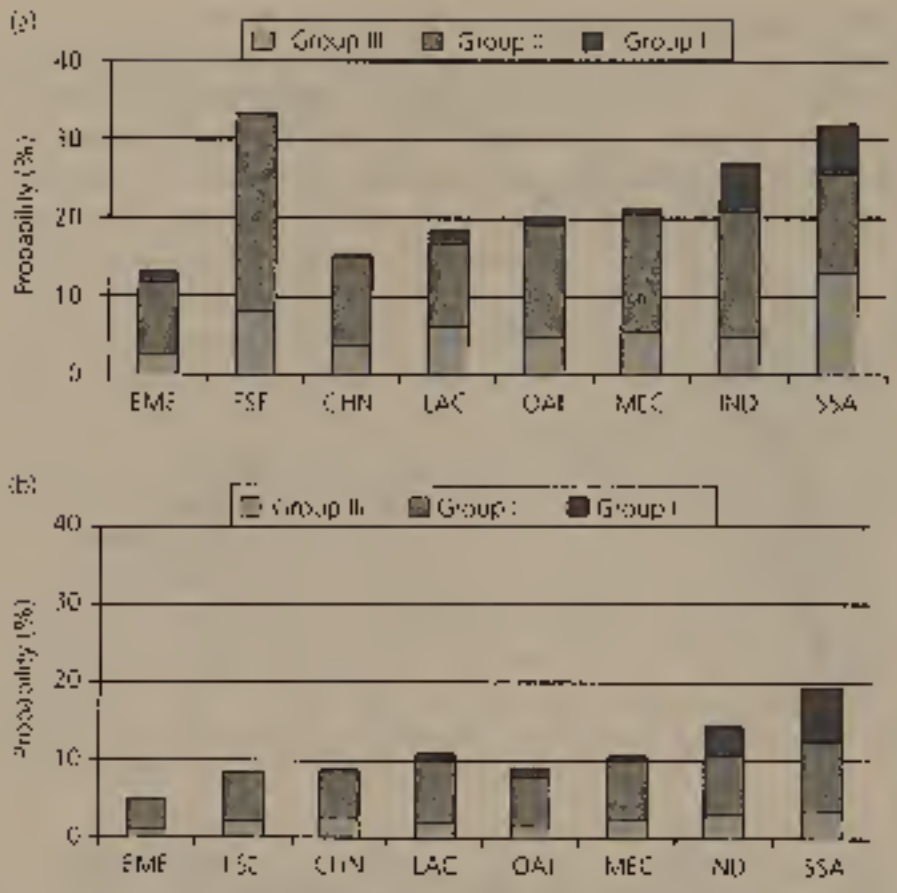

Fig. 1.3 Probability of death between ages 15 and 60 in year 2020: (a) males, (b) females. Group I, infectious, perinatal, nutritional, maternal. Group II, cardiovascular disease, cancer, respiratory, other. Group III, external causes. EME, Established market economies. FSE, formerly socialist economies of Europe. CHN, China. LAC, Latin America and the Caribbean. OAI, other Asia and islands. MEC, Middle Eastern crescent. IND, India. SSA, Sub-Saharan Africa. (From Murray and Lopez 1996.)

than the group including infections, perinatal, nutritional, and maternal deaths. Figure 1.3b shows the probability of death between 15 and 60 to be considerably lower in women than men. The death rate due to external causes is lower and, once again, the chronic diseases including cardiovascular disease emerge as the major cause of death.

Figure 1.3 shows the high mortality in middle-age in the former socialist economies of central and eastern Europe. In men, mortality rates were actually higher in these countries than in any other region of the world. This is a new development. Figure 1.4 (a and b) shows that around 1970 life expectancy in the countries of central and eastern Europe was similar to that in the European Union (Marmot and Bobak 1997). Over the subsequent two and a half decades life expectancy continued to improve steadily in the EU and Nordic countries and declined in the countries of central and eastern Europe. In women there was not a decline in life expectancy but the gap between 'west' and 'east' increased. The former Soviet Union, and then

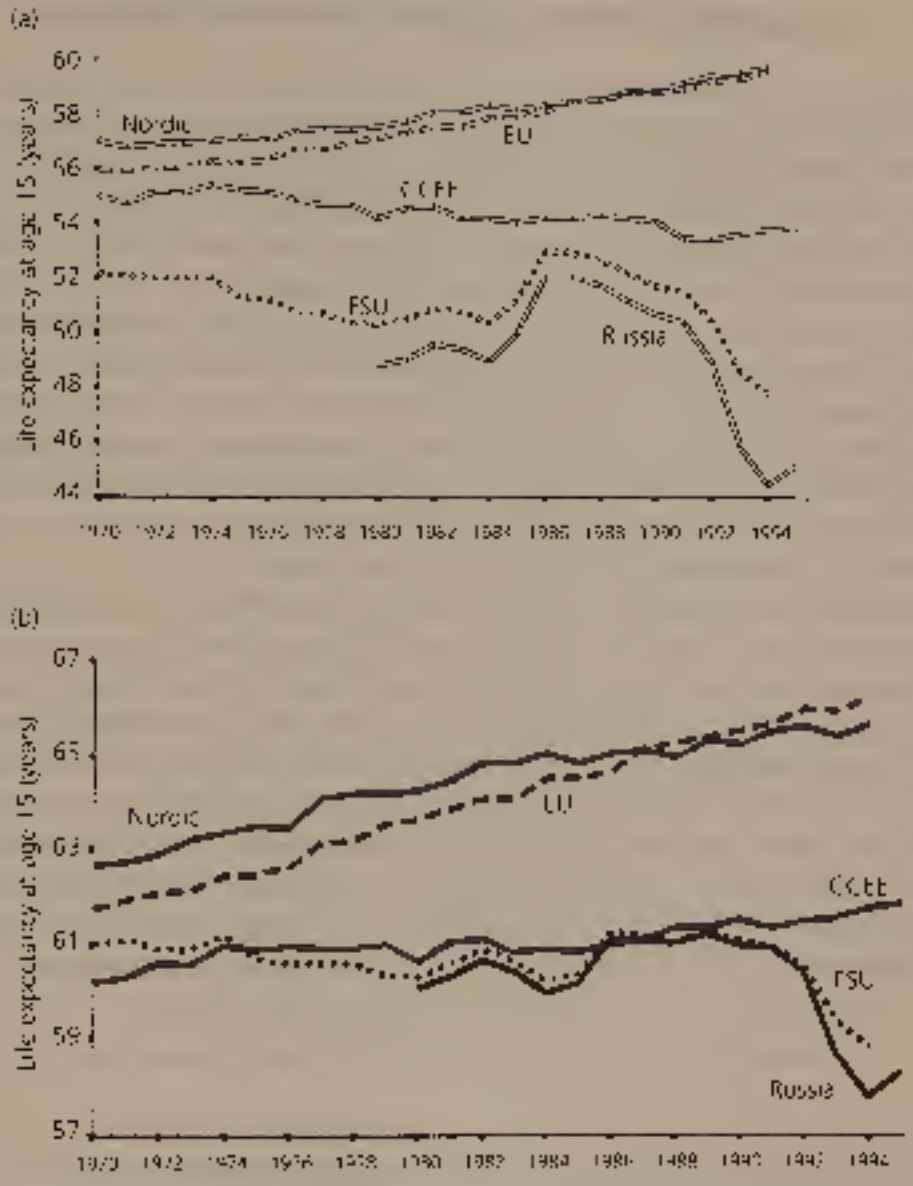

Fig. 1.4 Life expectancy at age 15 in Europe: (a) men; (b) women. CCEE, Countries of Central and Eastern Europe; EU, European Union; FSU, former Soviet Union. (From Marmot and Bobak 1997.)

Russia, shows even more marked divergence from the 'west'. The apparent increase in life expectancy in Russia around 1985 has been attributed by some to the Gorbachov reforms designed to reduce alcohol consumption (Leon et al. 1997). Similarly, it has been argued that alcohol has made a major contribution to the marked decline in life expectancy in more recent years (Leon et al. 1997), although the magnitude of this contribution has been questioned (Bobak and Marmot 1996).

More than half of the east/west difference in mortality is due to cardiovascular disease and a further 20 per cent per cent to external causes of death (Marmot and Bobak 1997).

1.3 Accounting for the global burden of disease

Figure 1.5 is adapted from the work of Murray and Lopez (Murray and Lopez 1996). It shows their best estimates of how much of the global burden of deaths could be attributed to different risk factors. In their analyses the largest single contributor is malnutrition, accounting for nearly 12 per cent of deaths. This, and all the other major risk factors that they consider account for about 40 per cent of the global burden of deaths. How are we to think about these figures? One obvious response is to assume that measurement error or other data analytical problems has led to an under-estimate of the contribution of risk factors. Possibly, but it seems unlikely that this would change the conclusion that about half of the global burden of deaths remains unexplained by major risk factors. Certainly the figures fit well with analyses of cardiovascular disease that suggest a similar conclusion in relation to international differences (Tunstall-Pedoe et al. 1994).

It also seems unlikely that Murray and Lopez (1996) have 'forgotten' a major risk factor. Better specification of 'malnutrition' could perhaps encompass the nutritional causes of cardiovascular disease and cancer, and thereby account for a larger proportion of deaths. Be that as it may, there are other reasons for believing that something important is not included in this analysis of risk factors. There is a developing research base that relates disease patterns to the organization of society and the way society invests in its human capital (for example, Amick et al. 1995; Blane et al. 1996; Wilkinson, 1996). Not only may these social determinants of health start to fill in the 'other' category in Fig. 1.5, but several of the risk factors in Fig. 1.5 themselves have social determinants.

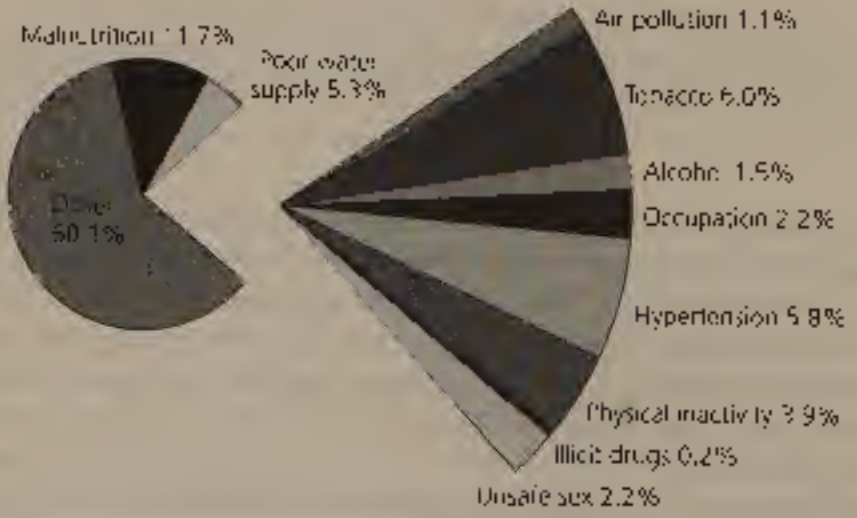

Fig. 1.5 Global burden of deaths attributable to risk factors, 1990 (from Murray and Lopez 1996).

1.3.1 Sustainable development and chronic disease

One formulation of sustainable development is:

> 'development that meets the needs of the present without compromising the ability of future generations to meet their own needs' (Interdepartmental Working Group on UK's Sustainable Development Strategy of 1994).

One way of thinking about it is the developing of goods and services which meet people's needs but involve the use of fewer natural resources. This implies managing and protecting the natural environment and resources. To take one example, Fig. 1.6 shows projected global energy use up to the year 2010. Although beyond the present purpose, we may note the inequities here in that the projected increase in energy use of non-OECD countries still does not bring them up to the level of use in the OECD (Organization of Economic Co-operation and Development) countries (Joint publication by World Resources Institute, United Nations Development Programme, 1998). We may point to two problems relevant to our current concern. First, this increasing use of energy will lead to increasing levels of air pollution, not to mention global warming due to emission of greenhouse gases. Murray and Lopez (1996) estimate that about 5 per cent of deaths in the former socialist economies could be attributed to air pollution. The second problem relates to transport. A significant proportion of this global energy use will be from the automobile. The downside to the convenience afforded by the car is decreasing use of walking and cycling as modes of transport. These have the advantage to individuals of being readily accessible to all and, in the richer countries, reducing the burden of obesity and of cardiovascular disease.

