22

Stress, anxiety and psychosomatic disease

- STRESS and AROUSAL are separate concepts, stress representing a psychological response and arousal a physiological response. The combination is ANXIETY.
- Pre- and post-operative anxiety can be reduced by preparation in which the patient is told the physical and psychological consequences of the operation and is taught strategies for dealing with events such as pain.
- Stress has deleterious physiological consequences via the GENERAL ADAPTATION SYNDROME, which mediates via the adrenal cortex, in contrast to the FIGHT-OR-FLIGHT MECHANISM which mediates via the adrenal medulla.
- High cortisol levels have wide-ranging physiological effects, including a suppression of immune functioning which may be important in the progress of malignant disease.
- LIVE-EVENTS such as death of a spouse, divorce and job loss are associated with illness such as myocardial infarction.
- Individuals with the TYPE A PERSONALITY have higher levels of blood cortisol, glucose and triglycerides, and have a higher rate of coronary artery disease.

STRESS as a psychological concept derives from physics, where it has two meanings: a force *imposed* upon a system, and the effect of a force *upon* the system (which may fatigue or break). Both meanings occur in psychology and are usually clearly delineated, although occasionally STRESSOR is used for the stimulus, and DISTRESS for the response.

Stressors take many forms (overwork, high temperature, loud noises, surgical operations) and if prolonged and severe, they produce a complex, non-specific set of behavioural and physiological changes described by Hans Selye (1907–1982), a Canadian endocrinologist, as the GENERAL ADAPTATION SYNDROME (GAS). In phase I (the ALARM REACTION) there is an initial brief fall in RESISTANCE TO STRESS during the SHOCK, but then the COUNTERSHOCK is followed by phase II (the STAGE OF RESISTANCE), which shows the behavioural changes of increased resistance to stress,

until eventually in phase III COLLAPSE, the STAGE OF EXHAUSTION is reached, with FAILURE TO COPE and a precipitous fall in resistance to stress.

AROUSAL is a separate concept from stress, primarily physiological in origin, and reflecting sympathetic activity, with increased heart-rate and raised metabolism. It is produced by many behaviours and need not be at all distressing. The physiology of an athlete crossing the finishing line, of an actor on the stage, or of sexual orgasm, all involve arousal, but it is not stressful, better being described as 'joyous excitement'.

Since arousal and stress are independent, all combinations occur. The separate components are measured easily by simple questionnaires. Low stress and low arousal are associated with DROWSINESS, and low arousal and high stress produce UNDERSTIMULATION or BOREDOM. High arousal and low stress is described as EXCITEMENT, whereas high arousal with high stress is a state of overstimulation labelled as ANXIETY, 'a vague, unpleasant emotional state with qualities of apprehension, dread, distress and uneasiness'; it has been described as the archetypal emotion of the twentieth century. Anxiety is often accompanied by autonomic over-arousal (seen particularly as tachycardia, but also tremor, hyperventilation, urinary frequency and diarrhoea, symptoms known to all exam candidates). Objective measurements of stress by recording simple heart-rate are not successful because many other confounding processes also cause tachycardia. However FOURIER ANALYSIS of heart rate extracts a component varying at about 0.1 Hz (i.e. every ten seconds) which reflects vasomotor control and relates to perceived stress in situations such as driving in heavy traffic (Fig. 22.1).

Anxiety impairs efficiency on many tasks, although not in a straightforward way. The YERKES-DODSON LAW says performance shows an inverted-U relation to anxiety, increasing anxiety improving performance until a maximum is reached, after which performance falls away, being poor at high anxiety levels. A little anxiety can benefit performance, but a lot is harmful, and optimal anxiety decreases as task difficulty increases, probably because otherwise useful cognitive activity is wasted on monitoring the effects of anxiety, leaving less resources available for actual processing.

Anxiety is readily assessed by questionnaires such as Spielberger's STATE-TRAIT ANXIETY INVENTORY (STAI), which measures both STATE and TRAIT ANXIETY (see Chapter 8). As an example, Figure 22.2 shows state anxiety levels in medical students immediately before a preclinical viva examination, and before or after their medical school selection interview, in comparison with age-sex norms for four different situations. Anxiety is slightly greater before the selection interview than after, but in each case is low compared with the very high levels before a viva examination.

