CLINICAL ANXIETY

by

MALCOLM LADER
B.Sc., Ph.D., M.D., D.P.M.

Member of External Scientific Staff, Medical Research Council; Honorary Senior Lecturer, Department of Psychiatry, Institute of Psychiatry, University of London; Honorary Consultant, Bethlem Royal and Maudsley Hospital; Honorary Research Fellow, Department of Pharmacology, University College London

ISAAC MARKS
M.D., D.P.M.

Senior Lecturer, Department of Psychiatry, Institute of Psychiatry, University of London; Honorary Consultant, Bethlem Royal and Maudsley Hospital

WILLIAM HEINEMANN · MEDICAL BOOKS · LIMITED
LONDON

First published 1971

I.S.B.N. 0 433 19000 0

Printed and bound in Great Britain by R. J. Acford Ltd., Industrial Estate, Chichester, Sussex.

Authors' Preface

Over the past few years there has been a vast increase in interest in the topic of anxiety as witnessed by the number of papers published. Much of the interest has been in two particular areas. Firstly, there have been many studies on the psychology of anxiety in normal subjects and on anxiousness as a personality trait. Secondly, in psychoanalytic writings anxiety in one form or another still appears to play a pivotal role. However, there has been more interest shown recently in anxiety in the clinical sphere—as a morbid affect complained of by patients with anxiety states. It has been the subject of some symposia (notably two under the auspices of the World Psychiatric Association) which have summarised selective aspects, but in general there has been little systematic work on the clinical, experimental or theoretical levels.

We set out to present a general account of this common, abnormal emotion, namely, clinical anxiety. However, it soon became apparent that the literature on anxiety was scattered, amorphous and varying in quality and we were forced to be more selective than we originally intended. Firstly, we have not dealt in depth with the extensive psychoanalytical writings as we felt that we could not do justice to them within the planned length of this book. Secondly, we have only briefly summarised the psychological literature as its relevance to the clinical sphere is limited at present due to its chief concern with anxiety in normal subjects and not patients.

Accordingly, we have attempted to give a representative selection of those aspects of anxiety which fall into the broad rubric of clinical science. As one of us is particularly interested in psychophysiology and psychopharmacology, the other in psychopathology and psychological treatments, some concentration on these areas was inevitable: the book is not a comprehensive account of all aspects of anxiety. Nevertheless, we hope that it will be of value to psychiatrists, general physicians, general practitioners and others who diagnose and treat clinical anxiety.

We are grateful to Dr. R. E. Kendell and Dr. P. J. Noble for their many helpful comments on our manuscript which Mrs. A. Ginger typed with such care.

Institute of Psychiatry M.L.
University of London I.M.
April 1971

Chapter One

INTRODUCTION

Anxiety is an emotion which is usually unpleasant. Subjectively it has the quality of fear or of closely related emotions. Implicit in anxiety is the feeling of impending danger, but there is either no recognisable threat or the threat is, by reasonable standards, disproportionate to the emotion it seemingly evokes.[292]

The English language is rich in expressions which connote feelings of anxiety or subtly allied states. Among these are: apprehension, uneasiness, nervousness, worry, disquiet, solicitude, concern, misgiving, qualm, edginess, jitteriness, sensitivity, being pent-up, troubled, wary, unnerved, unsettled, upset, aghast, distraught or threatened, defensiveness, disturbance, distress, perturbation, consternation, trepidation, scare, fright, dread, terror, horror, alarm, panic, anguish, agitation. All these terms convey the fine nuances of emotions related to anxiety.

Emotional terms overlap considerably in their meaning, and closely related terms like anxiety and fear can be hard to differentiate. One way to distinguish between them is to find out the "average" person's associations to each term. Davitz[95] examined the common meaning of emotional terms amongst 50 normal Americans. He found some associations which were distinctive for each term and many which overlapped. These are seen in Table 1.1.

In general the emotional states of anxiety and fear are very similar, though fear has more physiological concomitants. However, this could reflect intensity of the emotion rather than its quality. More definite distinctions might be made on the basis of value judgments regarding cause of the emotion. If the cause is readily apparent to the outside observer or to the subject, then the emotion tends to be labelled fear. If no causal agent is evident it is likely to be called anxiety.

Subjective bodily discomfort occurs during anxiety. There is a sense of constriction in the chest, tightness in the throat, difficulty in breathing, epigastric discomfort or pain, palpitations, dizziness and weakness in the legs and dryness of the mouth. Other bodily disturbances during anxiety are also objectively visible, e.g. running in panic, screaming, tremor, sudden micturition and defaecation, sweating and vomiting.

Although anxiety is usually thought of as an unpleasant emotion, people do not always try to avoid it. On the contrary, some subjects actively seek anxiety and gain intense satisfaction from their mastery

Table 1.1
Associations to "anxiety" or "fear" in 50 normal Americans[95]

Associations to *anxiety* but not fear:
There's a sense of uncertainty about the future; I have no appetite; I can't eat; a tension across my back, my neck and shoulders; it's involved with other feelings; a gnawing feeling in the pit of my stomach; everything seems out of proportion; I try to stop thinking of the situation and try to think of other things.

Associations common to both *anxiety* and *fear*:
I'm wound up inside; there is an intense concern for what will happen next; there is a sense that I have no control over the situation; a sense of anticipation waiting for something to happen; my whole body is tense; I'm jumpy, jittery; a sense of being gripped by the situation; there is a narrowing of my senses, my attention becomes riveted on one thing; I want to do something, anything, to change the situation and relieve the tension; there is a tight knotted feeling in my stomach; I seem to be caught up and overwhelmed by the feeling; there is a sense of aloneness, being cut off, completely by myself; there is a queasy feeling in my stomach; a clutching, sinking feeling in the middle of my chest; there is a yearning, a desire for change, I want things to hurry up and begin to change; I want to fight against it, not let the feeling overcome me.