1.3.2 The natural environment and the social environment

There is now active work enlarging the concept of sustainable development to include the building of sustainable communities for people to live and work in

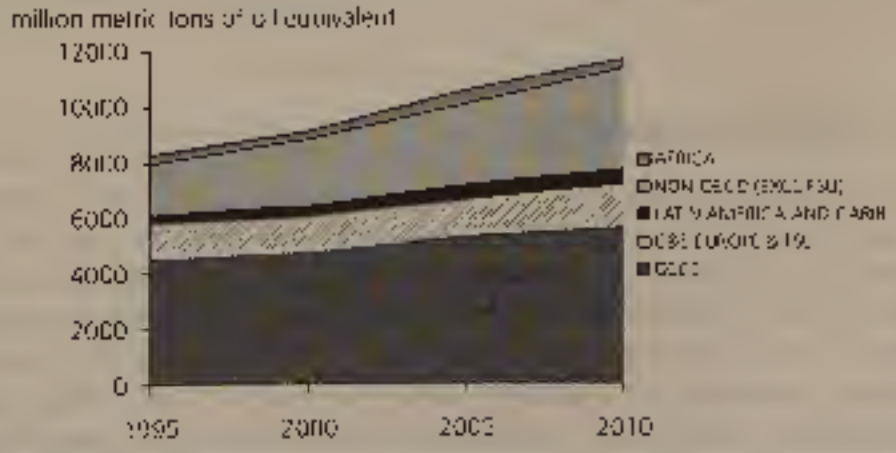

Fig. 1.6 Projected global energy use 1995–2010. FSU, former Soviet Union; OECD, Organization of Economic Co-operation and Development. (from World Resources Institute and United Nations Development Programme 1998).

Although the major focus of this work is not the improvement of health, the areas it covers are relevant to the social determinants of health. In the broadest terms, the relevance of social determinants was illustrated above in Fig. 1.2, which showed the association between GNP and life expectancy.

There are three further observations to be made about Fig. 1.2. First, for a given level of income (standardized to $1991), life expectancy has been increasing over the four time periods shown. This could be attributed to improvements in public health and medical care. But it could also be related to the causes underlying the other two observations. Second, there is a scatter of life expectancy around a given GNP level. This is illustrated further in Fig. 1.7 (a, b and c). It compares countries with equivalent levels of GNP and shows that adult mortality is inversely related to levels of adult literacy. The suggestion here is not necessarily that adults who are literate will have better health than those who are not, although that is plausible. Rather, one should view adult literacy as an indicator of investment in human capital. Even poor countries who invest in human capital will have better health than those who do not.

The third observation relates to the flattening of the curve in Fig. 1.2. Above a GNP per capita of about $5000, the relationship between GNP and life expectancy is weak. Wilkinson shows that, for these richer countries, there is a strong relation between income inequality of a country and life expectancy (Wilkinson 1996).

In the final chapter of this book Wilkinson develops the argument that income inequality reflects the social environment. His thesis is that a more fragmented society goes along with wider income inequalities. Income inequalities may be a driver of the system. It is possible, however, that fragmentation of the social system may have profound adverse effects on health, whatever is happening to income inequalities. This may be relevant to the trends in central and eastern Europe illustrated in Fig. 1.4 (Walberg et al. 1998). They may be a reflection of a decline in the degree to which these countries provide suitable circumstances for people to live and work in. This may be thought of as erosion of social capital, or unsustainable development.

1.4 Social inequalities

If the social environment is an important cause of ill health, this is likely to be manifested as social inequalities in health. For three decades we have been following the health of British civil servants in the Whitehall studies. This may, at first, seem to be an unlikely choice of population to use in order to study social inequalities in health. These people all live in a relatively affluent part of a relatively affluent country. They are office based, non-industrial employees in stable jobs, and, in the first Whitehall study, they were all white males. The results of 25 year follow-up of the first Whitehall study are shown in Fig. 1.8 (Marmot and Shipley 1996). At the

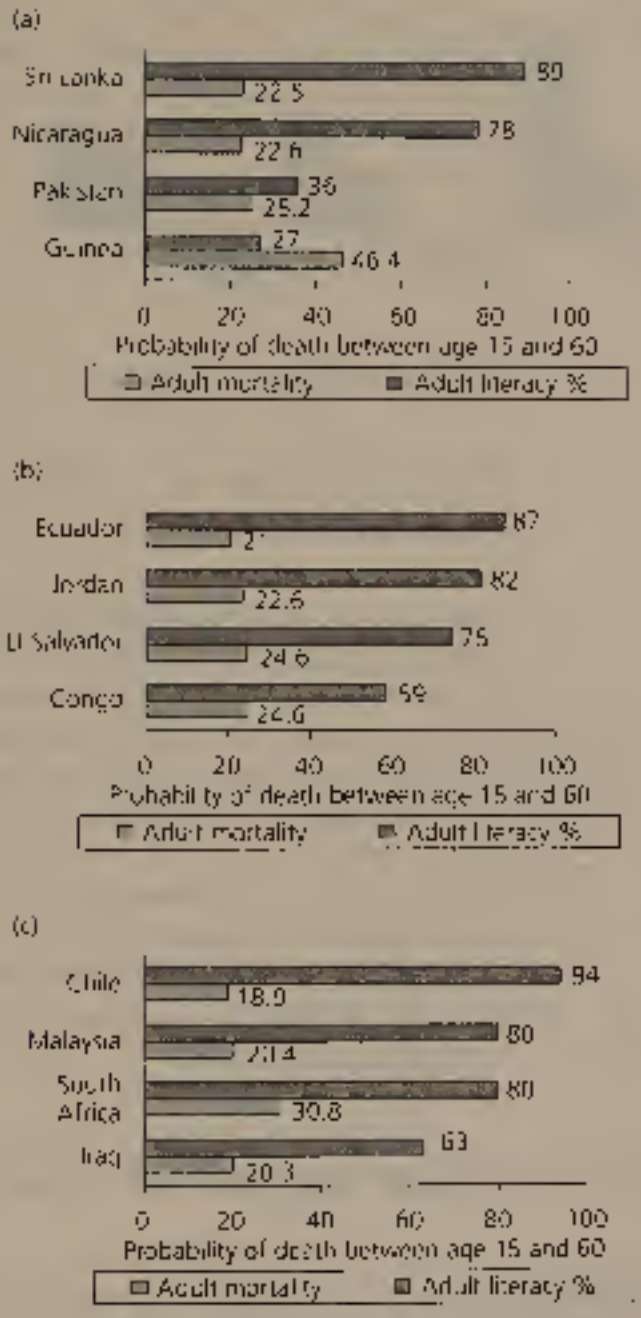

Fig. 1.7 Male mortality and literacy: (a) GNP per capita $400–500; (b) GNP per capita $1000–1100; (c) GNP per capita $2200–2600. (From Human Development Report 1994.)

younger ages, men in the lowest, office support, employment grades have a four times higher mortality rate than men in the highest administrative grade. Just as striking as the difference between top and bottom is the gradient. Position in the hierarchy shows a strong correlation with mortality risk. Men second from the top have higher mortality than top-grade civil servants; clerical officers have higher mortality rates than the men above them in the hierarchy.

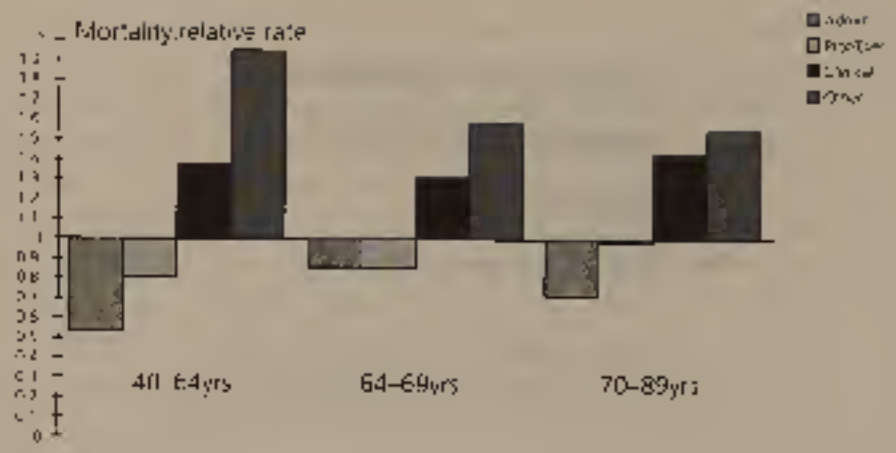

Fig. 1.8 All cause mortality by grade of employment, Whitehall men 25 year follow-up (from Marmot and Shipley 1996).

There are abundant data showing a link between poverty and ill health. These results from Whitehall have influenced us in coming to the view that inequality is also important. The problem of inequality in health is not confined to the poorest members of society but runs right across the social spectrum. In Whitehall the social gradient was seen not only for total mortality, but for all the major causes of death, including coronary heart disease and stroke (Marmot et al. 1984).

In several of the countries of central and eastern Europe, all-cause mortality and heart disease mortality are higher in people with less education. As mortality has increased in those countries between the early 1980s and early 1990s, the mortality disadvantage in those of lower status has increased (Blazek and Dzurova 1997; Shkolnikov et al. 1998).

1.5 Social determinants: selection or causation?

As David Blane explains in chapter 4, the causal direction may be two-way: health may determine socio-economic position as well as social circumstances affecting health. Where the link is between individual social status and health outcome, this has superficial plausibility. Health could be a major determinant of life chances. This has been termed health selection. The implication being that health 'selects' people into different social strata.

Perhaps one way of judging the social causation hypothesis is to consider the merits of the alternate, health selection hypothesis. For the purpose of argument, let us consider the extreme case to see whether *all* the observed relations could be the result of health selection. This would lead to the argument that ill health led to: lower position in the social hierarchy, social exclusion, having a job that offered less opportunities for control and imbalance between efforts and rewards, increased risk of unemployment and job

insecurity, living in a deprived neighbourhood, having less participation in social networks, eating worse food, indulging in addictive behaviour, and breathing in polluted air, as well as being sedentary.

These have varying degrees of plausibility. Plausibility, however, is no guarantee that selection is actually operating. Apart from judging the relative plausibility of the causation and selection arguments, there have been a number of other research strategies, of which two are worth highlighting. The first deals with the question head on. Longitudinal studies allow a judgement to be made as to which came first, health or social circumstances. This has been examined in considerable depth by a number of studies (Goldblatt 1990). Perhaps the clearest answers come from the birth cohort studies referred to by Wadsworth (Chapter 3) and studied also in the 1958 birth cohort (Power et al. 1991). In the 1946 birth cohort, children who showed evidence of illness were less likely to be upwardly mobile than healthy children and more likely to be downwardly mobile (Wadsworth 1986). The effect was small however and could not account for the relation between social position and ill health in adulthood (Blane et al. 1993).

The second approach to dealing with selection is to examine the effect of social circumstances that could not have plausibly been affected by health status of individuals. For example, it is plausible that sick individuals may be more likely to lose their jobs and remain unemployed than healthy people. Where unemployment is imposed from the outside, as in large-scale factory closures, individual illness is unlikely to be a determinant of unemployment status. This evidence is reviewed in the chapter by Bartley (Chapter 5). Similarly, geographic and population differences in disease rates could not all be attributed to selective migration of healthy people to 'good' areas or of unhealthy people to 'bad' areas. More plausibly, as elaborated in the chapters by Shaw et al. (Chapter 10) and Wilkinson (Chapter 12), these area differences in disease rates relate to characteristics of the social environment. The causal direction, therefore, is likely to be from social environment to illness, not the other way.