Anxiety is common in all hospital patients, and should always be

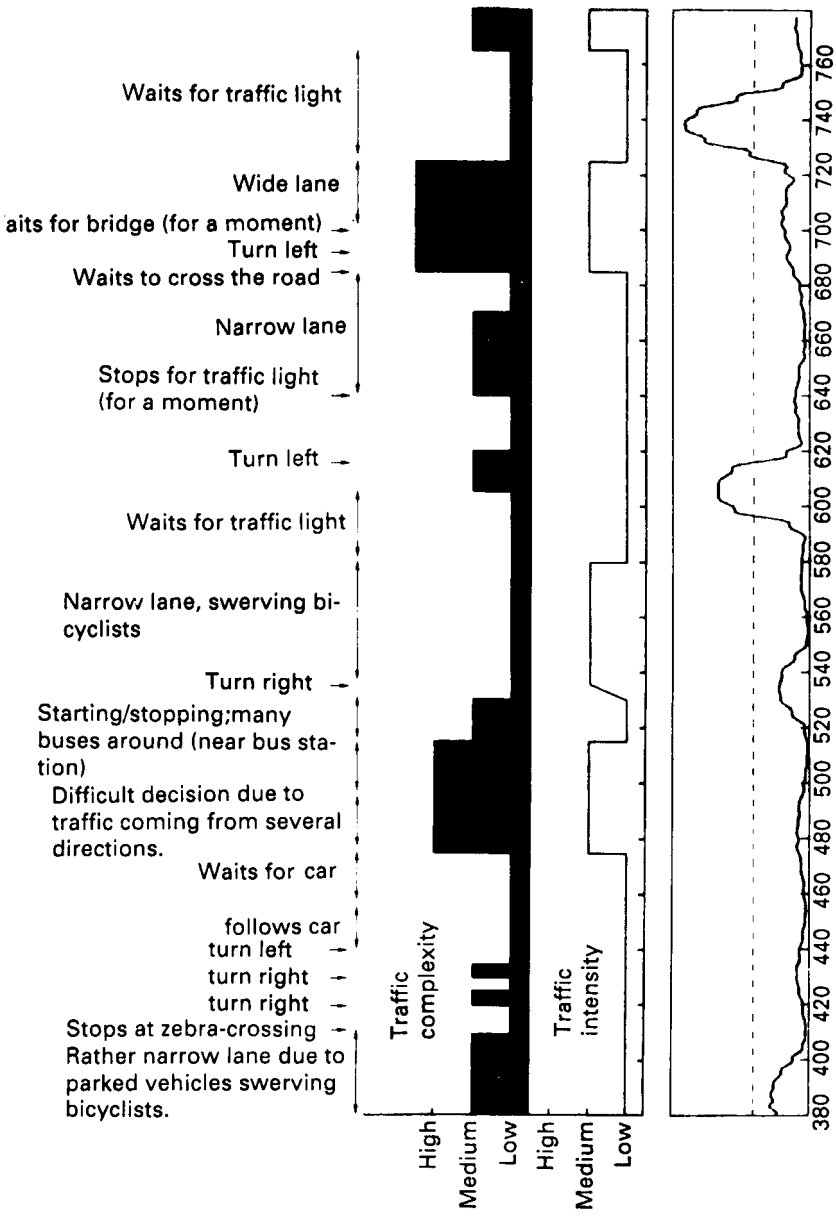

Fig. 22.1 The amplitude of the 0.1 Hz component of the heart rate (which relates to perceived stress, via the hypothalamico-pituitary-adrenal axis) of a person driving in heavy Dutch traffic (and hence turning *left* is a particularly difficult manoeuvre). Note that stress *suppresses* the 0.1 Hz component, so that low levels indicate high stress. Reproduced with permission from Mulder G (1980), *The Heart in mental effort*, unpublished PhD thesis, University of Groningen.

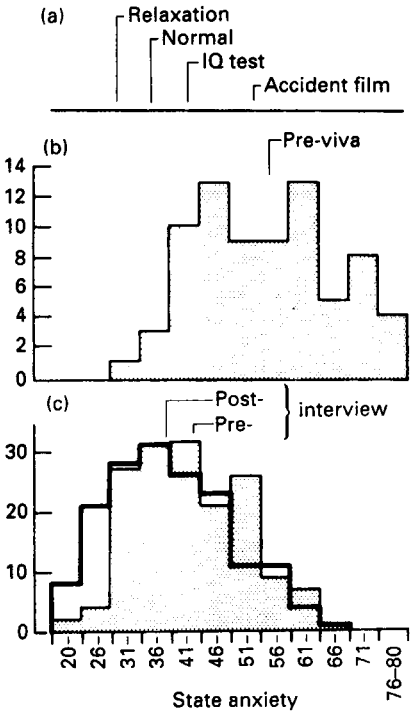

Fig. 22.2 State anxiety levels: *a*) of control subjects while relaxing, when they had just entered the laboratory ('normal'), when they had taken a timed IQ test, and when they had just seen a film of 'gruesome woodworking accidents'. *b*) anxiety levels of preclinical medical students just prior to an important *viva voce* examination. *c*) anxiety levels of medical school applicants just before or after their selection interview. Reproduced with permission from Arndt C B, Guly U M V and McManus I C (1986). Pre-clinical anxiety: the stress associated with a *viva voce* examination. *Medical Education*, **20**, 274–80.

thought about. Figure 22.3 shows anxiety levels before major, minor and dental surgery, showing that anxiety is almost universal before surgery, and extends both before and after the procedure. Careful studies show that pre-operative anxiety is reduced by psychological preparation; giving a clear, realistic description of what to expect physically (will there be drainage tubes? will they be in Intensive Care?) and psychologically (the degree, extent and treatment of pain, etc.). In comparison with controls, reduced post-operative morphine doses are required in patients undergoing intra-abdominal operations who have received pre-operative psychological preparation emphasizing active self-control of pain (e.g. by relaxing abdominal muscles and avoiding tensing muscles while moving) (Fig. 22.4).