Associations to *fear*, but not anxiety:
There's a quickening of heartbeat; my pulse quickens; my heart pounds; I feel vulnerable and totally helpless; the feeling fills me completely; I sweat; the feeling is all involuntary, there is no anticipation on my part, it all just comes; a muscular rigidity; my face and mouth are tight, tense, hard; I'm cold, yet perspiration pours out of me; my blood pressure goes up, blood seems to rush through my body; there's absolute physical turmoil; I can't believe what's happening is true; I have clammy hands; my hands are moist; an excitement, a sense of being keyed up, overstimulated, supercharged; being totally unable to cope with the situation; there is a churning inside; I'm stunned; a heavy feeling in my stomach; I want to be comforted, helped by someone; I'm afraid of the feeling; I'm intensely here and now; my body seems to speed up; thoughts just race through my head without control; there is a sense of not knowing where to go, what to do; I'm momentarily immobilised; paralysed, unable to act or move; my stomach shivers and trembles, there is a tremor in my stomach; I can't smile or laugh; my reactions seem to be exaggerated.

of dangerous situations. Racing drivers, bullfighters and mountaineers willingly expose themselves to needless hazards. Furthermore, thousands of spectators throng to experience vicariously the tension which is engendered by dangerous sports. Thriller films and books are important forms of entertainment. Certain kinds of anxiety are therefore pleasurable.

At lower levels anxiety is a useful state which is associated with mastery of the environment. It expands an individual's awareness of potential threat. However, extreme anxiety can be so intense as to disrupt ongoing behaviour. In the acute panic produced by a fire or an earthquake, people flee blindly in any direction which is possible, and may disregard their usual social responsibilities, e.g. a mother running out of a burning house may forget to take her baby with her. Soldiers under bombardment may vomit, defaecate and become paralysed with fear, so that they fail to take shelter or to shepherd others

they are responsible for into shelter. Anxiety can become so severe that no response is able to lessen it.

Less intense anxiety can also be refractory to any attempt to reduce it. Patients with anxiety states often report episodes of panic which come repeatedly out of the blue, last for a variable length of time, and then disappear without regard to what the patient does. These spontaneous variations in levels of anxiety may sometimes be wrongly attributed to that behaviour which the patient happened to be engaged in at that time. (By "spontaneous" is meant "not in response to an external situation".) The patient may then perform some unusual task or take some avoidance measures in the belief that it helps his anxiety, e.g. a patient who has just started a new drug will attribute his panic to it and cease taking the drug forthwith, even though identical symptoms occurred repeatedly before he ever took the drug. This is a form of superstitious behaviour.

Etymological considerations

The origin of the term "anxiety" has been traced in detail by Lewis.[292] It derives from a Greek root denoting "to press tight" or "to strangle". The Latin term "anxious" and its derivatives all had the notion of narrowness or constriction, usually with discomfort. Although these roots denoted distress, they did not include the idea of uncertainty and fear which has become an important feature in modern usage, but they tended to stress sadness and disquiet. The idea of constriction is also implicit in the French "angoisse", German "angst", Italian "ansieta" and Spanish "ansiedad", and remains in the English "anxiety". The relevant English terms include (O.E.D. and [292]):

Ange = trouble, affliction: in plural, straits.
Anger = trouble, sorrow (now obsolete).
Anguish = excruciating or oppressive bodily pain, or severe mental suffering.
Anxious = 1. Troubled in mind about some uncertain event, being in painful suspense.
2. Full of desire and endeavour; solicitous, earnestly desirous.
Anxiety = 1. Uneasiness about some uncertain event.
2. Solicitous desire to effect some purpose.
3 (at least from 1661). A condition of agitation and depression, with a sensation of tightness and distress in the precordial region.

Psychiatric use of the term anxiety

Anxiety was used by Wernicke for the agitated depression of melancholia in his title "anxiety psychosis". This meaning is now little used.

Freud[135] described anxiety in its modern sense as the state of expecting danger or preparing for it even though it may be an unknown one. He differentiated it from fear, which requires a definite object of which to be afraid. Freud[136] also introduced the term "anxiety neurosis" for a syndrome in which subjective alarm is associated with visceral disturbances. The main features are general irritability, anxious expectation, acute dread, e.g. of death, night terrors, vertigo, phobias, digestive tract disturbances and paraesthesiae. The term "anxiety neurosis" remains in common use today to indicate the same syndrome, while "anxiety" on its own denotes an emotion which can occur both normally and in any psychiatric disorder.

Psychological writings separate "state anxiety" from "trait anxiety".[471] "State anxiety" refers to anxiety felt at a particular moment—"I am feeling anxious right now". "Trait anxiety" refers to a habitual tendency to be anxious over a long period of time—"I generally feel anxious".

Persons with trait anxiety will have a lowered threshold for becoming anxious in a wide variety of situations which are perceived as threatening. Of course, a person with high trait anxiety may not be experiencing state anxiety at any particular moment but is more likely to be doing so at that time than a person with low trait anxiety. Also, a person with high trait anxiety may, by minimising stress situations in his life, avoid experiencing state anxiety. However, as it is only by experiencing state anxiety that any person can become aware that he is anxiety-prone, it is theoretically possible for someone to be unaware that he is high in the trait of anxiety proneness. Because there are always stresses in everyday life such a situation is unlikely. If such a person's life situation changes to become continually more anxiety-provoking he will experience much state anxiety, the continuing of which will change his assessment of his anxiety-proneness or trait-anxiety. In some respects, state and trait anxiety merge into one another at some point in time in a manner similar to the terms acute and chronic.

One can make a similar distinction in clinical anxiety. Some patients describe anxiety symptoms as a change in their emotional status; in other words, they think they were relatively free from anxiety previously and see their present symptoms as a departure from their previous norm ("state anxiety"). In contrast, other patients admit to always having been more anxious than their peers (high "trait" anxiety). Many factors may bring such a person to the psychiatrist, i.e., change him from an anxious "normal" to an anxious "patient", including a change in life-situation such as promotion at work, marriage, the birth of offspring, awareness of possible therapeutic help, e.g. after a relevant television programme or newspaper article, increased availability of psychiatric services and a sympathetic general practitioner. However, the two types of condition commonly occur together, with increased life-stresses

raising the anxiety of an already anxiety-prone individual beyond the point of tolerance.

Anxiety occurs with stress or threat. According to Spielberger and his colleagues,[471] *stress* refers to variations in environmental conditions which observers regard as objectively dangerous to some degree, while *threat* refers to an individual's perception of a particular situation as dangerous.

Psychiatric terms related to anxiety

(1) *Fear.*—This comes from the old English "faer" for sudden calamity or danger, and was later used to describe the emotion of uneasiness caused by the sense of impending danger (O.E.D.). In Middle English it continued to denote a state of alarm or dread, and does so still today. Fear is an emotion very similar to that of anxiety and phobias. It is a normal response to realistic danger or threat. *Timidity* indicates a lasting tendency to show fear easily.