1.6 How does the social environment affect health?

As stated above, in the discussion of Fig. 1.2, for the poor countries of the world an increase in living standards that reduces malnutrition and infectious disease will make a major contribution to improving health. These are the most obvious ways that the social environment can affect health. This book is concerned primarily with the health problems of the developed world, although, as the Global Burden of Disease study shows, these will increasingly become the problems of the developing world.

This book attempts to unpick the social environment in a way that is susceptible to scientific inquiry and relevant to policy. It focuses on the environment rather than on individual psychology and behaviour, although

these may be influenced by the environment. The categories in the chapters may overlap, because the more we attempt to unpick the environment in which people live and work and separate it into discrete analytical categories, the further we retreat from reality. Nevertheless, the attempt to be specific is potentially important for the development of policy. We have not recommended specific policies but areas where our judgement of the scientific evidence suggests that policies should be developed. Our hope is that we may rouse awareness of these important issues and contribute to informed debate.

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2 Social organization, stress, and health

Eric Brunner and Michael Marmot

2.1 Introduction

Two major health problems have been described in this book that illustrate the social determinants of health: the social gradient in disease, and the striking differences in life expectancy between the countries of western Europe and those of central and eastern Europe that have emerged over the last 25 years. In relation to the social gradient, observed in the Whitehall studies of British civil servants (Marmot et al. 1984, 1991), we argued that it is significant that it runs right across the social hierarchy from the top employment grades to the bottom. The fact that civil servants in the second grade from the top have worse health than those at the top shows that we are not dealing only with the effects of absolute deprivation. Rather, position in the hierarchy is important. This suggests some concept of relative rather than absolute deprivation. This is a psychosocial concept. What this might mean is discussed in other chapters of this book, for example chapters 6 and 8. Is it plausible that circumstances in which people live and work, which differ according to where they are in the hierarchy, could powerfully influence health by acting through psychological pathways?

Similarly, when we review the evidence from central and eastern Europe (Bobak and Marmot 1996), we come up with the hypothesis that psychosocial factors play an important role in accounting for the worse health of those countries compared to the more favoured countries of the 'West' Fig. 2.1. Is it again plausible that these factors might be crucial and, if so, how do they operate to cause disease?

This chapter takes up the issue of biological plausibility (Brunner 1997). There are, in fact, two broad issues here. First, is it plausible that the organization of work, degree of social isolation, and sense of control over life, could affect the likelihood of developing and dying from chronic diseases such as diabetes and cardiovascular disease? The answer is an emphatic 'yes'. As we shall discuss, a variety of biological pathways can plausibly change the risk of developing major disease. The second issue is more complicated: do any of the

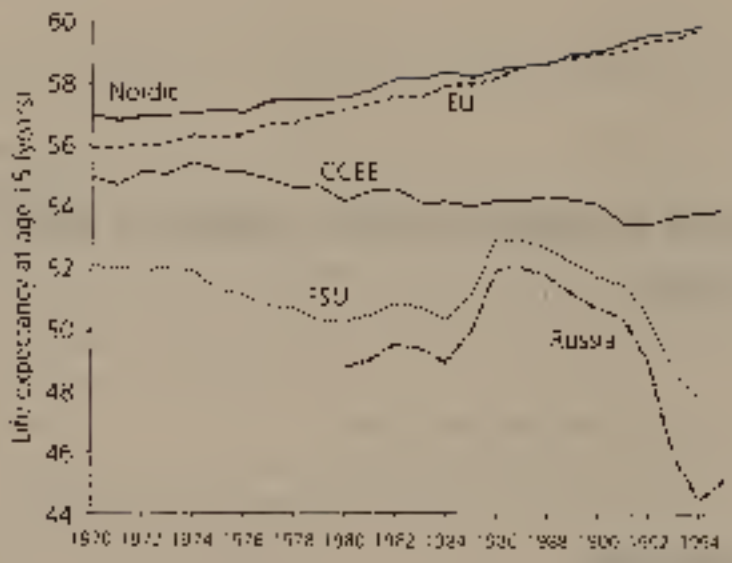

Fig. 2.1 Life expectancy trends in the EU, Nordic countries, and countries of the former USSR and central and eastern Europe, 1970–95. The powerful impact of social organization on health is seen over the period of transition from the centrally planned to the free market economy in central and eastern Europe. CCEE, Countries of Central and Eastern Europe; EU, European Union; FSU, former Soviet Union. (Source: WHO Health for all data.)

plausible biological pathways actually operate: that is, not could they cause disease, but do they? The evidence on this is incomplete and is an important topic for current and future research, but it is sufficiently suggestive to point to hypotheses for testing.

The issue of biological plausibility is, of course, important as a contribution to discussion of whether the variety of associations observed in this book represent causation. To take one example: does low socio-economic status lead to poor health, or does poor health lead to low socio-economic status? This is variously described as health selection, reverse causation, or, for economists, endogeneity. There are various ways of designing studies or analysing data to address this question. One contribution is to set out a plausible model of how socio-economic status could influence health and then test the various stages of the model. We set out an example of such a model in this chapter. Part of the model describes how factors in the environment, acting through the central nervous system, could influence biology to cause ill health.

2.2 The personal and the social

In the past, the debate about stress and health has seen stress as a property of individuals. This has led to the view that what is stress for one person is stimulation for another. The approach we take is different. We relate the biological response of the individual to the social environment acting upon

him or her. The response will clearly be influenced by previous experience and perhaps genetic make-up, but there is sufficient regularity of the response to suggest that the right approach is to understand how the social environment impacts on biology to cause disease.

Selye's approach calls the response of the organism 'stress' (Selye 1956). Others have used an engineering analogy, in which external demands are considered to be the stressor, and the biological response may or may not (depending on the resilience of the subject) have undesirable consequences. What is clearly known is the physiology of the fight-or-flight response. What has been more difficult to tie down is how the fight-or-flight response relates to chronic stress, and later on, to disease. The model elaborated by Sapolsky is that the fight-or-flight response is adaptive to acute stress, but may be maladaptive to chronic stress in today's urban environment (Sapolsky 1993). Thus, for example, the average life span of African-American men in Harlem is shorter than that of men in Bangladesh.

Psychosocial factors and their influences on health are active areas of research. There is now enough evidence to suggest that this is an important field for those concerned with improving public health in both economically developed and developing countries. Plausible mechanisms linking psychosocial factors to health are described in the first half of this chapter. We then look to the evidence from both human and animal literature to illustrate the ways in which social organization can influence our biology, and therefore the health of individuals and populations.

2.3 Biological pathways in a social context

Biological processes must be involved in the connection between social structure and health. But, perhaps even more than health, biology is thought of as an individual rather than a social attribute. Individuals develop some disturbance of their biology. They become sick so they go to see the doctor. The doctor treats individuals, except perhaps when there is an outbreak of infectious disease, or when a vaccination programme is undertaken. The individual, clinical view of health determinants is vitally important. It underlies medical training and biomedical science, and provides the framework for the treatment, cure, and amelioration of disease.

We can extend the conceptual framework to provide a public-health view in which the emphasis is on prevention rather than cure. Figure 2.2 is an example of such a framework, in which factors operating beyond the level of the individual, as well as individual characteristics, are recognized. Thus, social structure, top left of the diagram, influences well-being and health, bottom right. The influences of social structure operate via three main pathways. Material circumstances are related to health directly, and via the social and work environment. These in turn shape psychological factors and health-related

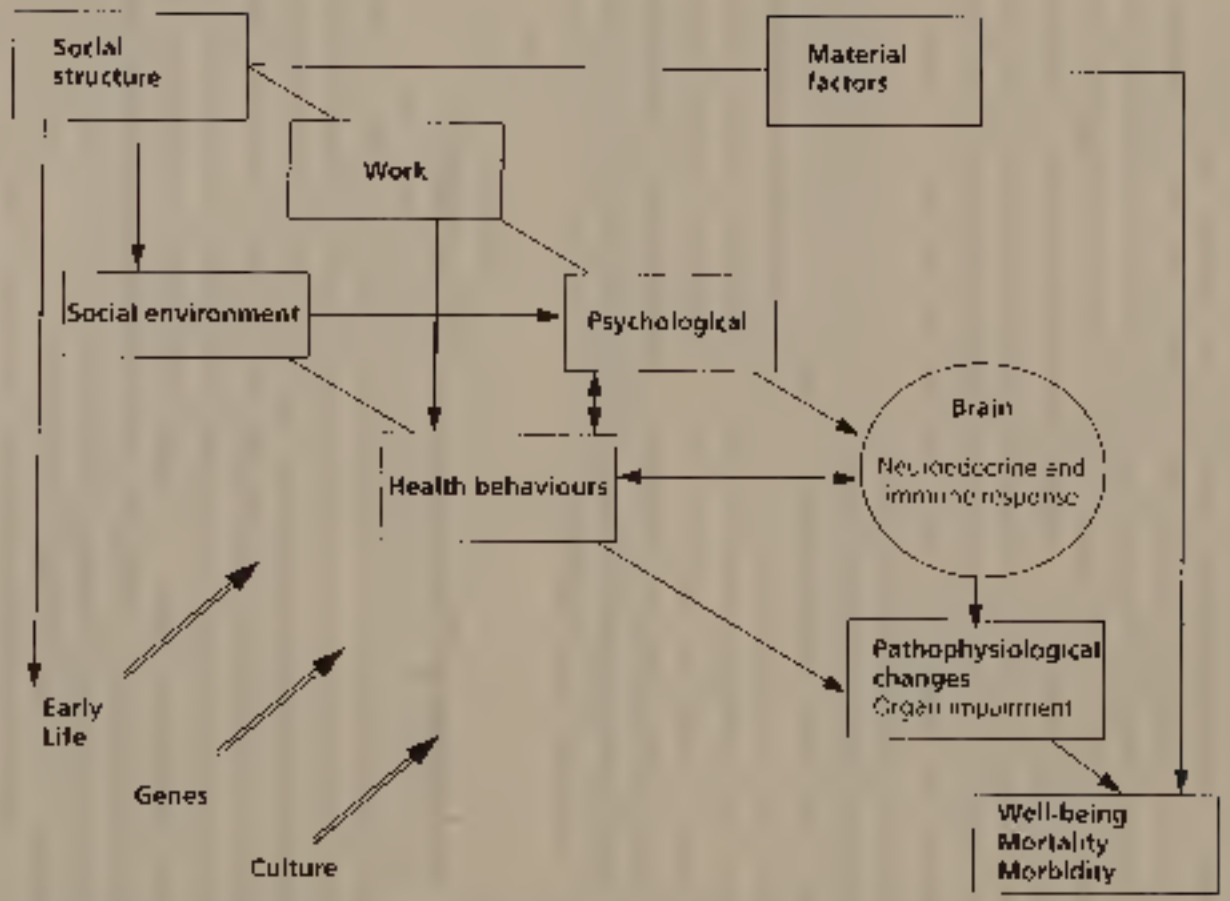

Fig. 2.2 Social determinants of health. The model links social structure to health and disease via material, psychosocial and behavioral pathways. Genetic, early life, and cultural factors are further important influences on population health.

behaviours. Early life experiences, cultural, and genetic factors also exert influences on health. Figure 2.2 is a generalization. A specific diagram for each disease category could be constructed, given the evidence. Further, the balance of influences on health depends on geographical location and historical circumstances of the population in question. For example, coronary heart disease is considerably more common in northern Europe than in the south of the continent, and within the UK and France similar north-south gradients exist. It should be noted however, that there is no evidence to suggest that lack of sunshine or northern latitude *per se* are risk factors for heart disease.