Stress is important in medicine because of the recurrent idea, expressed more by patients than doctors, that the stress of daily life causes illness. Stress-induced illness is an example of PSYCHOSOMATIC DISEASE in which instead of the more easily understood sequence of bodily disease affecting the brain and mind ('somatopsychic disease'), the primary event is thought to be behavioural or psychological, which then causes pathological change in the body. Psychosomatic causation for disease is easy to postulate, but difficult to prove convincingly, and several methodological problems are often ignored. Firstly, the mere correlation of two events, A and B, does not prove

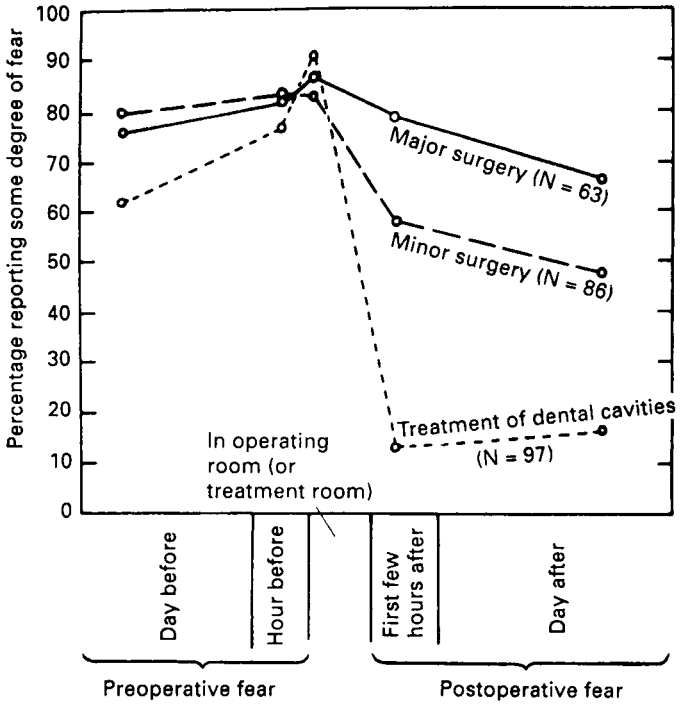

Fig. 22.3 Reported anxiety levels in relation to severity of surgery. Reproduced with permission from Janis I L (1958), *Psychological Stress*, New York, John Wiley, 284.

causation; although A may indeed cause B, B may also cause A, or A and B may be caused by some third event C. Thus it may be that persons regularly attending football matches might be more likely to develop lung cancer, but there is no point in postulating a psychosomatic effect, with the stress of the game *causing* lung cancer, when far more likely is that social class or cigarette smoking correlate with both variables, and create a spurious correlation. A second error is to think that behaviours occur in isolation, whereas in reality they are part of a broader nexus of behaviours. As an example, a recent book claimed that since divorcees had a higher rate of carcinoma of the cervix, then this must be caused by the stress of divorce, and hence cancer of the cervix should be classified as psychosomatic. Divorcees, however, are different from the general population, tending to have had their first sexual intercourse at an earlier age, to have had more sexual partners, more sexually transmitted disease, and married younger. Since strong evidence suggests that carcinoma of the cervix can be caused by infection with *herpes simplex* type II viruses, which are spread like other sexually transmitted diseases, the most parsimonious explanation of the excess of cervical malignancy in divorcees is that they have a higher rate of herpetic infection. Such