(2) *Panic* denotes a sudden surge of acute terror. The term was in use by 1603 (O.E.D.) and derives from the Greek rural deity Pan. Not only was Pan supposed to preside over shepherds and flocks, and to delight in rural music, but he was also regarded as the author of abrupt and inexplicable terror. In later times he became a personification of Nature. Psychiatrically, panic can be found in any condition which causes severe anxiety.

(3) *Phobia* derives from the Greek "phobos" indicating fear and terror, and from the deity of the same name who provoked panic and flight in one's enemies. It came into usage about 1801 (O.E.D.) to denote intense fear provoked by particular situations, and is used today in the same sense, viz. a morbid fear which is disproportionate to the stimulus feared, is involuntary, cannot be explained away, and leads to avoidance of the feared situation.[330] An earlier term which used to be synonymous with phobia is *aversion*, but its meaning is altering today. When in contact with the feared situation the phobic individual experiences acute anxiety, and *phobic anxiety* is synonymous with the term "*situational anxiety*". In contrast, "*free floating*", "*generalised or non-situational anxiety*" is not related to any particular situation, realistic or otherwise.

In Chapter 2 we have touched on some aspects of anxiety which are to some extent experienced by all human beings in the course of their lives. Such "normal" anxiety tinges many human activities, may be the fount of much creative activity, and is sometimes actively sought rather than avoided, but it differs only quantitatively from clinical anxiety, which is discussed in Chapter 3. This clinical anxiety differs from normal anxiety in being more severe, more persistent, and inappropriate to the patient's situation at the time. As such it is the concern of the psychiatrist, the physician and many other medical specialists in hospital

practice. It is also an important part of the work of the general practitioner who sees the vast majority of such patients in the first instance. Indeed, most patients with anxiety states are successfully treated by the general practitioner using human understanding and sympathy together with the newer pharmacological aids.

These aspects of treatment are set out in Chapter 4 but because of the preponderance of drugs in the modern management of anxiety state a separate chapter (5) is devoted to the clinical pharmacology and therapeutics of these compounds and some general guidelines for treatment are presented.

The latter half of the book is concerned with less clinical matters. Chapter 6 reviews methods of rating anxiety, an important topic because the progress of any clinical subject from the empirical to the rational depends on accurate recognition and measurement of the phenomena with which it is concerned. The psychiatrist assessing symptoms he cannot measure is often akin to a haematologist without laboratory aids.

The psychological aspects of anxiety are selectively reviewed in Chapter 7 although the relevance of much of the experimental work and the theoretical superstructures raised on those results is as yet unproven. The physiology of anxiety (Chapter 8) has attracted attention in the past twenty years. Although it has helped us to measure anxiety it has brought us no nearer to understanding its pathological mechanisms.

The final chapter (9), examines theoretical aspects of anxiety such as the concepts of arousal and adaptation, the importance of cognitive factors, physiological feed-back mechanisms, implications for psychosomatic medicine and attempts a synthesis of views concerning the protean phenomenon of anxiety.

Chapter Two

NORMAL ANXIETY

INTRODUCTION

In this chapter the topic of normal anxiety will be briefly discussed. This anxiety is normal in the sense that it is widespread, and affects almost all individuals. It is often related to specific situations which vary from one person to another, but certain activities regularly evoke some anxiety in most people. As such, anxiety is part of the fabric of everyday life.

Our daily routine commonly involves some element of danger. On crowded roads during the rush-hour constant vigilance and anticipation is necessary, near-misses are not infrequent and the unexpected is always happening. Anxiety is often experienced and may lead to excessive caution on the one hand or reckless behaviour on the other. The emotion which is experienced can legitimately be labelled "anxiety". During definite and immediate danger such as imminent collision the emotion is called fear. Obviously it may be impossible to decide whether a given situation is definitely or only potentially dangerous. Whether that situation is evoking fear or anxiety may be similarly impossible to tell. Of necessity the two emotions overlap. Often the emotion is experienced only *after* a tricky situation has been successfully negotiated.

Anxiety is engendered in many other areas of life. The insecure assistant perpetually worrying over his job, the responsible executive dithering over every decision, and the harassed switchboard operator exemplify the ubiquity of threatening situations and the anxiety they provoke. Similarly, marital friction, parental problems and even leisure activities may be tinged with anxiety. Anxiety is thus part of the normal coping process.

There are two aspects of normal anxiety which are dealt with in more detail in later chapters but which should be briefly adumbrated at this juncture. Firstly, anxiety bears a complex relationship to behavioural performance. In general an inverted U-shaped curve describes this relationship with a little anxiety facilitating optimal performance; too much or too little anxiety is associated with a drop in performance (see p. 113). For easy tasks, e.g. everyday household duties, anxiety does not interfere much, but with difficult tasks, such as learning new skills, even a little anxiety may be disruptive. The second aspect, in

some ways related to the first, concerns the attainment of a consistent anxiety level for each person. There is some evidence that each individual in some way "chooses" his own anxiety level and then regulates his activities so as to maintain that level (see p. 150). The anxiety level may or may not be optimal for that individual's activities.

ANXIETIES OF EVERYDAY LIFE

Some of the common anxieties of everyday life are reviewed by Levitt.[289] Examinations and other tests are a frequent focus of anxiety in young people who are particularly exposed to them. Test anxiety of some degree is widespread in countries like America and Britain, though only rarely does it become so intense as to disrupt performance. Test performance, of course, is of great importance to the future of individuals in Western cultures, where education so largely influences one's destiny. Stage fright is a similar source of tension. It is to be found not only among actors but in anybody who has to perform some action in public at school or at work. Even experienced politicians confess to nervousness before making important public speeches.

Fear or anxiety are regular accompaniments of stressful situations like combat or parachuting. This can be a useful emotion. Of men in aerial combat 50 per cent reported that mild fear had a beneficial effect, and 37 per cent thought they performed their duties better even when very afraid[522]. Anxiety normally accompanies activities like parachuting and fluctuates with other feelings at different phases of the act. During preparation fear and enthusiasm increase together. In experienced parachutists, fear then becomes inhibited during the jump run while enthusiasm increases to a peak when the parachute is opened. This wanes towards landing, when fear increases. Upon touching the ground fear drops to a new low and enthusiasm is heightened even more than at the first peak. Fear and enthusiasm are thus negatively correlated at successive points during parachute jumps.[248]

The timing and amount of anxiety during parachuting changes with experience. Walk[501] noted that subjective anxiety diminished with experience. Fenz and Epstein[127] showed that the inhibition of anxiety was just before the moment of jumping, and regarded it as an adaptive mechanism which prevented the jump from being disrupted by excess fear (see also p. 131). Too much anxiety is correlated with poor performance in trainee parachutists,[501] and even trained paratroopers become so afraid that they "lose their nerve" and become unable to jump.