The left-hand side of Fig. 2.2 adds social causes to our picture of the determinants of health. The social and cultural environment, and organization of work, are among the upstream factors now re-emerging in thinking about public-health policy (Blane et al. 1996), partly as a response to the weaknesses of the education behaviour change model which dominated the field between the 1960s and the 1980s. Moving towards the right of Fig. 2.2, we encounter the psychological and biological dimensions. These downstream factors are, to use anatomical terminology, the proximal causes of disease which tend to be the main focus of medical attention. These factors are the intermediates on the pathway from the social level to well-being or disease in individuals. Put another way, there can be no doubt that the effects of social organization on population health are mediated by psychological and biological processes. The two big questions, outlined in the introduction, are, first, what are the processes involved and, secondly, given the plausibility of stress pathways, what is the importance of 'stress biology' in comparison with behavioural explanations which place factors such as smoking, exercise, and diet at centre stage?

The plausibility question is answered illustratively below. Even if the reader is initially sceptical about the pubic health importance of direct stress pathways operating independently of health-related behaviours, the social patterning of health-damaging habits, such as smoking, suggests that psychological and biological processes are at least indirectly important in understanding health differences within and between populations.

2.3.1 The fight-or-flight response

Humans evolved to rise rapidly to the challenge of external, potentially lethal, but short-term threats. Such threats may be physical, psychological, or biological, and often are a combination of all three. From a physiological point of view, the fight-or-flight response is very similar in all mammals, whether man, woman, mouse, or lion. Sensory information is the trigger – unless the threat comes from an invading virus or bacterium, when the alarm is sounded by other means – for a set of nerve and hormone signals which prepare the brain and body to respond to the emergency. The resulting physiological changes can be the key to survival in the face of a predator's attack or physical

injury. For the mouse and particularly the lion, such stressors are brief and fairly unusual, and the accompanying disturbances to the body's internal status quo are likewise uncommon events. For humans, the contemporary environment is radically different. Physical and biological emergencies are comparatively rare, but instead life is filled with psychological demands and challenges which may activate the fight-or-flight response too hard and too often.

The mechanism of the fight-or-flight response involves two main pathways, which together co-ordinate an array of metabolic and physiological changes. Because these rely on parts of the nervous system and several hormonal or endocrine transmitters, they are known collectively as neuroendocrine pathways. Both are signal pathways that originate in the brain, where the threat is perceived and evaluated, and the resulting signal is initiated. The first pathway comes into action very rapidly, utilizing the sympathetic (as opposed to the parasympathetic) branch of the autonomic nervous system. The hormonal products of the pathway are noradrenaline, released at nerve endings, and adrenaline, secreted into the bloodstream by the medulla, or middle part, of the adrenal glands. This system is the sympatho-adrenal pathway. One effect of this involuntary reaction is known to us all: the unpleasant tightening of the gut we feel in response to a sudden shock. The second pathway comes into operation over minutes and hours instead of milliseconds. Its key components are three hormone-secreting glands, the hypothalamus and pituitary, respectively in and just below the brain, and the adrenal glands, located on the kidneys; hence the name of the second pathway, the hypothalamic–pituitary–adrenal axis. The adrenal glands secrete the important hormone cortisol, among other steroid hormones.

The sympatho-adrenal pathway

The almost instantaneous release of noradrenaline from sympathetic nerve endings and adrenaline from the adrenal medulla evoke responses throughout the body (Table 2.1). The effects are due, in varying degrees, to the presence of sympathetic nerves in the target organs, and to increased secretion of adrenaline into the circulation. One important target organ is the heart (Fig. 2.3) which is controlled directly by nerves of the autonomic nervous system, and indirectly by the level of adrenaline in the blood. The combined effects of sympatho-adrenal activation on the mind and body are psychological arousal and energy mobilization, and inhibition of functions which are irrelevant to immediate survival, such as digestion and growth. The precise nature of the activation varies according to the stressor and its duration, but its function is essentially to prepare for, or to maintain, physical exertion. The sympatho-adrenal pathway can be switched off rapidly. Even the circulating adrenaline has short-lived effects because its half-life is just a few minutes.

Table 2.1
Effects of circulating adrenaline and sympathetic nerve activity in the fight-or-flight response

Accelerate heart rate
Increase metabolic rate
Increase blood pressure
Increase sensory vigilance
Dilate pupils
Dilate airways
Constrict blood vessels in skin and gut
Dilate blood vessels in skeletal muscles
Inhibit salivation
Increase sweat secretion

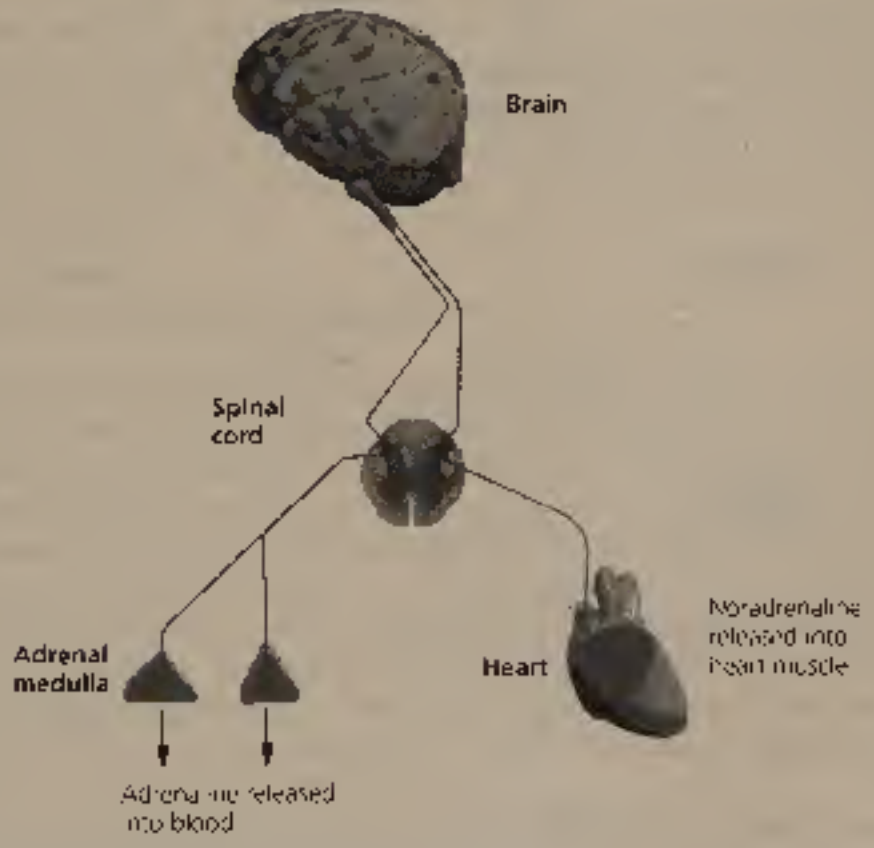

Fig. 2.3 Sympathoadrenal pathway and the heart. The heart rate is influenced directly by sympathetic nerve impulses and indirectly by the circulating adrenaline level.

There is much evidence of wide variations between individuals in the size and duration of responses. These variations appear to be partly constitutional and partly due to social and individual differences in psychological coping resources. The impact of these variations on the development of chronic disease is uncertain.

The hypothalamic–pituitary–adrenal axis

The second, slow component of the stress response is the hypothalamic–pituitary–adrenal (HPA) axis. This pathway results in cortisol release into the bloodstream (Fig. 2.4) from the adrenal glands. The hormonal cascade starts in the brain with the release of corticotrophin releasing factor (CRF) into small vessels that carry it the few millimetres from the hypothalamus to the pituitary gland. Here, specialized cells respond to the presence of CRF by secreting the second hormone, adrenocorticotrophic hormone (ACTH) into the circulation.

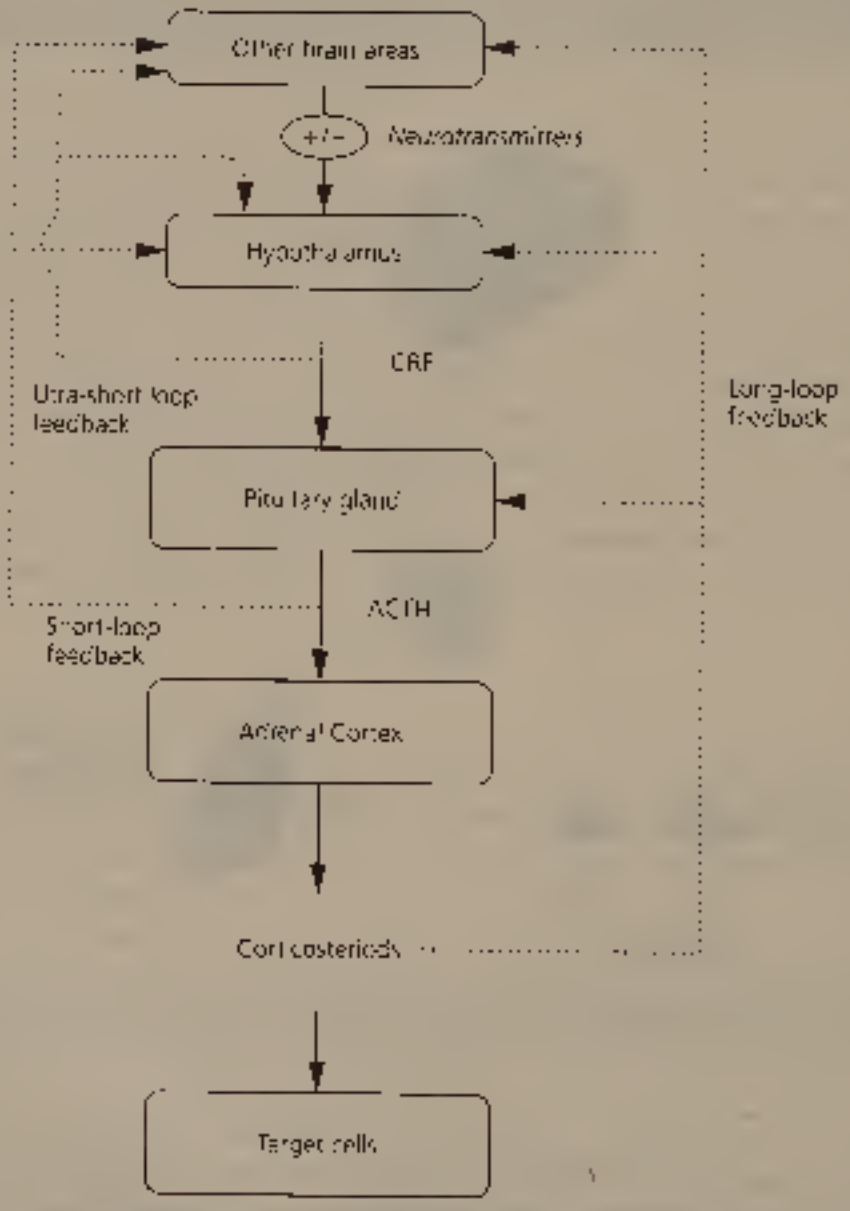

Fig. 2.4 The hypothalamic–pituitary–adrenal axis. The diagram shows how stimuli in the brain influence metabolic and immune functions in other parts of the body. The dotted lines show feedback controls which regulate release of cortisol and other corticosteroids from the adrenal cortex. CRF, corticotrophin releasing factor; ACTH, adrenocorticotrophic hormone. (Redrawn from Brown 1994.)

Within a few minutes, the level of ACTH in the adrenal cortex is sufficiently raised to stimulate cortisol release. As Fig. 2.4 shows, there are several feedback loops which regulate the activity of the HPA axis. The control system, involving each of the three hormones, provides sensitive mechanisms for adjustment of the circulating cortisol level during everyday life and in stress situations.

Cortisol and other related glucocorticoid hormones have both metabolic and psychological effects. They play a key role in the maintenance and control of resting and stress-related metabolic functions. As antagonists of the hormone insulin, they mobilize energy reserves by raising blood glucose and promoting fatty acid release from fat tissues. During an emergency this is a desirable effect, but in the physically inactive situation the superfluous availability of energy tends to increase output into the blood of cholesterol-carrying particles from the liver. The brain is also a target for glucocorticoids, which promote vigilance in the short term. However, a prolonged high level of cortisol, such as occurs in Cushing's syndrome, can provoke paranoia or depression. Some depressed patients respond to the drug metyrapone, which inhibits the production of cortisol within the adrenal gland (Checkley 1996), while in others, alterations of HPA axis functioning appear to override the effect of the drug, and cortisol output from the adrenal continues at a high level.

