introduction to the course, and changing the venue because of complaints about noise levels. The structure of courses will also change in the light of changes to the examinations. As with most of the colleges, the Royal College of General Practitioners continues to develop its examination, and preparation courses need to keep pace with such changes.

After each course, we compile a report, which has two functions. Firstly, it provides a report and evaluation of the course for its sponsors and supporters. Secondly, it provides feedback and continued motivation for the organisers, tutors, and examiners who contribute to the course.

Why bother?
Why should anyone want to get involved in running a course or tutoring on a course? We have found that it provides an important role in personal and professional development and it ensures that we keep up to date with core knowledge, current thinking and research, and changes within our college. Furthermore, we have found that if the course is organised and administered well it is not stressful to be involved but is fun.

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Socioeconomic determinants of health
Stress and the biology of inequality
Eric Brunner

Summary
It is well established that health depends on socioeconomic circumstances, but the biology of this relation is not well described. Psychosocial factors operating throughout the life course, beginning in early life, influence a variety of biological variables. Research with non-human primates shows the effects of dominance hierarchy on biology, and similar metabolic differentials are evident in a hierarchy of white collar civil servants. The neuroendocrine “fight or flight” response produces physiological and metabolic alterations which parallel those observed with lower socioeconomic status. The biological effects of the psychosocial environment could explain health inequalities between relatively affluent groups.

Impact of early experience
The quality of nurturing seems to have long term effects relevant to health inequalities. Deprivation in childhood is linked to poor educational attainment and behavioural problems such as hyperactivity and other conduct disorders, which may be precursors of a lifetime of material and emotional insecurity. Studies of the attachment patterns of parents and their children suggest that early experiences of caregivers may contribute to the intergenerational transmission of physical and psychological vulnerability. We can view childhood social disadvantage, therefore, as a first sign of an unfavourable social stress history. This risk may interact with other early factors, such as low birth weight, which are associated with lower parental social class, to produce adverse effects on later health.

Such early life influences should not be taken to imply a fixed trajectory. Studies of young rhesus monkeys suggest 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 stressful conditions in adulthood. Psychosocial growth retardation of a less dramatic nature was unintentionally documented in Widdowson’s famous study of orphaned children in postwar Germany.

Under identical food rationing, those who lived in the Bienenhaus orphanage, initially under the control of the stern and forbidding Fraulein Schwarz, gained less weight and grew more slowly than children cared for at the Vogelnest orphanage by the affectionate Fraulein Grün. By chance, Schwarz replaced Grün during the study and the growth rates reversed, despite the provision of extra food at Vogelnest. The limited evidence from lifelong follow up studies that included measures of socioeconomic status suggests that risk of premature cardiovascular death is sensitive to early deprivation, while cancer and risk of death from non-cardiovascular, non-cancer causes depends more on adult circumstances.

Stressors in the hierarchy
The Black report concluded that smoking, diet, and other behavioural factors with biological effects contribute to, but do not fully explain, health inequalities. Psychosocial influences, such as self esteem, relate to the social distribution of behavioural risks. Distinct from these indirect psychosocial mechanisms, there is evidence of direct connections between the psychological characteristics of social position and biological functioning.
If exposure to psychosocial as well as to physical adversity is able to explain the continuous gradient in health inequalities, which extends into the highest social strata, can we identify candidate stressors? A necessary but not sufficient condition for such factors is that their prevalence is linked with lower socioeconomic status. On the basis of current evidence, key contenders in adult life include perceived financial strain, job insecurity, low control and monotonity at work, stressful life events and poor social networks, low self esteem, and fatalism. A stepwise relation was found between civil service paranoia or depression. Some depressed patients such as in Cushing’s syndrome, may provoke cortisol/ such as in 9ushing’s syndrome, may provoke cortisol/ also seems to be conditioned by psychosocial factors usee below. / cortisol/ interacts with protective factors, each of which is influenced by social status, which extends into the highest social strata, and the prevalence of several of these factors at the employment grade uyKK1 salary range £VU3VR£3V 21S.  