SURGERY AND DENTAL TREATMENT

Surgery and dental treatment are performed on a major section of the population each year. In self-reports by patients, over 75 per cent indicate moderate or marked preoperative anxiety.[215] The number

expressing anxiety increases as the hour for surgery approaches and is maximal in the operating room (fig. 2.1). 80–90 per cent of people are at least moderately anxious immediately preoperatively, whether for dental treatment or for minor or major surgery. Anxiety drops off sharply, shortly after dental treatment, less rapidly after minor surgery, and slowly after major surgery.

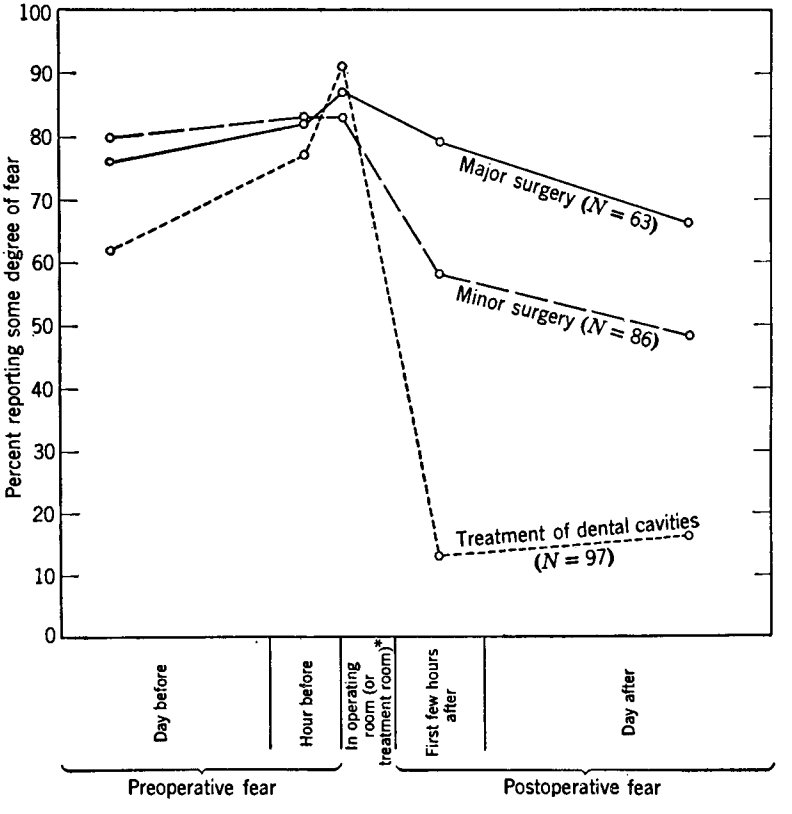


Fig. 2.1: Temporal course of fear responses reported by three groups exposed to different degrees of stress: major surgery, minor surgery and dental treatment. (Reproduced from Janis[215] by kind permission of the author and John Wiley and Sons, Inc.)

Preoperative level of anxiety relates to postoperative behaviour.[215] Patients with moderate preoperative anxiety developed fewer post-operative emotional symptoms like acute anxiety, depression and hostility than did patients with low or high preoperative anxiety. A moderate degree of anxiety appears optimal for adjustment and occurs in stable subjects who face up to their difficulties. In contrast, unusually

low anxiety is often associated with a denial of real problems. When suffering occurs, therefore, it is not regarded as an unavoidable consequence of surgery but is instead blamed on the caring staff who are perceived as unhelpful or inefficient. Patients with high preoperative anxiety, on the other hand, have shown excessive anxiety in past situations and are difficult to reassure.

Anxiety about dental treatment is widespread, being admitted to by 89 per cent of people in one survey.[405] This was not related to educational level nor to anxiety about general illness. Tooth extractions cause as much anxiety as major surgery immediately before treatment.[215] Dental anxiety also leads to avoidance of the dentist. Kegeles[238] noted that of those who had dental anxiety only 49 per cent made routine check visits, compared to 65 per cent of those who were not anxious.

DEATH

A horror of death is ubiquitous in most cultures. As La Rochefoucauld commented, "neither the sun nor death can be looked at with a steady eye". The dread is not necessarily about the process of dying itself. Diggory and Rothman[101] found that people feared it as the end of all opportunity to pursue goals important to their self-esteem. In a large sample of people aged 15–55, subjects were mostly agreed that their worry concerned death as an end to purposive activity and the ability to have any more experiences.

A penetrating analysis of anxiety about death is provided by Hinton,[198] who reviewed much of the literature. Children on the whole speak quite freely of death and avoidance of the topic is unusual. In a vocabulary test in which the word "dead" was added to the list of words, it was accepted quite readily; only 2 out of 91 deliberately avoided it.[12]

In contrast, the topic of death is largely avoided from adolescence onwards, especially when it has a personal connotation. It is usual not to speak of another's death in his presence. In speaking of dying, euphemisms are employed—"passing on", "departing this life", and "going to heaven". In more hardened circles a different idiom appears —"pegging out", "kicking the bucket", "croaking", "throwing a wobbler". Burial and mourning ceremonies in many religions soften the impact of loss by emphasising continuing contact with the deceased in Heaven or the Spirit World. The well-known "American way of death" is a sophisticated denial of the finality of bereavement, a denial which gives witness to the anxiety it causes.

Towards old age more people become resigned to the inevitable, and fear of death is less common over age 60 than one might suppose. In one study 10 per cent admitted fear of death and 44 per cent were "distinctly evasive", preferring not to think about it.[480] In another study,[216] 10 per cent again answered "yes" to the question "Are you

afraid to die?", though only 35 per cent gave an unqualified "no" to the question. In dying patients, Hinton[198] found less than a third of those over 60 were clearly apprehensive, while two-thirds of those under fifty were anxious. This is understandable, as death in earlier life disrupts more expectations and hopes. Young mothers and fathers of dependent children showed greater unease.

Some of the greater anxiety found in younger dying patients might be caused by their mode of death. Persistent pain, nausea and vomiting, and especially breathlessness, are serious sources of distress to the dying. Younger adults tend to have longer-lasting illnesses with more physical distress. Hinton reviews evidence that in one sample of dying hospital patients physical distress was considerable in 45 per cent of those aged under 50, 32 per cent of those aged 50 to 70, but in only 10 per cent of those over age 70.