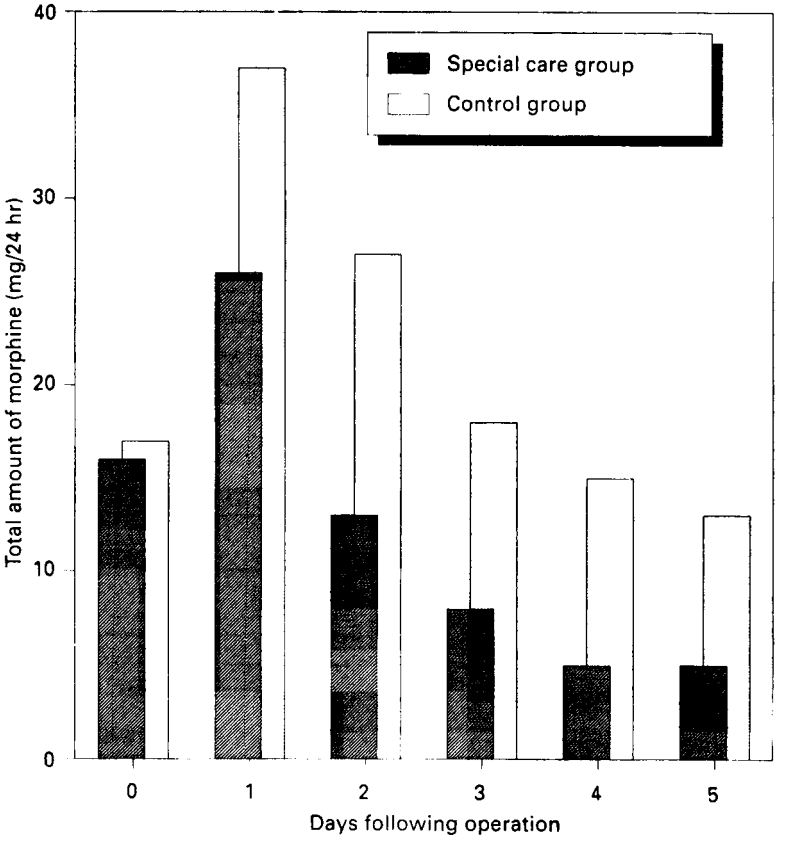

Fig. 22.4 Total daily post-operative morphine requirements of patients who had special psychological preparation for surgery, compared with a control group. Redrawn with permission from Egbert L, Batit G, Welch C and Bartlett M (1964), Reduction of post-operative pain by encouragement and instruction of patients, *New England Journal of Medicine*, **270**, 825–7.

analysis begs the question of *why* these individuals had more sexual behaviour, and it cannot exclude the possibility that the stress of divorce either precipitated disease, prevented its early detection, or enhanced its growth. These possibilities might all be true, but still the original hypothesis of psychosomatic disease causation cannot be supported by the original data. Merely suggesting a psychosomatic aetiology does not dispense with the need for rigorous scientific analysis of cause and effect.

An interesting example of a psychosomatic process that seems beyond serious doubt concerns the simple association of dates of birth and death. Birth dates are known accurately, and are recorded systematically in national statistics. Comparison of dates of birth and death shows individuals are slightly less likely to die in the months before their birthday, and are more likely to die in the months after

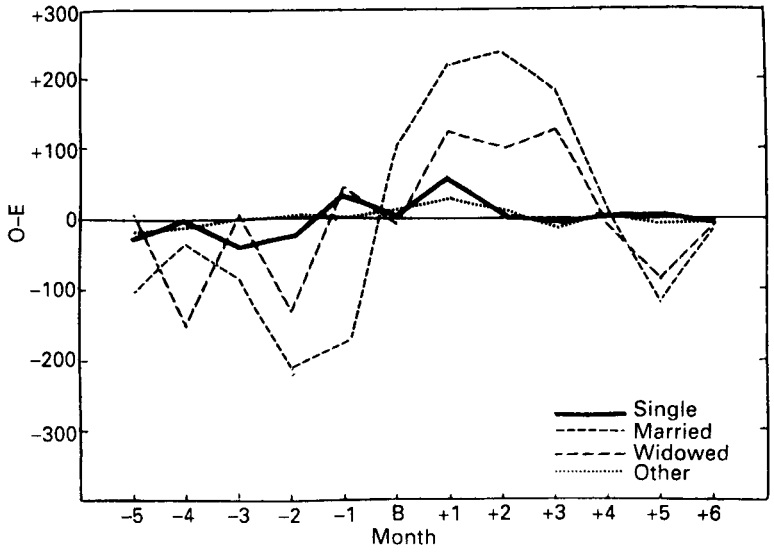

Fig. 22.5 Difference between observed (O) and expected (E) number of deaths of men aged over 74, in England and Wales in 1972, in relation to their birthday (B), according to whether the death was before (minus values) or after (positive values) their birthday. Reproduced with permission from Alderson M (1975). Relationship between month of birth and month of death in the elderly. *British Journal of Preventive and Social Medicine*, **29**, 151–6.

(Fig. 22.5); and the effect is greater over the age of 60, and for the 'important' birthdays, which end in a '5' or a '0'. The simplest explanation is that individuals wish to live until their next birthday, they set this as a goal or challenge, and they successfully strive to achieve it; after the birthday they have less to live for and succumb. The effect is small, affecting only 1% of deaths, but it must be seen as an indubitable triumph of mind over the vicissitudes of body, since basic pathophysiology cannot possibly appreciate the calendar. The converse process, of patients willing themselves to die, and just fading away over days or weeks, is also well documented, and is related to the 'evil eye' phenomenon in primitive tribes in which a person cursed by a witch doctor dies within a matter of days.

Such studies say little of the role of stress in psychosomatic disease, and to understand that we must look at the physiological responses to stressful events that occur. Two separate physiological systems must be distinguished. Cannon's FIGHT-OR-FLIGHT system was discovered first, in which an organism experiences a THREAT TO CONTROL, due to some external event, and there is sympathetic hyperactivity, principally dependent upon adrenaline and noradrenaline from the ADRENAL MEDULLA, although other hormones such as testosterone also increase their levels; corticosteroid levels do not change. The increased arousal