All stressed out and nowhere to go?慢性 stresses associated with social position may be translated into modified neuroendocrine and physiological functioning, with later consequences for susceptibility to disease. Humans evolved to rise rapidly to the challenge of external, potentially lethal, but short term threats. Frequent and prolonged activation of the ‘fight or flight’ response seems, however, to be maladaptive and may prove to be central in understanding the social distribution of cardiovascular and other diseases.

The main axes of neuroendocrine response, the hypothalamic-pituitary-adrenocortical systems, coordinate an array of metabolic and physiological changes. Rapid release of adrenaline from the adrenal medulla and noradrenaline from sympathetic synapses is able to produce cognitive arousal, sensory vigilance, bronchodilation, raised blood pressure, haemoconcentration, and energy mobilisation. The precise nature of the activation varies according to the stressor and its duration, but its function is essentially to prepare for or maintain physical exertion. Wide variation in the size and duration of endocrine responses is attributed to individual differences in psychological coping resources. Laboratory animals have different physiological responses to a given stressor, reflecting differences in their stress history. There is thus potential for immediate and chronic psychosocial adversity to interact with protective factors, each of which is influenced by social status.

The second and less rapid adrenocortical component of the stress response, which results in release of cortisol, also seems to be conditioned by psychosocial factors (see below), which are unevenly distributed across social classes. A large response seems to be characteristic of actual or projected failure to cope with the apparent threat, and this corresponds to Selye's proposed general and non-specific stress mechanism. Endogenous opioids, linked with vigorous exercise and psychological wellbeing, may be important in the counterregulatory system by inhibiting pituitary release of adrenocorticotropic hormone (see box). Glucocorticoids have many effects, including profound suppression of immunity. Centrally, the hippocampus is a target for glucocorticoids promoting vigilance in the short term. Prolonged high levels of cortisol, such as in Cushing's syndrome, may provoke paranoia or depression. Some depressed patients respond to metyrapone, an inhibitor of cortisol biosynthesis. Stress from physical restraint is associated in rats with reversible loss of hippocampal neurones, probably as a result of high glucocorticoid concentrations. Aspects of aging may be connected to similar irreversible processes, but evidence is scant in humans. Glucocorticoids have a key role in metabolic responses related to stress, as insulin antagonists acting to raise blood glucose and to promote mobilisation of fatty acids. During physical inactivity these superfluous energy substrates will lead to increased output of hepatic lipoproteins. Among captive rhesus monkeys, those with heightened stress responses tend to occupy lower positions in the dominance hierarchy.

Stress mechanisms and cardiovascular disease

It is a plausible but unproved hypothesis that neuroendocrine mechanisms are involved in the production of some cardiovascular diseases. The precise nature of the activation varies according to the stressor and its duration, but its function is essentially to prepare for or maintain physical exertion. Wide variation in the size and duration of endocrine responses is attributed to individual differences in psychological coping resources. Laboratory animals have different physiological responses to a given stressor, reflecting differences in their stress history. There is thus potential for immediate and chronic psychosocial adversity to interact with protective factors, each of which is influenced by social status.

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**Protective effect of wellbeing**

Neuroendocrine pathways interact to pattern the stress response. In a study where the acute stress response was obtained by administration of methoxamine (an α1-adrenergic agonist), rising concentrations of cortisol were provoked over a period of two hours. This rise could be blocked by giving subjects a synthetic endorphin, which mimics the action of endogenous opioids. These findings are consistent with a protective effect of wellbeing — induced, for example, by exercise, which limits the adverse effects of stress.
of social inequalities in coronary heart disease. Reduced variability in heart rate, indicating predominance of sympathetic over parasympathetic activity, is linked with adverse work characteristics and anxiety and separately with increased risk of sudden death. Depression, which is linked with excessive production of glucocorticoids, predicts future coronary disease. Cushing's syndrome is characterised by central obesity and increased risks for hypertension, diabetes, and coronary disease. Central obesity is linked with both of these degenerative diseases and is a feature of low socioeconomic status. The metabolic syndrome of central obesity, glucose intolerance, insulin resistance, lipoprotein disturbances, and reduced fibrinolysis, secondary to altered functioning of the hypothalamic-pituitary-adrenocortical axis, may mediate effects of the psychosocial environment on coronary risk. The challenge of a car driving simulation showed that, consistent with a neuroendocrine conditioning effect, low reactivity was linked with high self esteem. Assessed by a standard psychometric method, self esteem was unrelated to cortisol concentration at baseline but was inversely related to the amount of increase during the challenge.