The process of dying is often free of discomfort. The dying physician William Hunter said: "If I had strength enough to hold a pen, I would write how easy and pleasant a thing it is to die." Apprehension or agony can be mistakenly attributed to the dying by onlookers who do not know the protective value of diminished consciousness. Dying is commonly more distressing to the onlookers who are about to be bereaved than to the one who is departing.

Once someone has died his body is liable to become the focus of new fears. In many cultures strong taboos prohibit the touching of a corpse, from which evil powers are said to emanate. Ghosts and evil spirits hover around the corpse and later the grave.

Some anxiety about dead bodies centres over its altered state at death and during decomposition. Where there is belief in a future life disfigurement at death threatens this promise. Elaborate steps are taken in different cultures to ensure there is no handicap to resurrection. The body is embalmed to preserve its shape; food, valuables and retainers are buried with it; easy exits are built into the grave. Precautions like these emphasise that much anxiety concerning death relates to the way it ends ongoing activity. A premium is attached to ideas that some kind of existence can continue after death.

Religious belief can influence the degree of anxiety felt about death. Hinton cites findings in England that of dying patients who had firm faith and attended church frequently only a fifth were apprehensive. However, religious faith appears less important than confidence in one's views, whatever they are. Of those who frankly said that they had practically no faith, only a quarter were anxious. In contrast, lukewarm believers who claimed faith but showed little observance of it were twice more anxious than the regular churchgoers or firm unbelievers.

Uncertainty of knowledge also increases apprehension about death in other ways. Terminal patients who are not sure what is happening to them but suspect they are dying can be particularly anxious until they

are told the truth. Anxiety might then abate and be replaced for a while by depression which gradually passes off. This gloom is like a grief reaction in which the patient comes to terms with the loss of his own future.

Some people are so afraid of dying, however, that they avoid learning about their progress at all costs. Even when they are told the truth they forget it immediately, or deny it. Denial may not be effective for long and the patient may then break down in acute perturbation. There can therefore be no golden rule about concealing or telling the truth about dying. One has to decide in the light of the patient's past responses to other stress, the stability of his personality, and whether he genuinely wants to know or strives to avoid learning about his position.

Separation anxiety

Separation anxiety is another normal response to stress of a different kind, namely, the threat of loss of a love object. Grief is a special form of separation reaction to the actual loss of a love object. Since these phenomena have been stressed in psychopathological states, it is necessary to examine their normal characteristics.

The features and origins of separation anxiety have been well described by Bowlby.[43] Separation anxiety has been defined as "the subjective accompaniment of awareness of the danger of loss".[372] It is shown by young individuals of many mammalian species and also occurs in most adults. It is evoked by separation from a familiar figure. When members of a bonded pair become separated from one another they eventually try to find each other. Should reunion be delayed or prevented, then separation anxiety is likely to occur. Separation anxiety is thus thwarted attachment behaviour.

The stranger the surroundings in which a separated child finds himself, the more the anxiety which is provoked in him.[43] When the child subsequently rejoins familiar figures, people and events that remind him of his period away often re-evoke this anxiety.

Origins of separation anxiety.—Young animals and other vertebrates are born with a strong bias to approach certain classes of stimuli and to avoid other classes.[438] This approach and avoidance behaviour emerges at slightly varying ages in different species and is modified to some extent by experience. Approach behaviour usually precedes avoidance behaviour. Approach responses appear shortly after birth in animals which are born mature and are readily elicited by any stimuli of moderate to low intensity which change gradually, e.g., a quiet repetitive sound or an object that moves slowly. At a slightly later phase, avoidance reactions are evoked by stimuli of high intensity that change abruptly, e.g., sudden loud noises or fast moving objects. Once a young animal has gained some experience, whatever has become familiar tends to be

approached whilst strange objects are avoided or treated with caution. At about one year of age most infants go through a phase during which they are afraid of strangers[358] and slightly later any novel stimulus may evoke fear. Sometimes this effect is enhanced if the novel stimulus is juxtaposed to a familiar one. These phenomena have been reviewed in detail elsewhere.[330]

The role of affectional bonding.—Separation anxiety develops out of the foregoing elements and probably results from the importance of affectional bonds in animals. These have been reviewed by Bowlby.[43] Strong persistent bonds between individuals are the rule in many species of birds and mammals. The function of such attachments* is probably protection from predators. The commonest types of bond are those between one or both parents and their offspring and those between adults of opposite sex. In mammals the first bond is usually that between mother and young. The essential feature of affectional bonding is that both partners tend to remain near one another and if separate they eventually renew their proximity. Separation of the bonded pair by a third party is resisted, and the stronger of the partners attack the intruder whilst the weaker flees or clings to the stronger partner. When bonded partners are separated and cannot find one another they become agitated and distressed, i.e., they show separation anxiety.[43] Once a young creature has become attached to a mother figure his behaviour in her presence is different to that in her absence. With her he is relaxed and adventurous, whereas in her absence he becomes tense and inert.

This difference is emphasised during alarm. If a primate is alarmed when his mother figure is present he will run to her and cling. In contrast, a goat kid alarmed in the absence of its mother will remain tensely rooted to one spot, preferably a corner, while a primate or human toddler is likely to curl up on the floor and cry.

Bonding behaviour in man is often accompanied by a subjective feeling of love or dependency. The wish to be loved or need for dependency is termed *amae* in Japan, and is regarded there as a key emotion with positive connotations not always present in the English concept of dependency.[283]

In summary, attachment behaviour is as intrinsic a system of behaviour as feeding and sex, develops earlier than sex, and is active more continuously. Normal separation anxiety results whenever bonding behaviour is disrupted or threatened.

Grief reactions.—This special kind of separation anxiety has been studied by Parkes[372] in two investigations involving 138 bereaved adults who were interviewed at intervals during their first year of bereavement.

---

*The importance of bonding behaviour was expressed by Freud in a different language. The terms "to make a bond" or "to be attached to" refer to the same events as Freud's terms "to cathect an object" or "to invest an object with libido".[43]

Major bereavements do not become "established facts" in the eyes of the bereaved for some time after their loss and until they do separation anxiety remains the dominant aspect of a grief reaction. This is reflected in yearning for the deceased person which is a characteristic feature of the "pang" of grief. Pining is accompanied by crying and searching for the lost object. Searching implies loss or absence of an object and is regarded as the central component of grief. Searching behaviour involves: (1) restless movement about and scanning of the environment; (2) thinking intensely about the lost person; (3) developing a perceptual "set" for the lost person with a tendency to perceive and attend to stimuli which suggest the presence of that person and ignoring other items; (4) attending to those parts of the environment in which the person might be; and (5) calling for the lost person.