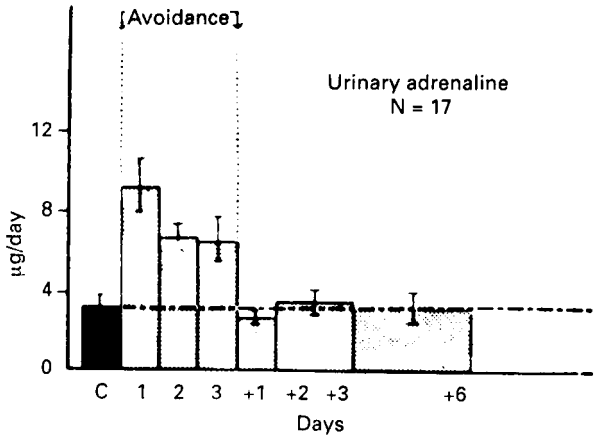

Fig. 22.6 Hormonal responses of monkeys to three days of conditioned avoidance learning (days 1–3) in comparison with the pre-conditioning baseline (C) and the six days after conditioning had ceased. *a*) Urinary adrenaline levels from Mason J W, Tolson W W, Brady J V, Tolliver G A and Gilmore L I (1968), Urinary epinephrine and norepinephrine responses to 72-hr avoidance sessions in the monkey, *Psychosomatic Medicine*, **30**, 654–5 and *b*) other hormones, from Mason J W (1968), Organisation of the multiple endocrine responses to avoidance in the monkey, *Psychosomatic Medicine*, **30**, 775.

makes the organism better capable of taking emergency action demanded by the threat. Cannon's system must be contrasted with Selye's General Adaptation Syndrome, which has already been mentioned. LOSS OF CONTROL results in high levels of corticosteroid secretion from the ADRENAL CORTEX, reduction in testosterone levels, and little change in adrenaline or noradrenaline levels. The GAS proceeds through the three stages mentioned earlier, during which RESISTANCE changes (it is measured experimentally by exposing animals to cold or infection, and monitoring survival). Resistance decreases during shock, but then recovers and increases above normal levels in phase II, before falling precipitously during exhaustion and death. The fight-or-flight mechanism is probably controlled by the AMYGDALA and the GAS by the SEPTO-HIPPOCAMPAL SYSTEM. Figure 22.6 shows endocrine responses of monkeys coping for three days with a CONDITIONED AVOIDANCE TASK, in which lever presses helped avoid electric shocks. The fight-or-flight response of increased adrenaline occurred on day 1, but decreased thereafter, whereas GAS responses continued throughout the three days, and in some cases, such as urinary 17-OHCS (17-hydroxycorticosteroid, a principal metabolite of the corticosteroids), thyroxine and growth hormone were still raised several days after the schedule had ceased.

Corticosteroids have a wide range of physiological effects, and

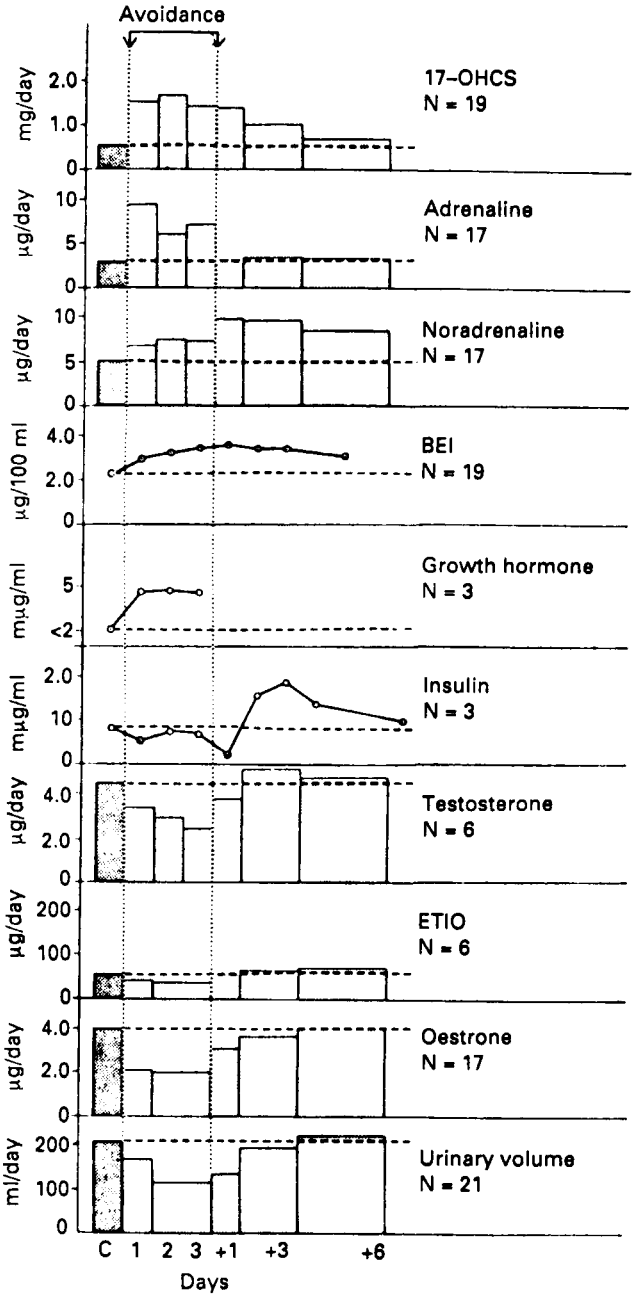

Fig. 22.6 *b) continued*

when administered in large quantities produce peptic ulceration and haemorrhage, diabetes, amenorrhoea, growth retardation, osteoporosis, thinning of the skin, poor wound healing, thrombosis, sodium retention, hypertension and immune suppression. It is therefore possible that the GAS may well underlie diseases such as peptic ulceration, hypertension, rheumatoid arthritis and diabetes, all of which have been claimed to be psychosomatic. Cortisol's effects upon the immune system have resulted in PSYCHONEUROIMMUNOLOGY, which studies the links between brain, behaviour and immune function (and which has argued that the brain views the immune system as another sensory system, which tells it about the internal milieu of the body). Cortisol suppresses immune function, decreasing circulating lymphocytes, and causing a decrease in thymic, splenic and lymphatic tissue. If stress causes cortisol secretion it can then impair immune rejection, as is seen experimentally in mice injected with tumour cells (Fig. 22.7).