2.3.2 Acute and chronic stress

The neuroendocrine pathways outlined above, which generate the fight-or-flight response, are valuable properties of human biology because they provide the means by which to survive in the face of environmental challenge. From an evolutionary perspective it is easy to see that systems which gave survival advantage during the past million years, and have therefore been inherited by modern *homo sapiens*, may not be without a downside for the health of the present-day city dweller. The material and social environment has changed beyond recognition over the past 10 000 years since agriculture began, and in the past 200 years successive waves of industrial development have altered living conditions at a great pace. Yet our underlying biology is essentially the same as it was in ancient Babylon.

What, then, is the effect of living in social isolation on a shabby housing estate? Of growing up with parents who have no work and little self-respect? Of being a low-paid office worker surrounded by high-income executives? In advanced industrialized countries such groups of individuals will usually have adequate material circumstances, food, and clean water. Financial strain, lack of social support, and monotonous work may, however, produce a low level of psychosocial stress as a feature of daily life. Modern populations are largely free of the risks of fatal infectious disease, but not of the more subtle exposures which may repeatedly and frequently activate the fight-or-flight response over a period of decades. The increased risks of

diabetes and cardiovascular disease among those lower down the social hierarchy fit this interpretation very well.

This is not to argue for stress counselling rather than poverty alleviation and social reform. The point is to dispel a common misconception that 'stress' is predominantly a health risk for senior managers, stockbrokers, and others in positions of corporate and public responsibility. Acute stress in such contexts provides challenges which often will be exciting, stimulating and, after the event, emotionally and intellectually satisfying. As Siegrist and his group have shown, high effort linked to high reward is generally health promoting (Siegrist 1996). In contrast, ill health is associated with prolonged exposure to psychological demands when possibilities to control the situation are perceived to be limited and chances of reward are small (Bosma et al. 1997). How might such repeated activation of the fight-or-flight response relate to the development of chronic disease?

2.3.3 The limits of stress reactivity

A principle of animal physiology is that an organism requires a stable internal environment in order to live successfully. Claude Bernard saw this to be true almost 150 years ago when he wrote '*La fixité du milieu interieur est la condition de la vie libre*'. Constant temperature, carbon dioxide concentration, and osmotic pressure are essential for the well-being of cells, tissues, and organs, and therefore for the integrity of the whole organism. At the same time, blood sugar, other circulating nutrients and waste products, blood pressure, and heart rate are also controlled, but the controls have wider margins. Variability in these factors is a fact of life, and the maintenance of a constant internal environment, termed homeostasis, is about balancing necessary variation against the need for physiological stability. Neuroendocrine regulation, based on complex and interlocking positive and negative feedback mechanisms, is central to this function.

The nature and size of the biological response to psychological demands can influence health in several ways (Steptoe 1998). First, a particular type of response may be directly responsible for disease. Secondly, it might be that reactivity increases vulnerability to certain illnesses, such as colds or flu, but does not cause them. Thirdly, the pattern of reactivity may disrupt existing disease processes, and finally, it might act as trigger for acute events such as heart attack.

There is good evidence for the disruptive effect of stressors, such as life events, on existing medical conditions, including diabetes and rheumatoid arthritis, and for the precipitation of myocardial infarction by emotional trauma. But although a habitual pattern of high blood pressure reactivity has been seen to be a likely cause of hypertension, it has proved difficult to demonstrate that heightened blood pressure reactions are more common in those who go on to develop disease than in those who do not (Steptoe 1998).

An explanation for these findings may be found by considering the ways in which blood pressure may depart from and return to its baseline level. Figure 2.5 depicts three types of reactivity pattern which might apply to adrenaline and cortisol and other stress hormones, as well as to blood pressure. Time is on the horizontal axis, measured in minutes for adrenaline and blood pressure, and hours in the case of cortisol. Blood pressure level (or hormone concentration) is on the vertical axis. In Fig. 2.5a, the stimulus produces a sharp reaction with a fast return to baseline; in Fig. 2.5b, the initial reaction is similar but the return to baseline is delayed, and there is a prolonged departure from the resting level. In Fig. 2.5c there is a blunted response and an elevated baseline. Other combinations of baseline and stimulated levels are also feasible, such as blunted response with a low basal level. The optimal reactivity pattern for each physiological system may be different.

For the blood pressure response to a psychological challenge, it appears that a large reaction may not be harmful, provided there is a fast return to baseline, as in Fig. 2.5a. If, however, such a response is provoked too frequently, the reactivity pattern may become like that shown in Figs 2.5b or c, and elevated blood pressure might follow. This example illustrates how feedback controls within the neuroendocrine system may be reset to a new level by environmental factors.

The allostatic load hypothesis (McEwen 1998) links the psychosocial environment to physical disease via neuroendocrine pathways. Allostatic load, or stress-induced damage, is considered relevant in cardiovascular disease, cancer, infection, and cognitive decline, and has been described as a sign of accelerated ageing. The concept of allostasis – the ability to achieve stability through change – extends the idea of homeostasis to include processes leading to disease. The price of adaptation to external and internal stress may be wear and tear on the organism, the result of chronic over- or

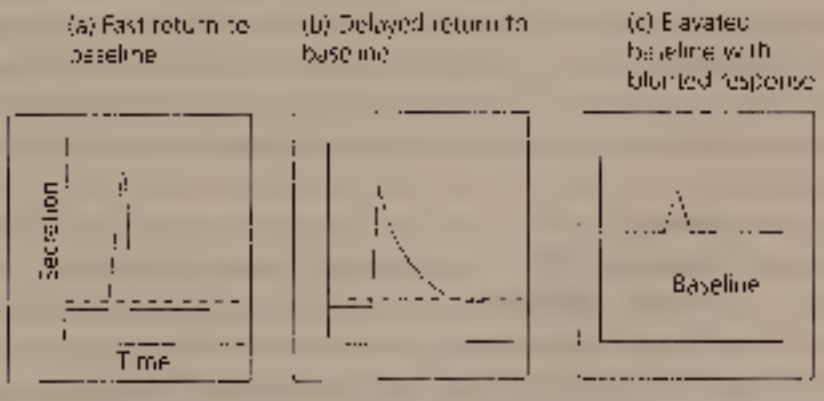

Fig. 2.5 Stress reactivity patterns: idealized representations of neuroendocrine and metabolic reactivity. (a) Fast return to baseline: reactivity is responsive and flexible. (b) Delayed return to baseline: reactivity is responsive with slow recovery. (c) Elevated baseline with blunted response: overreactivity and abnormal resting level.

underactivity of allostatic systems to produce allostatic load. For instance, the physiological system controlling blood glucose may be pushed towards diabetes. Allostatic load was investigated in a longitudinal study of older Americans (Seeman et al. 1997), where it was defined by measures of five established cardiovascular risk factors, plus urinary adrenaline and cortisol, and serum dehydroepiandrosterone sulphate (an adrenal androgen). Subjects with lower baseline allostatic load scores had better physical and mental functioning. Over the follow-up period the same group showed less decline in functioning and were less likely to develop cardiovascular disease.

The general description of stress reactivity in this section leads to many questions about individual and social differences in response to the same stimulus, which may or may not threaten homeostasis. This topic will be taken up later in the chapter.

2.3.4 The blood clotting system

Blood flow is vital for the transport of gases, nutrients, and waste materials to and from body tissues. It is also important that physical injury does not result in massive blood loss, and the clotting, or haemostatic, system provides the mechanism to prevent such a disaster. The sensitivity of this system to a variety of triggers suggests that it may be an important stress pathway in heart disease.

The change of blood from the liquid to the solid state involves a series of chemical reactions in which more than a dozen blood proteins take part. When the first protein is activated, it in turn activates the second protein, and so on. At the end of this cascade, the thrombin molecule catalyses the splitting of fibrinogen into fibrin. The fibrin molecules so produced condense to form threads which intermesh, trapping red blood cells and platelets, and very quickly a blood clot is formed. Major abnormalities of the haemostatic system are life-threatening; in haemophilia, for example, loss of blood after injury results from a defective clotting mechanism. An increased tendency for the blood to clot even in the absence of injury is very dangerous, and may be provoked in susceptible individuals by hormones such as those found in oral contraceptives.

The clotting system is, like other physiological systems, influenced by environmental stressors. The fight-or-flight response produces, via the increase in circulating adrenaline, increased 'stickiness' in platelets. The blood tends to become more concentrated and viscous at the same time, and stress-related hormones can increase the output of fibrinogen from the liver. It is plausible that, over decades, such small changes may add to the formation of arterial plaques, and therefore increase risks of heart disease and stroke.

2.3.5 Infection, inflammation, and immunity

Infectious disease continues to contribute to ill health, particularly among poorer groups, in developed as well as in developing countries. Standards of housing and sanitation, vaccination, and other infectious disease control programmes are crucial to reducing this public-health burden. Recent research suggests that infection and immunity may also be important in two poorly recognized ways. First, as a contributory cause of diseases not previously considered to be due to infection (Vallance et al. 1997), and secondly, because chronic stress may alter susceptibility to infection and its severity. Though the evidence is incomplete, immunity has been implicated in a variety of conditions, such as peptic ulcer, gastric, cervical and other cancers, and coronary heart disease. The brain is able to influence immune function. Nerves of the autonomic nervous system are found in all relevant tissues – bone marrow, thymus, spleen, and lymph nodes – and hormones, including cortisol, have large effects on the immune system.

It is now evident that long-term, but low-level, inflammatory processes resulting from undetected infection alter circulating levels of hormones and proteins in ways which increase the risk of heart disease by damaging the walls of blood vessels and promoting the development of atherosclerosis. Modification of these processes by stress is possible. For example, in the absence of infection the stress of space flight was shown to produce a rise in urinary output of interleukin-6 (Stein and Schluter 1994), a hormone considered to be important in immune and inflammatory responses.

2.3.6 Integration

The endocrine, immune, haemostatic, and nervous systems are often studied as distinct and separate entities. This simplification has been useful and probably essential because it allows laboratory scientists to focus on the details of their chosen mechanism. In this way, each discipline has come to understand the complexity of the relevant pathways, each with its set of feedforward and feedback controls. The reality, of course, is that there are not clear boundaries between these systems.