Several of these features confirm Lindemann's[297] classic description of grief reactions: "The activity throughout the day of the severely bereaved person shows remarkable changes. There is no retardation of action and speech; quite to the contrary, there is a push of speech, especially when talking about the deceased. There is restlessness, inability to sit still, moving about in an aimless fashion, continually searching for something to do. There is, however, at the same time, a painful lack of capacity to initiate and maintain organised patterns of activity."

The urge to search for the lost object is thus an integral part of grief reactions, and pining, or separation anxiety, is the subjective component of this behaviour. Separation anxiety alerts a person to the threat of loss, and searching behaviour maximises the chances of reunion with the lost object. As Parkes has noted, in the animal and young child who have no means of distinguishing between temporary and permanent loss the function of searching is obvious. When the loss is permanent, unrewarded searching does not continue indefinitely. After repeated failure to achieve reunion the intensity and duration of searching gradually diminishes and extinguishes until the "grief work" has been done, and the attachment to the lost person is finally broken.

Lindemann[298] has shown that the pain of grief is partly the result of disrupted role functions between the bereaved and the deceased. During early mourning these roles are rehearsed repeatedly and painfully. After a while the bereaved ceases these abortive attempts at interaction with the deceased and develops new role ties with other people instead.

Coping (defence) mechanisms

The anxieties of everyday life can be dealt with in many different ways. Many of these have been described in psychoanalytic terms as defence mechanisms. They are detailed by Fenichel.[126] Some of these include the following: *Denial* is a common way in which anxiety is

handled, particularly in children. *Repression* is a variant of this. Here the subject is not aware of his emotions yet they continue to affect his behaviour. *Reaction formation* results from repression. It is recognised by cramped and rigid attitudes that are obvious attempts to deny contrary impulses which nevertheless sometimes break through in various ways. An attitude is taken that contradicts the original one. In *undoing* one more step is taken. Something positive is done which actually or magically cancels what occurred before. Such behaviour is often seen in obsessive-compulsives. In *projection* a person sees his own attributes in someone else without recognising them in himself. Occasionally people cope with anxiety by *counterphobic behaviour.* "Sometimes the original anxiety situations are not avoided but are sought at least under certain conditions; the person shows a preference for the very situation of which he is apparently afraid; even more frequently a person develops a preference for situations of which he formerly had been afraid. . . . The obsessive manner of the search for the once feared situations shows that the anxiety has not been completely overcome. The counterphobic pleasure is a repetition of the child's 'functional' pleasure of 'I do not need to be afraid any more'. And, as in the child, the type of pleasure achieved proves that the person is by no means really convinced of his mastery, and that before engaging in any such activity, he passes through an anxious tension of expectation, the overcoming of which is enjoyed."[126] Another possible response to stress is *regression.* This is a tendency to revert to earlier modes of behaviour corresponding to earlier periods in a subject's life when his experiences were more pleasant and satisfying.

Many forms of behaviour are used to reduce anxiety and to seek comfort. Anxious people solicit reassurance and the company of others. They may seek rhythmic stimulation by touch or sound. They might engage in distracting activities or in oral habits like smoking, chewing gum, drinking alcohol or taking drugs. Tension can lead to laughing or crying. It can produce overtalkativeness or other overactivity and tension habits like scratching or head rubbing. The opposite can also happen. Anxiety can lead to retreat into fantasies, daydreaming, or even sleep.

Anxiety and other responses to extreme stress

Acute extreme stress

Anxiety is a normal response to acute stress, and it is useful to consider it together with other reactions which are found in times of disaster like fire, aeroplane and train crashes, and tornados. Sociologists have studied such situations by detailed interviews of involved persons shortly after a disaster. Janis[214] noted five typical patterns of reaction to danger:

1. *Apprehensive avoidance* (anxiety) occurred when danger was rapidly approaching or at hand. During this brief period there was acute fear with attempts to escape the danger. Long after the danger had subsided some persons continued to show fear, flight tendencies and jittery alertness to minor threats that are ordinarily disregarded.
2. *Stunned immobility* occurred during and immediately after the disaster. This was an acute freezing reaction, usually of short duration, but some people might wander about for hours in a distracted, dazed state.
3. *Apathy and depression* was observed among people who had just been severely injured either physically or emotionally by the disaster. Such people became depressed and apathetic, lacked energy, initiative and interest, and were narrowed in their attention. Suicide and suicidal thoughts were not very prevalent.
4. *Docile dependency* was found when people first became aware of their loss, and in the early stages of recovery of the community. Such people were not necessarily depressed or apathetic but clung passively to authority and showed automatic obedience.
5. *Aggressive irritability* became evident in populations recovering from a disaster after the most urgent rescue and relief operations were already over.

The same persons might show all five reactions in a definite sequence: (1) during the brief period of maximum threat, (2) during the period when disaster struck, (3) and (4) shortly after the obvious signs of danger had disappeared and (5) during the recovery period.

In extreme stress, anxiety and panic is not the major problem in saving the community involved.[138] Rather, the problem is lack of coordination among many people all acting on their own different personal definitions of the situation at the time. Interestingly, these workers felt that very brief warning of impending disaster (less than a minute) was associated with more serious subsequent loss than no warning at all. They noted that emotional reactions to disaster might be increased by separation from family and by intimate contact with dead or injured people.

Somewhat surprisingly, panic is a rare reaction to disaster.[138,392] Panic has been defined in sociological terms as an acute fear reaction marked by loss of self-control which is followed by non-social and irrational flight.[392] Panic is generated when a person feels immediately threatened and believes escape is possible at the moment but will shortly become impossible. Panic behaviour is non-social and disrupts organised group activity. During panic ordinary social relations are disregarded and pre-existent group patterns fail to be followed. This distinguishes panic from controlled withdrawal behaviour, where the

conventional patterns of response are still maintained, despite some confusion. Panic is highly individualistic behaviour during escape from danger, and prevents collective cooperation. It occurs when possibilities for escape still seem available, not when a person feels completely trapped. Panic is accompanied by a sense of helplessness, impotence and aloneness, and is more likely to happen when there is contact with other agitated individuals who feel in similar danger. During panic there is blind flight from the threatening situation, with no attempt to deal directly with the danger itself.[440]

Relatively little contagion of anxiety under stress was found in air crew during the Second World War.[41] In an experiment, 110 emotionally disabled airmen lived for a week with 550 healthy airmen on leave in a rest home, with no attempt at segregation. It was generally known that the sick men were out of combat and often would be going home. Conversation was virtually confined to aviation and to combat, and no therapy was given to the ill air crew. The experiment lasted 9 months. Follow-up of the healthy men showed only 6 of the 550 were removed from combat for emotional reasons—a very low figure, especially as many of the healthy men had been sent to the rest home to recuperate after a bad crash or a ditching.