The size of the GAS response depends upon the extent of perceived loss of control, and can be assessed biochemically. Figure 22.8 relates urinary hydrocortisone levels in women awaiting breast biopsy for possible malignancy to the degree of failure of psychological defence mechanisms (and these mechanisms are themselves a strong predictor of survival in breast cancer: Fig. 22.9). Perceived control need not be real to be effective, as in experiments in which rats received unpredictable, uncontrollable electrical shocks; isolated rats showed higher ACTH levels than paired animals, which responded to shocks by fighting, apparently 'blaming' the other for the shock, and hence treating it as controllable. Social pressure also produces loss of control; subordinate animals in a dominance hierarchy have higher corticosteroid levels than dominant animals, although eventually levels do fall as the animals cope with low status. Social effects also interact with genetic factors; the stress of living in social groups produces higher blood pressure in rats which are genetically spontaneously hypertensive (Fig. 22.10). Finally it must be emphasized that danger alone does not cause the GAS and there must also be a threat to control. In a study carried out during a threatened attack on a group of Vietnam War soldiers, only the officer and radio-operator had increased urinary 17-OHCS levels. The other men were not suffering a threat to control, since they were trained to act precisely and efficiently under orders, and hence had less threat to control than did the officer, who did not know what to expect in the coming attack, and whose sense of control was therefore threatened.

Stress is also a risk factor in disease in the way individuals respond to life events. Any life, however well-ordered, suffers changes. Some changes, or LIFE-EVENTS, are bad (deaths, financial difficulties, job loss, etc.) and others are good (marriage, children, new job, new house, etc.); however, each requires *change*, and threatens a loss of control,

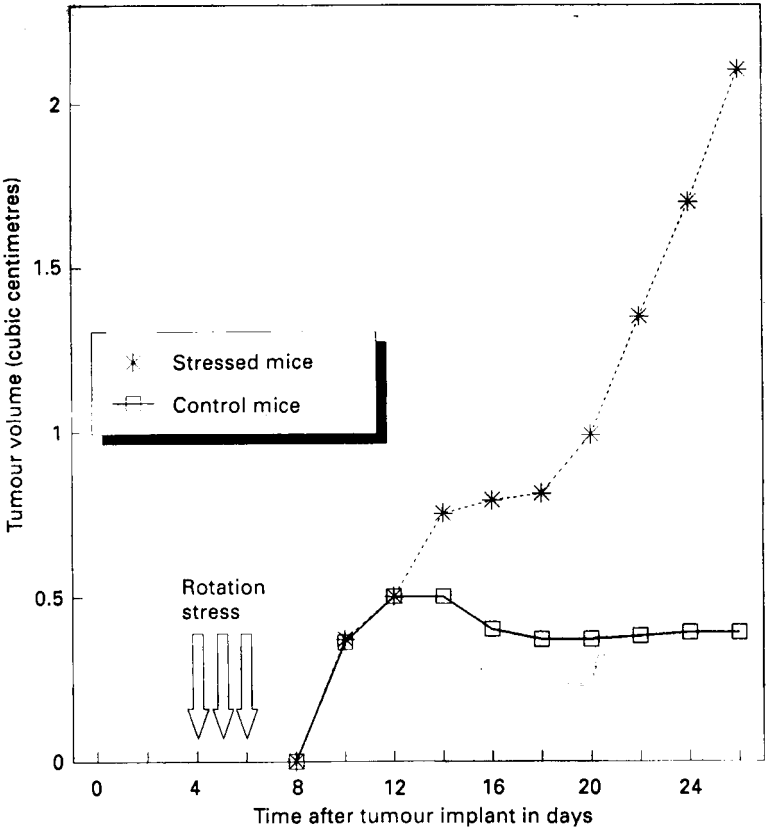

Fig. 22.7 The weight of tumour tissue present in mice which have had the 6C3HED lymphosarcoma implanted subcutaneously on day 0. On days 4, 5 and 6 the experimental group was stressed by spending 10 minutes in each hour in a cage placed on a gramophone turntable rotating at 45 revolutions per minute. Adapted from Riley V (1981), Psychoneuroendocrine influences on immunocompetence and neoplasia, *Science*, **212**, 1100–9.