Figure 2.6 shows some of the interconnections between the neural, endocrine, and immune systems. The diagram shows how the brain and then the HPA axis are able to respond to non-cognitive stimuli, and conversely how the immune system has the capacity to respond to perception and emotion. The brain (central nervous system) cannot itself detect the presence of infection. One of the functions of the immune system is therefore to act as a sensory system, making the brain aware of infection by means of messengers of the immune system, the cytokines, which enter the brain via the bloodstream. Immune function responds to cognitive stimuli via the autonomic nervous system and the release of hormones from the hypothalamus

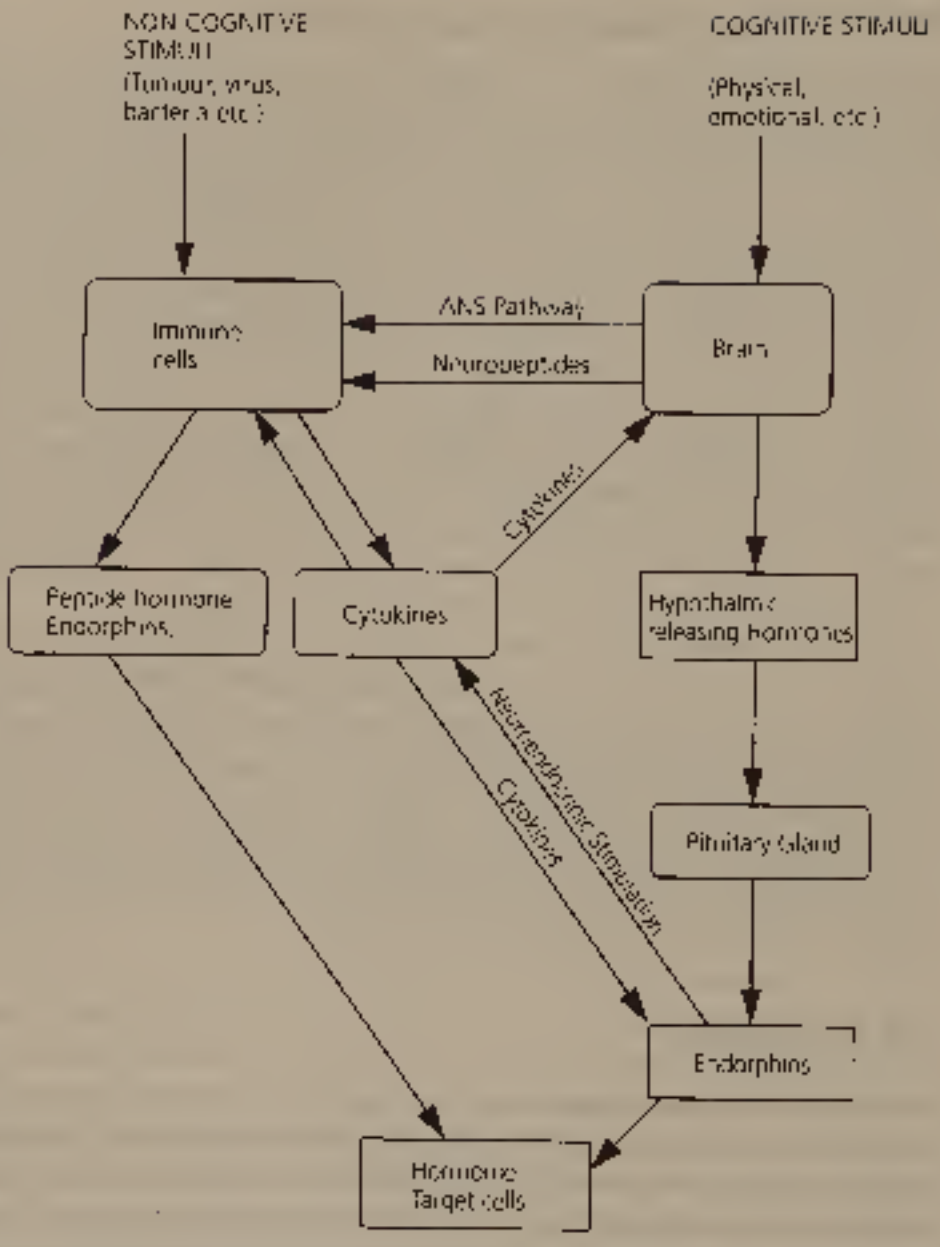

Fig. 2.6 Communications between brain hypothalamic-pituitary-adrenal axis, and immune system. The brain perceives cognitive stimuli which can influence immune function via neuropeptides, the autonomic nervous system (ANS), and the HPA axis. The immune system responds to non-cognitive stimuli (infection and tumour growth) by secreting cytokines (immune messengers) and peptide hormones which act on the brain and neuroendocrine system. The immune system thus has a sensory function. (Redrawn from Brown 1994.)

and pituitary gland. In animals, isolation rearing, crowding, low dominance status, and social stress influence the effectiveness of defences against infection (Brown 1994).

This brief account has emphasized the roles of the autonomic nervous system and the HPA axis in the stress response. However, it is important to recognize that there are at least 15 neurotransmitter substances which convey

sensory and cognitive information in the human nervous system. Among these, serotonin appears to be important in depression and hostility, and both psychological states have been linked with increased heart disease risk in a variety of studies. In animal studies, learned helplessness, the tendency to passivity in the face of repeated experimental stress, is associated with a reduced level of serotonin receptors in the hippocampus, an area of the brain which also responds to cortisol (Checkley 1996).

2.4 Human studies

The sections above have illustrated some of the major biological pathways that plausibly change risk of developing major disease according to social and psychological circumstances. Central to these processes is the concept of disturbance of homeostatic equilibrium and thus increased risk of ill health. We now turn to the second question posed at the beginning of the chapter: what is the evidence that these pathways do actually operate to produce or accelerate disease? Throughout this book there are numerous examples of the ways in which aspects of social organization are correlated with measures of health and disease. Here the aim is to examine some of the evidence for the biological pathways which intervene. The research findings are divided into two groups: those based on human subjects (discussed here), and those based on observational and experimental studies of animals (discussed later).

2.4.1 Psychological effect on growth

Psychogenic dwarfism is a rare syndrome associated with severe childhood deprivation. Psychosocial growth retardation of a less dramatic nature appears to have been documented in Widdowson's study of orphaned children in post-war Germany (Widdowson 1951). Under identical food rationing regimes, those who lived in the '*Bienenhaus*' orphanage, initially under the control of the stern and forbidding Fraülein Schwarz, gained less weight and grew more slowly than children cared for by the affectionate Fraulein Grün at the '*Vogelnest*' orphanage. By chance, Schwarz replaced Grün during the study and the growth rates reversed, despite the provision of extra food at '*Vogelnest*'. This controlled cross-over study provides evidence that adverse psychosocial circumstances in childhood can influence growth (although it is not clear whether this was the result of upset appetite and eating, or a direct psychosocial effect). Separately, there is evidence that attained height is a marker of health capital, or constitution, which is a protective factor for adult disease. Recent studies suggest that long-term effects on health may be produced by early deprivation, even among children born in the British welfare system of the 1950s (Montgomery et al. 1997; Power et al. 1998).

2.4.2 Social patterning of coronary risk factors in adults

Measures of social and economic status, including occupation, are extremely powerful predictors of premature heart disease. Employment grade proved, on its own, to be more powerful than the combination of classic risk factors including smoking, serum cholesterol, and blood pressure, in a follow-up study of 17 000 British civil servants (Marmot et al. 1984). This important observation prompted a new long-term study to investigate the possible psychosocial causes of heart disease and other important health problems. Biology is being given special attention in the Whitehall II study, in order to clarify the mechanisms involved.

At the baseline of the Whitehall II study in 1985–88 (Marmot et al. 1991) there was a stepwise relationship between civil service employment grade (1992 salary range £7400–£87 600) and the prevalence of several of health-related psychosocial factors: low control and lack of variety at work, lack of social contact with friends, distressing life events, difficulty paying bills, hostility, and health locus of control. These relationships were seen before employment security in the British civil service was reduced in the late 1980s (Ferrie et al. 1995) and it is likely that their prevalence is now higher, particularly within the lower grades of staff.

Biochemical and physiological risk factors were studied in detail at the second medical examination of Whitehall II subjects in 1991–93 (Brunner et al. 1997). Because total serum cholesterol levels were similar by employment grade, and resting blood pressure showed only a small differential in the expected direction at the baseline examination, we speculated that a particular pattern of risk factors might be associated with occupational status. This 'metabolic syndrome' pattern has previously been shown to predict diabetes and coronary disease in other populations, including South Asian migrants to the UK (McKeigue et al. 1991). Figure 2.7 shows that the metabolic syndrome is indeed linked with lower status in the sample of 4691 men and 1903 women.

As the grade hierarchy is descended, a progressively larger proportion of subjects exhibits adverse levels of each component of the metabolic syndrome (Fig. 2.8; moving from left to right in each block of histograms). The top four panels of Fig. 2.8 are components reflecting adverse homeostatic alterations in carbohydrate and lipid metabolism, and Fig. 2.8e shows that abdominal obesity, a fat pattern particularly associated with coronary risk, is also strongly associated with low status. Figure 2.8f shows that the blood clotting protein, fibrinogen, also shows a strong inverse social gradient (Brunner et al. 1996).

The findings for blood glucose are particularly interesting because they are based on a metabolic challenge rather than a measurement of fasting, or baseline, level. Subjects in the fasting state were given 75 g of glucose as a drink, and 2 hours later the level of blood glucose was measured. The results (Fig. 2.8a) show that the lower the position in the civil service, the greater was

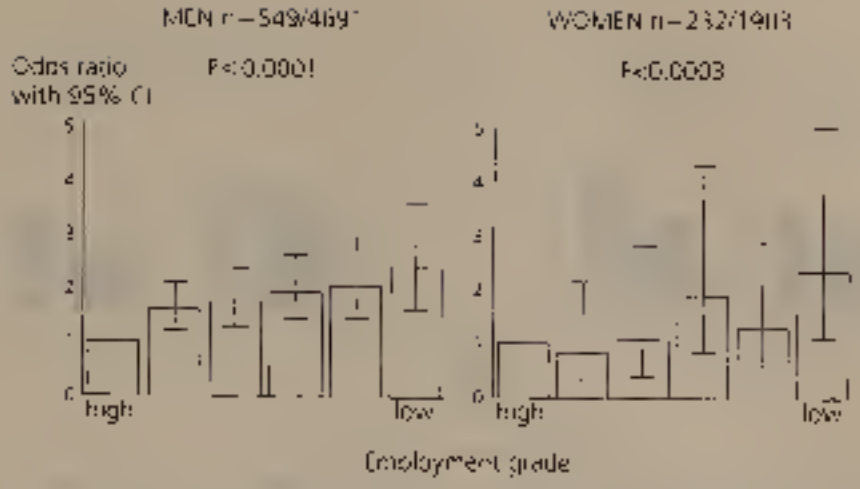

Fig. 2.7 Prevalence of the metabolic syndrome by employment grade in the Whitehall II study. Odds ratios and 95 per cent confidence interval (CI) adjusted for age and, in women, menopause status. *P* values are for trend test across grades. (From Brunner et al. 1997)

the probability that a subject had difficulty in clearing the glucose into body tissues for storage or energy functions and returning to the optimal baseline state. This finding corresponds to the condition shown in Fig. 2.5b, or perhaps in Fig. 2.5c. It illustrates that the ability to mount a hormonal response to the glucose challenge, and thus to maintain homeostasis, appears in some way to depend on occupational status.

The social gradient in prevalence of the metabolic syndrome is consistent with a psychosocial explanation for the social pattern of coronary risk. The alternative life-style explanation was only weakly supported by statistical analysis. When grade differences in rates of smoking, physical inactivity, and alcohol consumption were taken into account, 90 per cent of the grade differential in metabolic syndrome prevalence remained. Further adjustment for overall obesity (body mass index) but not central obesity (waist–hip ratio), which is itself a component of the syndrome, as well as the behavioural factors, reduced the grade differential by only an additional 22 per cent in men and 1 per cent in women. How then does the metabolic syndrome develop? One possibility, which is the subject of current research (Fig. 2.9), is that this cluster of risk factors may be the product of altered activity of the HPA axis (section 2.3.1) in response to long-term exposure to adverse psychosocial circumstances (Bjorntorp 1991; McEwen 1998).