Stress, infection, and immunity

The brain is able to influence immune function. There is autonomic innervation of all relevant tissues—bone marrow, thymus, spleen and lymph nodes—and glucocorticoids have large effects on the immune system. Infectious disease contributes to the social gradient in morbidity in countries such as Britain, and though evidence is scant, immunity may be implicated in a variety of conditions such as peptic ulcer; gastric, cervical, and other cancers; and possibly coronary disease. Recent stressful life events, which are more frequent in lower social strata (table 1), have been shown to increase susceptibility to and severity of respiratory infections.

Evidence for social stress and stress buffering effects on cell mediated immune function comes from recent animal studies. Macaque monkeys were randomised for two years either to stable social groups or groups which were changed every month. Repeated observations established individual levels of affiliative behaviour (grooming, passive physical contact, or close proximity). As measured by mitogen stimulated proliferation of T cells, the high affiliation group seemed to be protected from the stress of social instability. Although the importance of such effects for health is not known, the same research group has shown that social status predicts susceptibility to influenza virus (SB Manuck, personal communication).

The social patterning of coronary risk

The specific nature of the links between socioeconomic status and coronary risk supplies valuable information about inequalities. Among individuals and between populations, serum cholesterol is an important predictor of coronary risk. Total cholesterol does not, however, seem to explain the inverse gradient in risk according to social position. Thirty years ago, more affluent men who had lower risk had higher cholesterol concentrations, whereas mean blood cholesterol concentrations now vary by no more than 0.1 mmol/l across social classes in England. These observations substantiate the results of dietary surveys, which have found little evidence of social class differences in total intake of fat or intake of saturated fat. A dietary contribution to health inequalities seems related to antioxidants and other micronutrients, and indirectly through the excess energy intake which leads to obesity.

More detailed blood lipid profiles from the Whitehall II study and elsewhere indicate that protective high density lipoproteins, which promote "reverse transport" of cholesterol from the arterial wall, are involved in the social distribution of coronary risk. High density lipoprotein cholesterol concentrations rise incrementally with social status in both sexes.

Determinants of the protective lipoprotein fraction may be important in understanding socioeconomic differences in risk of coronary heart disease. The lipid and lipoprotein pattern observed in male civil servants reproduces the pattern found in the social hierarchy of male baboons. Sapolsky, who has studied the behaviour and physiology of wild baboon troops in the Serengeti for many years, argues that the animals are ideal subjects for investigating psychosocial factors. Food is plentiful, predators are scarce, and infant mortality is low. Only some four hours a 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 after anaesthesia under controlled conditions showed, just as in Whitehall II men, that total cholesterol and low density lipoprotein cholesterol were similar by rank position, and that high density lipoprotein concentrations were higher in the dominant than in the subordinate males, again mirroring findings in civil servants. Subordinate baboons were found to have higher resting glucocorticoid concentrations and fewer circulating lymphocytes.

Do these parallels reflect the common psychosocial effects of position within the two hierarchies of primates? Production of the more favourable physio-
logical profile in dominant baboons might be the direct consequence of their assertions of supremacy and consequent feelings of wellbeing, or perhaps 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 of captive macaques suggest that this is not the case.\(^{22}\) The initial rank in small groups of female monkeys who were fed an atherogenic diet was altered experimentally by switching animals between groups.\(^{23}\) The effects of manipulating social status were dramatic. Dominants who became subordinate had a fivefold excess of coronary plaques compared with animals who remained dominant, while subordinates who became dominant had a twofold excess of atherosclerotic changes in comparison to those remaining subordinate. Other findings are compatible with an interaction between a high cholesterol diet and psychosocial adversity.