and hence is stressful. Life-event stress can be measured using a checklist of life-events, the HOLMES-RAHE LIFE CHANGE EVENT INVENTORY (Table 22.1), each of which has been rated for its stress. There is also a special version for students (Table 22.2). Men suffering myocardial infarction have higher life-event scores in the previous six months than controls. That stress comes from *change*, be it good or bad, is seen in studies of death statistics in relation to unemployment and other economic indicators: the death rate rises as unemployment rates rise (as might be predicted) but also rises during rapid economic growth, when increasing wealth and prosperity are accompanied by industrial changes and the need to learn new skills. Following unemployment, death rates rise almost immediately for suicide, after a

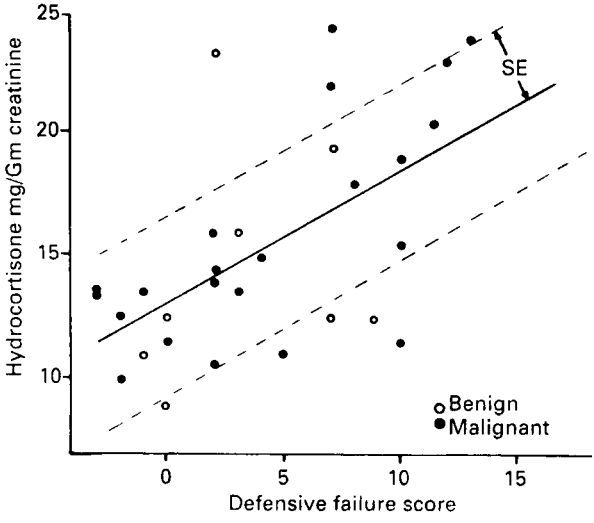

Fig. 22.8 The relation between urinary excretion of hydrocortisone and the failure of defence mechanisms, and development of a sense of loss of social and personal well-being in women undergoing breast biopsy for a lump. Reproduced with permission of author and publishers from Katz J L *et al.* (1969), *Ann NY Acad Sci*, **164**, 509–15.

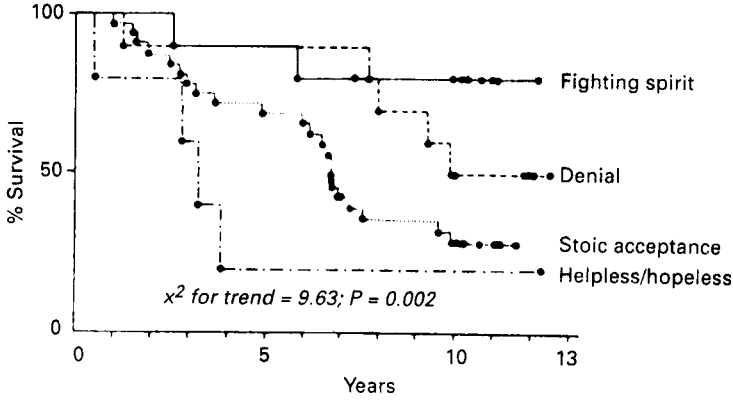

Fig. 22.9 The proportion of women still alive twelve years after breast cancer was diagnosed in relation to the woman's psychological response to the diagnosis (assessed by a psychiatrist within three months of the diagnosis). The difference between groups is not explained by other known predictors of survival such as age, severity at diagnosis, histology, appearance at mammography, or hormonal or immunological measures. Reproduced with permission from Pettingale K W, Morris T, Greer S and Haybittle S L (1985), Mental attitudes to cancer: an additional prognostic factor, *Lancet*, **i**, 750.

lag of two or three years for cardiovascular disease, and after longer lags for chronic diseases, showing the long latencies for psychosomatic effects.

Another source of stress with life-events arises from the person themself. In America, Friedman and Rosenman were studying the diet of patients with myocardial infarctions. The wife of one patient pointed out that she and her husband ate almost identical diets, and