2.4.3 Socio-economic status and cortisol secretion in two cities

Middle-aged men in Lithuania and Sweden had similar coronary heart disease mortality rates in 1978. Subsequently, rates rose in Lithuania and fell in Sweden, so that by 1994 coronary mortality was fourfold higher in Lithuania. The divergence in life expectancy, in addition to coronary disease rates,

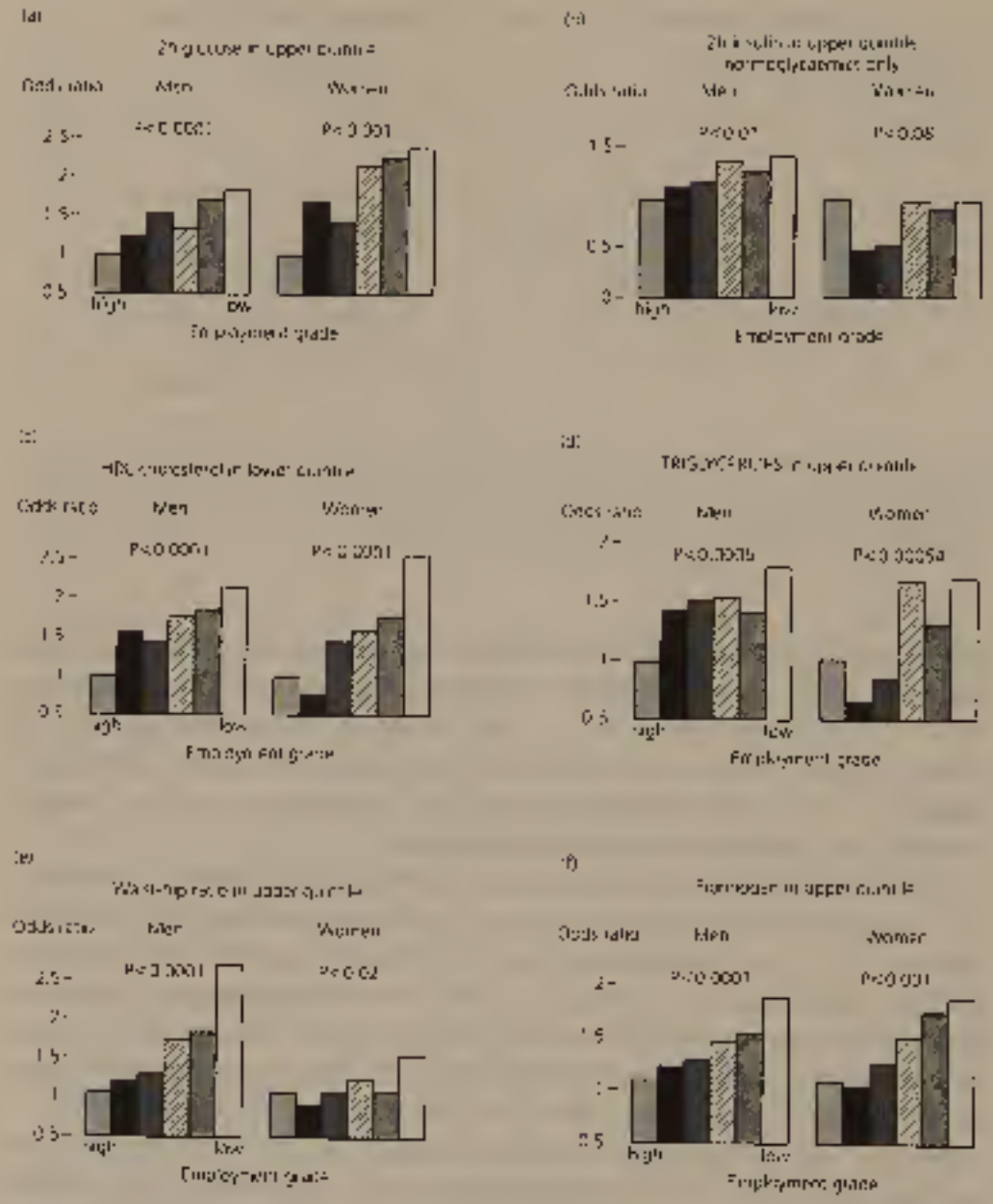

Fig. 2.8 Prevalence of adverse levels of metabolic syndrome variables and fibrinogen by employment grade in the Whitehall II study. Odds ratios and 95 per cent confidence interval for occupying top quintile (except HDL cholesterol: bottom quintile). Adjusted for age and, in women, menopause status. P values are for trend test across grades. (From Brunner et al. 1997.)

between the countries of eastern and western Europe around the time of the collapse of the Soviet system illustrates the importance of socio-economic factors in health (Bobak and Marmot 1996). The widening East–West health gap prompts the thought of a possible analogy with the widening socio-economic inequalities in health within countries. Could it be that the psychosocial environment is part of this analogy?

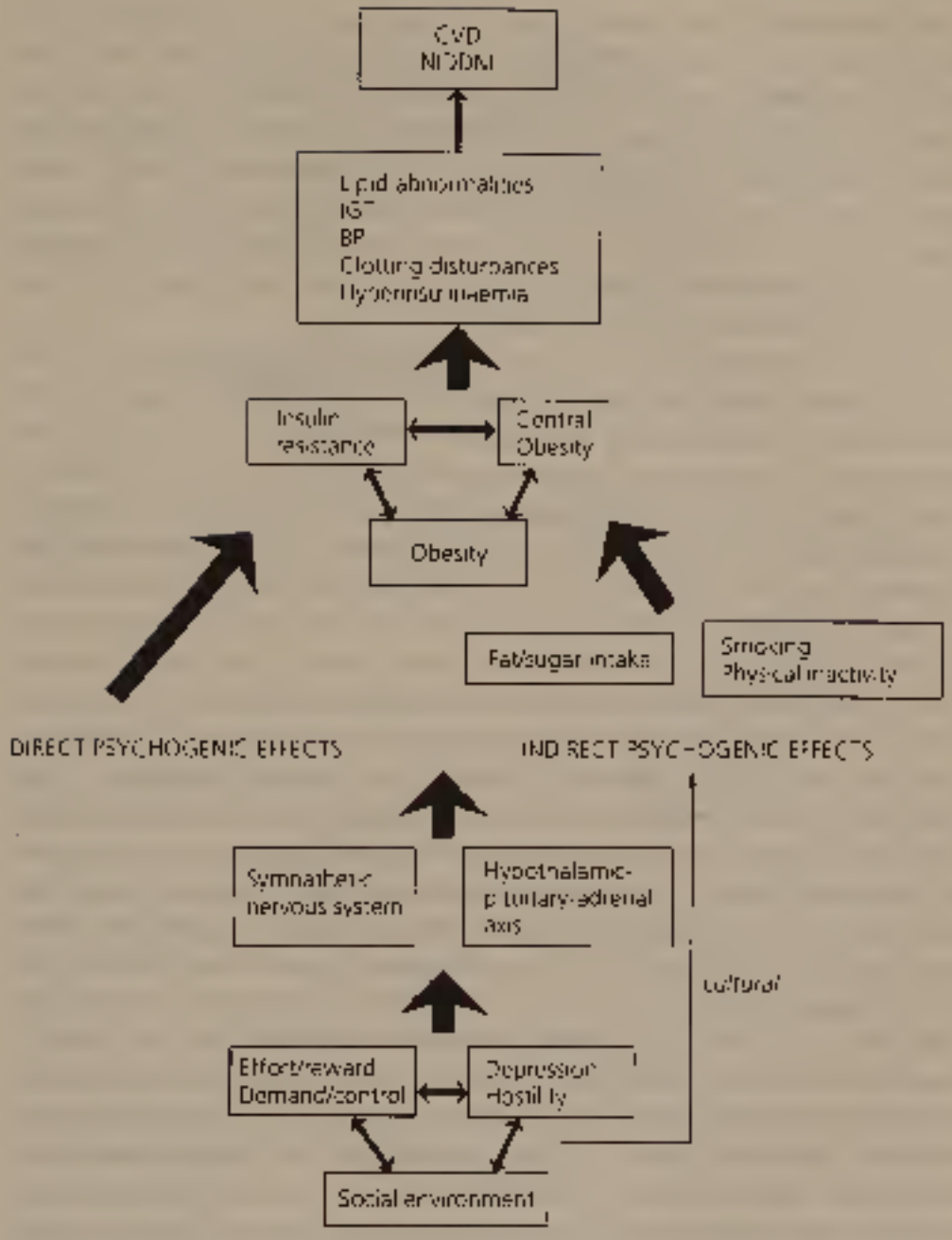

Fig. 2.9 Psychosocial and biological pathways in cardiovascular disease (CVD) and non-insulin-dependent diabetes (NIDDM). Hypothesized research model. IGT, impaired glucose tolerance. BP, blood pressure.

Kristenson et al. and co-workers examined the possible causes for the differences in coronary heart disease incidence between Lithuania and Sweden, and between men of high and low socio-economic status in each country (Kristenson et al. 1997, 1998). Random samples of 150 50 year-old men participated in each of two cities: Linköping in southern Sweden and Vilnius, the capital of Lithuania. Response rates were 82 and 76 per cent, respectively. The conventional risk factors (smoking, serum cholesterol, and

blood pressure) did not provide a good explanation for national differences in risk, as was the case in the Whitehall study (Marmot et al. 1984). There were substantial differences in blood levels of antioxidant vitamins, suggesting that dietary differences are important both between and within countries. Psychosocial factors were found to follow precisely the predicted pattern. Vilnius men reported more social isolation, more job strain, and more depression than those in Linköping. The low-income groups in both cities likewise reported higher levels of isolation and vital exhaustion, and greater difficulties coping than those on higher incomes.

Here then is evidence from a cross-cultural study, conducted in 1993–95, that certain dietary and psychosocial factors are important in explaining the differences in coronary risk both between Swedes and Lithuanians, and between those with financial insecurity and their relatively well-off neighbours. Other measures also revealed marked differences between the two populations. Quality of life and perceived health showed a large differential (one standard deviation) in favour of Linköping. Although depression was more common in Vilnius, the mean hostility score in Linköping was substantially higher than that in Vilnius. It may be that many men in Vilnius had a sense of defeat and a lack of confidence in their post-Soviet society.

The contrasting psychosocial environments in Linköping (population 130 000) and Vilnius (600 000) translate into different patterns of the HPA axis stress response. Subjects took a standardized laboratory stress test involving anger recall, mental arithmetic, and immersion of one hand in iced water. Subjects attended the test the morning after an overnight fast in order to standardize the biological measurements. Attending the clinic, and fasting, can be considered to be additional stressors, but since all men did the same it does not detract from the findings. Figure 2.10 shows that both the high- and low-income groups of Swedish men had what is considered to be an adaptive response to the experimental challenge: low baseline followed by a rise and fall in blood cortisol. The difference in findings with the Vilnius subjects is striking. The high-income group exhibited a low baseline level like the Swedes, but a relatively blunted response. However, the low-income group, showed a very different response from the other groups. There was a much higher baseline level of blood cortisol and a failure to respond to the challenge, corresponding to the condition shown in Fig. 2.5c.

The implications of these results, if confirmed in other studies, are dramatic. They highlight the significance of quality of life, in terms of the social and working environment, as key determinants of population health. The demonstration of a biological mechanism, involving altered functioning of the main neuroendocrine stress pathway, is evidence that the psychosocial hypothesis is not only plausible, but that it is a significant social policy consideration. A study of 63 German army recruits given a mental stress test (Hellhammer et al. 1997) further supports the view that social rank is related to HPA axis

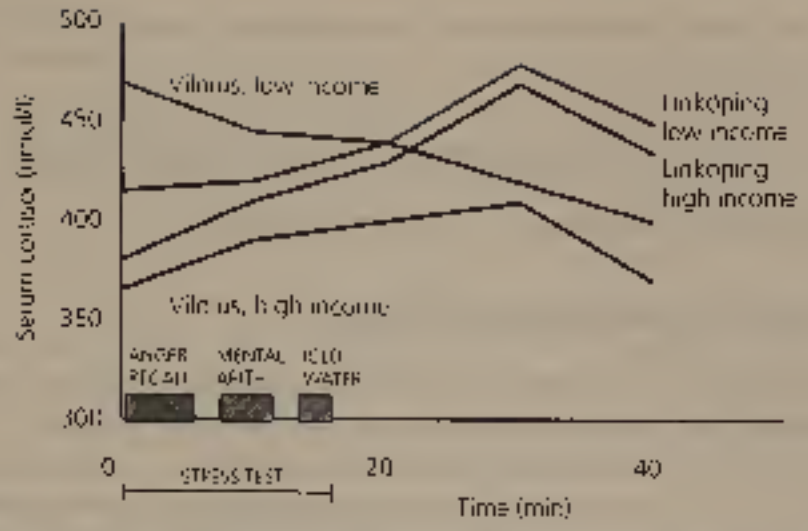

Fig. 2.10 Serum cortisol responses to a standardized stress test in Vilnius, Lithuania, and Linköping, Sweden, by income group. Low income group with lowest 25 per cent of income. High income group with highest 25 per cent of income. (Redrawn from Kristenson et al. 1998.)

functioning. Salivary cortisol levels showed a considerably larger response among psychologically dominant soldiers than subordinates.