Control and adaptation

An important characteristic of position in the social hierarchy is the individual’s level of control. Follow up of male and female civil servants in the Whitehall II study shows that self reports of low control at work (low autonomy and decision latitude) predict coronary heart disease.\(^{24}\) These prospective findings, although observational, add important evidence for an independent effect of low control at work because the risk remains after adjustments for socioeconomic status or coronary risk factors. The dose-response gradient—reports of low control on two occasions being more strongly linked to incident disease than a single report—further supports a causal interpretation.

In the social service, low perceived control is related to poor health and many factors relevant to it, including dietary behaviour\(^{25}\) and sickness absence rates.\(^{26}\) Low control is also associated with high concentrations of the blood clotting protein fibrinogen, a marker for cardiovascular disease.\(^{27}\) This linkage may be one example of the costs of stress related biological adaptation. Physiological variables such as body temperature and blood pH are under close homoeostatic control, while others such as fibrinogen concentration are less tightly constrained. Such adaptations have been defined as allostatics.\(^{28}\) Follow up studies are testing this concept with measures of the effect of allostatic load, which include glycosylated haemoglobin, waist-hip ratio, high density lipoprotein cholesterol concentration, and output of urinary cortisol and catecholamines.

Conclusions

There is incomplete evidence, but biological plausibility, for the view that psychosocial factors may be important determinants of population health. This short review shows that the stress history—the accumulation of psychosocial experiences beginning in infancy and continuing throughout the life course—seems to have biological effects that will influence the development of degenerative disease. Neuroendocrine stress mechanisms may contribute in particular to social gradients in risk of coronary disease and morbidity associated with reduced immunity. The observed social distribution of chronic diseases presents a challenge to understanding because the underlying pathophysiological processes, which take place over many years and involve many body systems, are incompletely understood. The biological perspective does not detract from the primary importance of social organisation in generating health inequalities, but it can provide an approach to determining the specific aspects of the psychosocial environment that influence health.

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Keeping in touch
A paper reunion

Medical school is a working life time away as retirement approaches. Contact with contemporaries may be tenuous and memories hazy. I went to my year’s 40th reunion out of curiosity. Most there were instantly recognisable by voice, mannerism, and surprisingly by appearance too. The conversations were of illness, bereavement, and death. Surely something good must be happening to someone? Finding out required an accurate list of names and addresses. No group’s progress through medical school is tidy—1st MB exemptions, intervening BScs, illness, and examination failure disrupt it. Class lists do not tell the whole story of who did what when. The medical school’s old student directory is not updated annually.

Cross referencing the school’s list with the Medical Directory and Medical Register could produce three different addresses. The register has ceased to hold dead records earlier than the mid 1970s. A missing name could mean a death or a permanent move abroad with a lapsed British registration. I suspected that a personal approach would bring the best response. But the information I needed had to be standardised and I wanted it to reflect personality and perceived achievement. The questionnaire devised was sent to 103 individuals identified as the 1953 1st MB intake and/or 1959 qualifiers.

The response was good; what was even better was the number of letters, full of gossip, that accompanied the returned questionnaires. These provided snippets of information about some of the inevitable non-responders. Networking from this was an effective tool and ultimately there were only nine people about whom nothing—apart from the consensus opinion that they were alive—was known.

Seventy five of 81 women and 19 of 22 men could be accounted for. Six students had not completed their training. Sixteen were dead, one a suicide and two since that 40th reunion. Forty four were settled abroad. Seventy one had married. There were lots of children (few doctors) and an increasing number of grandchildren.

Fellowships, MDs, master’s degrees, a single DSc had been acquired, and of course BScs en route to qualification. There were memberships and diplomas galore. Several had reached the top of the profession; one had even established a new specialty. Everyone had done some medical work, despite the establishment’s antipathy to women, especially if they were married and had children.

Involvement in a broad range of medical activity had created career portfolios before the concept had been defined. There had been an occasional change of specialty to match interest or need or both. A few had branched into other occupations.

The ability to combine medical and domestic commitments, with neither suffering, was a source of pride. Particular pieces of work, not necessarily of earth shattering significance, had brought satisfaction. Most would have changed little of what they had done and few regretted their medical careers.

There was anger about the way the NAS now conveyed instruction, pathos, or humour—by possible any other piece. A memorable patient. A paper that changed my life. A paper that changed my practice. My most unfortunate mistake, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.