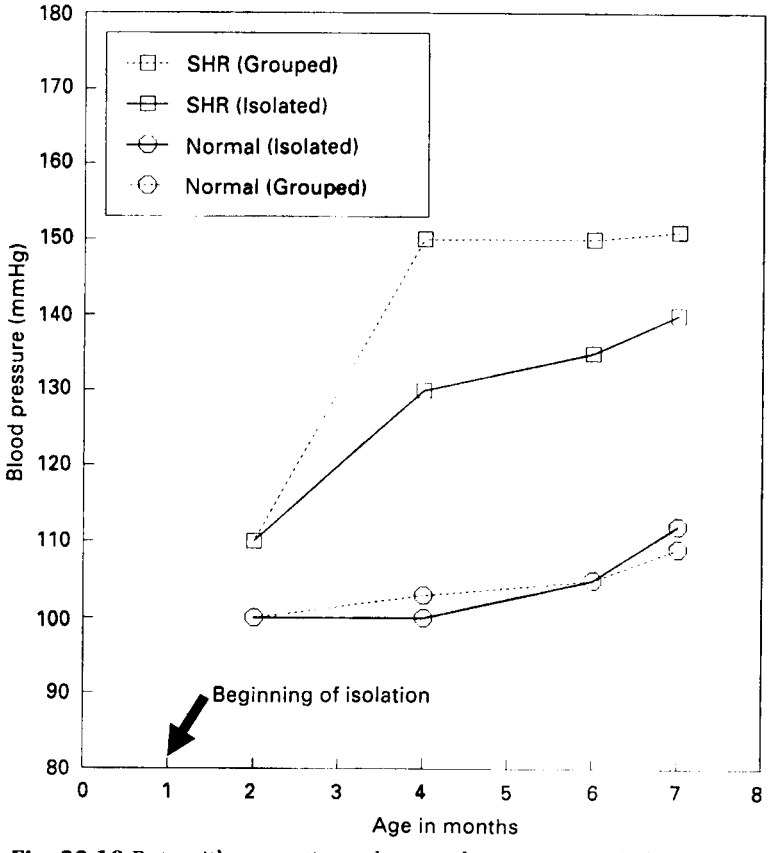

Fig. 22.10 Rats with a genetic tendency to be spontaneously hypertensive (SHR) show a higher blood pressure when kept in social groups than when isolated, whereas no difference is found for normal rats. Redrawn with permission from Hallbaeck M (1975), Interaction between central neurogenic mechanisms and changes in cardiovascular drive in primary hypertension, *Acta Physiol Scand, Suppl 424*.

therefore diet was unlikely to be the problem, and that instead behaviour differences might be the culprit. Spurred on by this, Friedman and Rosenman suggested that the problem might be the TYPE A PERSONALITY, a person aggressively involved in a chronic struggle to achieve too much and to participate in too many events, particularly when under challenge. Many characteristics of type A behaviour, such as a desire to compete, achieve and be successful are particularly prevalent in medical students and doctors, and are also found in 10% or more of the population. Type A behaviour is also associated with higher levels of serum ACTH and cortisol, noradrenaline, blood clotting factors, glucose and triglycerides, and with a higher rate of coronary artery disease, even after smoking, obesity, cholesterol and blood pressure have been taken into account.

Table 22.1
The Holmes-Rahe scale of life change events. The value of 50 was arbitrarily assigned to 'Marriage' and other events rated against it. From Holmes T H and Rahe R H (1967), The social readjustment rating scale, *Journal of Psychosomatic Research*, **11**, 213–18.

	LCU values
Family:	
Death of spouse	100
Divorce	73
Marital separation	65
Death of close family member	63
Marriage	50
Marital reconciliation	45
Major change in health of family	44
Pregnancy	40
Addition of new family member	39
Major change in arguments with wife	35
Son or daughter leaving home	29
In-law troubles	29
Wife starting or ending work	26
Major change in family get-togethers	15
Personal:	
Detention in jail	63
Major personal injury or illness	53
Sexual difficulties	39
Death of a close friend	37
Outstanding personal achievement	28
Start or end of formal schooling	26
Major change in living conditions	25
Major revision of personal habits	24
Changing to a new school	20
Change in residence	20
Major change in recreation	19
Major change in church activities	19
Major change in sleeping habits	16
Major change in eating habits	15
Vacation	13
Christmas	12
Minor violations of the law	11
Work:	
Being fired from work	47
Retirement from work	45
Major business adjustment	39
Changing to different time of work	36
Major change in work responsibilities	29
Trouble with boss	23
Major change in working conditions	20

Table 22.1 *Continued.*

Financial:	
Major change in financial state	38
Mortgage or loan over $10 000	31
Mortgage foreclosure	30
Mortgage or loan less than $10 000	17

Table 22.2
Scale of 'Life change events experienced by college students'. College entry was arbitrarily assigned a value of 50, and other items rated against it. From Marx M B, Gavrity T F and Bowers F R (1975), The influence of recent life experience on the health of college freshmen, *Journal of Psychosomatic Research*, **19**, 87–98.

	Unit score
Family	
Death of spouse	87
Marriage	77
Death of close family member	77
Divorce	76
Marital separation	74
Pregnancy or fathered a pregnancy	68
Broke or had broken martial engagement or steady relationship	60
Marital reconciliation	58
Major change in health or behaviour of family member	56
Engagement for marriage	54
Major change in number of arguments with spouse	50
Addition of new family member	50
In-law trouble	42
Spouse began or ceased work outside the home	41
Major change in number of family get-togethers	26
Personal	
Death of close friend	68
Major personal injury or illness	65
Sexual difficulties	58
Major change in self-concept or self-awareness	57
Major change in use of drugs	52
Major conflict or change in values	50
Major change in amount of independence and responsibility	49
Major change in use of alcohol	46
Revision of personal habits	45
Major change in social activities	43
Change in residence or living conditions	42
Change in dating habits	41
Outstanding personal achievement	40
Major change in type and/or amount of recreation	37
Major change in church activities	36
Major change in sleeping habits	34

Table 22.2 *Continued.*

Trip or vacation	33
Make change in eating habits	30
Minor violations of the law	22
Work	
Fired from work	62
Entered college	50
Changed to different line of work	50
Changed to new school	50
Major change in responsibilities at work	47
Trouble with school administration	44
Held job while attending school	43
Major change in working hours or conditions	42
Change in or choice of major field of study	41
Trouble with boss	38
Major change in participation in school activities	38
Financial	
Major change in financial state	53
Mortgage or loan less than $10 000	52