An outstanding question is whether the apparently adverse cortisol responses are indeed responsible for future ill health, or are merely markers of psychological state. Related to this is the issue of reversibility, since a stress response pattern which becomes fixed early in life would have specific policy implications. Barker's group has demonstrated, for example, that lower birthweight is associated with higher morning plasma cortisol level among 59–70-year-old men (Phillips et al. 1998). Their findings give evidence that plasma cortisol levels within the normal range are among the determinants of blood pressure and glucose tolerance. However, in this group of men, fetal programming of the HPA axis was more important than the effect of current socio-economic position, suggesting that interventions after infancy may be ineffective. Nevertheless, it seems likely that both fetal growth and experiences during the life course will turn out to be of importance in shaping neuroendocrine function in later life.

2.5 Animal studies

Animal studies provide some added dimensions to our understanding of the connections between social organization, stress, and health. Referring to our general model in Fig. 2.2, it is clear that direct analogies are to be avoided. The human social environment is immensely and uniquely complex. From a psychological perspective, the faculties of abstract thought, emotion, and memory appear largely to be limited to our own species. However, many

animals live within hierarchical social structures and mammalian biology is potentially comparable across species. An added value of such studies is that, unless required to by man, animals do not smoke, drink coffee or alcohol, take drugs, or sit in front of a computer all day. This truism means that we do not have the problem of separating these behavioural effects from purely psychosocial processes which may influence disease risks.

2.5.1 Genes, constitution, and destiny

With due attention to relevance, animal studies can tell us about the plausible links between psychosocial factors, biology, and health. Their value is not confined to the social gradient in health (see section 2.5.2), and is also a way to understand effects such as the interaction between genetic predisposition to disease and environmental factors. Our first example may provide a caution to those who view genetic susceptibility, in the absence of medical intervention, as an irreversible destiny.

The spontaneously hypertensive rat (SHR) is an animal model often used in the study of hypertension. An experiment in cross-fostering (Cierpial and McCarthy, 1987) shows the importance of early environment in expressing this characteristic. When pups of SHR rats were cross-fostered with Kyoto–Wistar mothers they did not develop hypertension as they matured. This 'pure' genetic characteristic did not manifest itself as the phenotype of hypertension in the absence of the appropriate environmental stimulus.

Another example of the impact of nurture on nature comes from Suomi's elegant long-term studies of rhesus monkeys (*Macaca mulatta*) (Suomi 1997). Some 20 per cent of any troop are 'high reactors' who are more likely than others to exhibit depressive responses to maternal separation, along with greater and prolonged activation of the HPA axis, more dramatic sympatho-adrenal arousal, and immunosuppression. These responses remain quite stable throughout development. The pattern of arousal appears to be determined genetically, but it can be reproduced in other non-susceptible animals by raising them without their mothers (suggesting that non-genetic inter-generational transmission may be an alternative explanation). Interestingly, the high reactors tend to end up at the bottom of the social hierarchy.

The genetic, or at least constitutional, high-reactor destiny can be interrupted by changing the environment. When reared with especially nurturing mothers, such animals showed no signs of the usual behavioural disorder. Instead, they showed signs of precocious behavioural development and rose to the top of the hierarchy as adults. Females adopted the maternal style typical of their especially nurturing mothers. Further evidence from the same research group (Suomi 1997) suggests that the consequences of experimental social isolation can be modified with timely intervention, and that

long-term effects are most likely to be seen under stress conditions in adult life.

2.5.2 Social dominance among wild baboons

Determinants of circulating levels of the protective high-density lipoproteins (HDL), which promote 'reverse transport' of cholesterol away from the arterial wall, appear be important in explaining the social differential in coronary risk. We have seen above that the HDL cholesterol level in civil servants is strongly related to employment grade, and is a component of the cluster of factors making up the metabolic syndrome (Fig. 2.8). To our surprise, the same pattern of blood fat levels was found in the social hierarchy of wild male baboons (Sapolsky and Mott 1987).

The neuroscientist Sapolsky has been studying the behaviour and physiology of wild baboon troops in the Serengeti for many years. He argues the animals are ideal subjects for investigating psychosocial factors. Food is plentiful, predators are scarce, and infant mortality is low. Only some 4 hours/day are required for foraging, leaving the animals, who live in groups of 50–100, plenty of time to engage in social activity. Attainment and maintenance of social rank is a preoccupation which determines access to a variety of resources. On the basis of these behaviours, Sapolsky classified males of the troop into dominants and subordinates. Blood samples obtained following anaesthesia under controlled conditions showed, just as in Whitehall II men, that total and low-density lipoprotein cholesterol were similar by rank position, and that HDL levels were higher in the dominant compared to the subordinate males, again mirroring findings in civil servants. Subordinate baboons were found to have higher resting cortisol levels, and levels of the hormone were inversely correlated with HDL.

Do these parallels reflect the common psychosocial effects of position within the two primate hierarchies? That the baboons are non-smokers and non-drinkers is consistent with a psychosocial explanation, since smoking is known to lower, and alcohol consumption to raise, HDL levels. Production of the more favourable physiological profile in dominant baboons might be the direct consequence of their assertions of supremacy and consequent feelings of well-being, or alternatively the result of easier access to the best available food. Equally, these observational data are compatible with the view that the fittest attain the highest rank, but studies utilizing captive macaque monkeys suggest that this is not the case (Shively and Clarkson 1994). Initial rank in small groups of females fed an atherogenic diet was altered experimentally by switching animals between groups. The effects of manipulating social status were dramatic. Dominants who became subordinate had a five fold excess of coronary plaques compared with animals who remained dominant, while subordinates who became

dominant had a two fold excess of atherosclerotic changes compared to those remaining subordinate.

2.6 Conclusions

Disturbance of usual homeostatic equilibrium by the repeated activation of the fight-or-flight response may be responsible for social differences in neuroendocrine, physiological, and metabolic variables which are the precursors of ill health and disease. Social and individual differences in the response to social and environmental stressors appear to be determined by many factors, including birthweight and conditioned hypo- or hyper-responsiveness. It seems likely that the optimal stress response in relation to health in the long term is associated with living and working environments typical of the materially advantaged. This optimal response can be characterized as one with a rapid return to a resting level, and thus a high resistance to stress-related disorder (Fig. 2.11). The level of demands does not in itself pose a risk to health, provided that the individual has adequate coping resources and the opportunity to control his or her environment.

The causal role of psychosocial factors in coronary heart disease has been reviewed recently (Hemingway and Marmot 1999). The evidence from longitudinal studies involving more than 500 healthy subjects was strongest for social isolation, depression and anxiety, and low control at work.

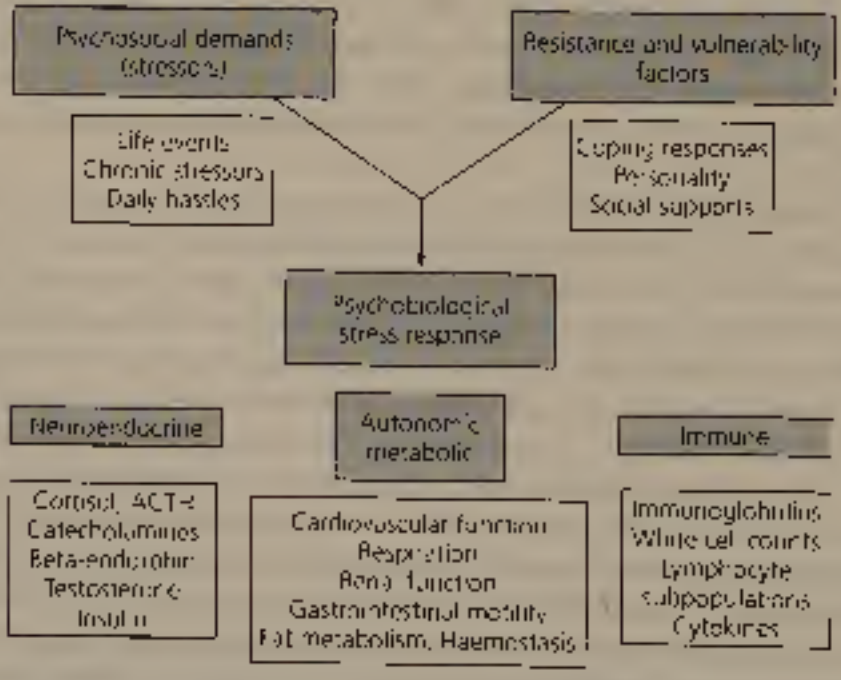

Fig. 2.11 The psychobiological stress response. Resistance and vulnerability factors influence the response to psychosocial stressors. The major neuronal, metabolic, and immune elements of the response are shown. (From Steptoe 1998.)

2.7 Summary

Stress has short-term effects on the human body and mind. The effects are positive if the situation is right, but everyone has his or her limits. We are now beginning to recognize that people's social and psychological circumstances can seriously damage their health in the long term. Chronic anxiety, insecurity, low self-esteem, social isolation, and lack of control over work appear to undermine mental and physical health.

The power of psychosocial factors to affect health makes biological sense. The human body has evolved to respond automatically to emergencies. This stress response activates a cascade of stress hormones which affect the cardiovascular and immune systems. The rapid reaction of our hormones and nervous system prepares the individual to deal with a brief physical threat. The heart rate rises; blood is diverted to muscles; anxiety and alertness increase. This response is highly adaptive: it may save life in the short term. But if the biological stress response is activated too often and for too long, there may be multiple health costs. These include depression, increased susceptibility to infection, diabetes, high blood pressure, and accumulation of cholesterol in blood vessel walls, with the attendant risks of heart attack and stroke.

These health problems increase progressively down the social strata in industrialized countries. Psychosocial and stress mechanisms have been studied in a variety of non-human primates, both in the wild and in captivity. In monkeys there is also a social hierarchy in cardiovascular damage. Submissive animals have a higher prevalence of atherosclerosis and a pattern of metabolic changes similar to that linked with increased cardiovascular risk in humans. In baboons, those of lower status in the troop have a higher level of the stress hormone cortisol, and this is associated with lower levels of protective high-density lipoprotein cholesterol in the blood.

Clustering and accumulation of psychosocial disadvantage, perhaps beginning with a poor emotional environment in early childhood, is a neglected area of public-health prevention and social policy. This is an area of active research.

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3 Early life

Michael Wadsworth

3.1 Introduction

Associations of poverty and social inequality and social exclusion with child health are found in all countries, regardless of methods and delivery of medical care and of culture (Williams et al. 1994; Helman 1994; Williams et al. 1994). Child health is of the greatest importance for the future of health of a nation, not only because today's children grow up to become the next generation of parents and workers, but also because recent research in child health shows that early life health is, for each child, the basis of health in adult life. Therefore investment in health in early life has beneficial effects, specifically on the future health of a nation as well as on the future functioning of its citizens.

The purpose of this chapter is to describe the biological processes that affect child health and that determine adult health, and then to outline the nature of the social factors that affect these biological processes, both at the family level and in terms of the cultural social context. Conclusions are drawn about the policies needed to improve health in early life.

3.2 Biological processes affecting child health

3.2.1 Biological processes occurring before birth

Disruption and curtailment of growth *in utero* may be caused by poor nutrient supply to the fetus. This is not only a matter of the mother's diet, but also includes oxygen.

> The nutrients that get into the fetus . . . are clearly related to the many aspects of the mother's physiology, her preconceptual stores, her competence to sustain fetal growth and maybe to a minor extent what she eats in pregnancy, and whether the mother exercises in pregnancy. Delivery of nutrients to the fetus is a very complicated agenda.
> *(Barker 1994a, p. 238).*

Although the effects of serious malnutrition in the mother, and the stage in pregnancy at which it occurs, are well documented (Perry 1997), it seems likely