The prime mover in causing breakdown during air combat was danger itself.[41] The number of emotional casualties among heavy bomber crew correlated +0·7 with the number of aircraft lost (fig. 2.2). Emotional casualties increased sharply when the loss rate exceeded 8 per cent and the chances of witnessing a disaster were much higher. Men repeatedly traced their initial difficulties to a mission on which heavy losses had been experienced. In contrast combat neurosis was not related to fatigue or to overall activity in the air. Even a personal or family history of neurosis played little part.

Chance factors largely determined the effectiveness of particular traumata. Position in a flying formation influenced visibility of harrowing events and attention at these moments. It mattered much whether the parachute of an escaping friend opened safely or caught fire or blew into another aircraft. "It makes a difference, too, whether a flak burst hits directly in the bomb bay so that all pieces of the ship and its occupants are blown beyond the field of vision, or whether the expression on a wounded or a parachuting man's face is immediately discernible. The physical appearance of the man in jeopardy, how well he is known to the spectator or how well liked, the details of his character and of his circumstances in life—all combine either to strengthen or to weaken ego defenses and to reinforce or to pass by unconscious conflict. . . . The unevenness of individual exposure to the details of danger was so widespread that it would be erroneous to regard combat as a uniform test" (p. 131–2).

The most frequent symptoms of a developing combat neurosis were

airsickness, pseudobends, headaches, vertigo and cautiousness in the air to the exclusion of other safety precautions. Phobias of flying often developed when something happened to remind the man of his precarious position. This might be a trivial accident, an unexpected gust of wind, a momentary sticking of the controls. Symptoms often began

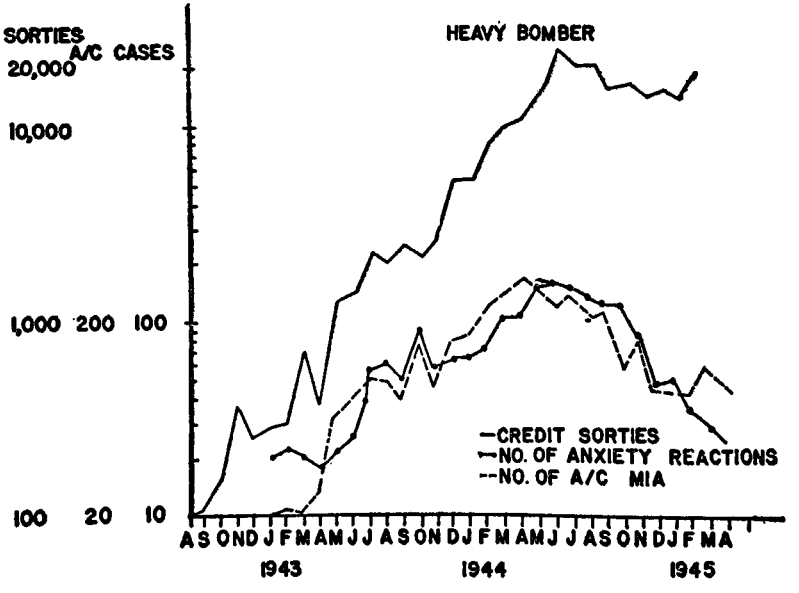


Fig. 2.2: Relationship of the activity of the Air Force, measured by the number of credit sorties; of the combat danger, measured by the number of aircraft missing in action (A/C MIA); and the number of anxiety reactions. It is evident that anxiety reactions bear a very close relationship to the combat danger and not to the activity itself. Ordinate shows number, from left to right, of sorties, A/C MIA, cases. Abscissa shows time in months. Semilogarithmic paper. (Reproduced from Bond[41] by kind permission of the author and International Universities Press, Inc.)

at the beginning of an advanced step in training—the first night flight, the first flight on instruments or in formation, the first flight in a more complicated or new type of aircraft. The phobia commonly spread in ripples to surrounding circumstances but always remained centred round flying.

Despite the severity of symptoms in combat neuroses, after 3 to 6 weeks' rest almost all men were fit for noncombatant duty, although many had persistent symptoms, particularly nightmares. However, practically none of them were able to return to combat flying. As an

example: One man's reaction had developed on a mission during which his plane was twice damaged badly and two men aboard were killed. At a rest home this man spent the first two weeks lying on the grass with his face down, deeply depressed, speaking to no one, preoccupied with guilt and whether or not he was alive. At first he was unable to eat, sleep or mingle with others. He was unable to talk about flying or to listen to others talk about it, and was extremely sensitive to noise of any kind. He had an intense phobia for the air base at which his group was located. He improved slowly at first and then suddenly quite rapidly. At the end of his 6 weeks he was able to do ground duty.

Prolonged extreme stress

The disturbance caused by extreme stress becomes more widespread and lasting as the stress is prolonged. Such is all too often the result of man's inhumanity to man, e.g. in tortured political prisoners or in concentration camps. Vivid accounts are portrayed in many poignant books by survivors.[164,419,457] Eitinger[108] systematically studied the adjustment of former inmates of Nazi concentration camps 12 years or more after they were liberated. Detailed medical and psychological investigations were made of 227 such survivors, including air encephalograms in the majority. Anxiety was still troublesome in 43 per cent of the survivors while the remainder had other problems. Anxiety was associated with nightmares and other sleep disturbances. Horrible associations with past events would be stirred up repeatedly and could not be discussed with closest friends or relatives. These associations would be triggered by the most harmless stimuli, e.g. seeing a person stretching his arms would revive memories of fellow prisoners hung up by their arms during torture; seeing an avenue of trees would be associated to rows of gallows with swinging corpses as were commonplace in the camps; children playing peacefully might suddenly call to mind other children, emaciated, tortured, murdered.

The presence of anxiety at follow-up did not correlate with the survivor's adjustment prior to arrest nor with the post-war circumstances. It did, however, correlate with the appearance of psychic disturbances during imprisonment, especially anxiety. The latter was also connected with a chronic brain syndrome. Chronic brain damage was correlated with the severity of torture, the incidence of head injuries and loss of weight.

Two-thirds of the survivors reported psychological disturbances while they had been in the camps—severe chronic anxiety, tension, inner restlessness, despair and severe depression. Anxiety was particularly experienced by those who had been in death cells for long periods or who had taken part in illegal organisations which had been exposed resulting in execution of other participants. The more serious the cause of arrest,

the greater was the likelihood of anxiety. Bombing attacks were terrifying for those locked in their cells while the bombs and buildings fell around them.

Eitinger summarised his findings as follows: "Prisoners who were very young when arrested, and those few who had suffered serious mental disorders before the war, seemed less able to withstand the stresses of concentration camp life than those who had the opportunity to develop their personality before they were arrested. The most important factor, however, was the total sum and combination of the different kinds of psycho-physiological stresses to which the prisoners were subjected. The greater the sum of this stress, the greater the immediate psycho-pathological reaction and . . . the greater the incidence of chronic long-lasting reactions."

Two points in particular were singled out. Anxiety phenomena which developed in prison or camp led to continued anxiety after release; the severity of psychological or physical torture seemed the main factor in this anxiety rather than emotional immaturity of victims prior to arrest. Secondly, the symptoms of anxiety were actively disturbing or incapacitating subjects up to quarter of a century after the traumatic experiences.

THEOLOGICAL CONCEPTS[196]

In conclusion, it is instructive to examine briefly some of the views of theologians on anxiety as their philosophical analyses of the problem help to maintain one's perspective. They take an essentially molar view, an extreme example being the tenet of the Arab scholar, Ali ibn Hazm (994–1064): "No one is moved to act, or resolves to speak a single word, who does not hope by means of this action or word to release anxiety from his spirit." The source of the anxiety, in the early Christian view, is described in the commonly quoted text of St. Augustine of Hippo (354–430): "You (God) motivate (man) to delight in praising you but you have made us in such relation to you that there is disquiet in the human mind until it reposes in your presence"—(*our translation*). This latter state is that of grace.

The nineteenth-century Danish theologian, Sören Kierkegaard devoted an entire book to anxiety—*The Concept of Dread*.[246] Anxiety is regarded as an inevitable consequence of knowledge and freedom. Man in a state of "innocence" (Adam before the Fall) is neither free nor sinful. Once alienation from this innocent, ignorant, natural state occurs, man looks at his situation as a being and dizzily contemplates the possibilities of freedom. Anxiety is recognition of the reality of freedom—that it contains potentialities for man and that he must bear responsibility for what is done with that freedom. Anxiety, therefore, is a form of knowing rather than an emotion. With alienation from the state of "innocence" comes "original sin" which is thus the concomitant of anxiety. In this regard, Kierkegaard writes "With sinfulness

was posited sexuality"; this adumbrates Freud's views. Kierkegaard's views have been echoed by the eminent contemporary American theologian, Reinhold Niebuhr:[365] "Anxiety is the inevitable concomitant of the paradox of freedom and finiteness in which man is involved." Thus, it is a normative function, the internal corollary to external temptation. Two outcomes are possible: sin, if temptation is succumbed to; creativity, if it is resisted.

Paul Tillich, another contemporary theologian, propounds a view concerned with ontology, the understanding of being.[489] Anxiety is comprehended as "the state in which a being is aware of its possible non-being". This anxiety cannot be eliminated but its form is culture-dependent. At the dissolution of Ancient Greek civilisation anxiety engulfed man relatively in terms of his fate and absolutely in terms of death; at the time of the Reformation, guilt and condemnation were the forms. At the present time anxiety appears relatively as emptiness and in absolute terms as meaninglessness. Tillich utilises the concept of pathological anxiety as a "state of existential anxiety under special conditions". It is "the result of contingent occurrences in human life". This morbid anxiety must be healed. Tillich, like Freud, attributes such anxiety to unresolved conflicts between structural elements of the personality, but regards anxiety not merely as an alarm signal but as an awareness of those conflicts.

One common strand through these formulations is the emphasis on cognition, knowledge, rather than on affect, feeling. Anxiety is conceptualised as a recognition or an awareness rather than as an affective response to that cognition. The asceticism of this view results in a restricted view of anxiety but one which is helpful in analysing the cognitive aspects psychologically. Clinically, its value is strictly limited, as it is not subject to systematic analyses nor is it clear when the anxiety under discussion is the normal phenomenon which everyone experiences at times or the pathological anxiety which is encountered in psychiatric patients.

Chapter Three

CLINICAL ANXIETY

In this chapter "anxiety" is used synonymously with the term "free-floating", non-situational or general anxiety to distinguish it from phobias or normal fear. We are concerned here with anxiety which is beyond the normal response to stress and which handicaps the everyday functioning of an individual. As outlined on p. 4, clinical anxiety may be defined as anxiety which is more marked, more frequent or more persistent than the intensity, occurrence or duration which the patient regards as his norm or as the norm for his peers. Like other emotions, anxiety can occur in a wide range of clinical states. It is a common feature of affective disorders, the agoraphobic syndrome, and obsessive-compulsive disorders, while it can also be a symptom of schizophrenia, conversion symptoms, organic confusional state or epilepsy. Where anxiety dominates the clinical picture in the absence of other gross disorders the term "anxiety state" is used.

In each syndrome anxiety is part of a distinctive pattern, which will be described in more detail in each instance.

Affective disorders

Anxiety is a common manifestation in depressive states and waxes and wanes together with other features of the affective disorder. Often anxiety is associated with motor agitation, which when prominent gives rise to the classical picture of agitated melancholia. Mild agitation is frequent, though severe depression is seldom seen today since the advent of early and effective treatment for depressive disorders. Of 35 patients with depression of moderate or severe degree, Lader and Wing[274] found 48 per cent to be agitated, 38 per cent to be retarded, and 14 per cent to be neither. Agitation was accompanied by physiological correlates of anxiety, namely a high mean skin conductance, increased fluctuations of spontaneous skin conductance, and decreased habituation of the galvanic skin response.

When anxiety is prominent and other depressive features are slight it can be difficult to know whether a given patient has a depressive illness or an anxiety state. Of a series of patients diagnosed as anxiety states 19 per cent were subsequently re-labelled as depressives.[90] The distinction might have some prognostic import. Walker[502] studied 111 outpatients in whom free floating anxiety was the cardinal symptom,

and classified them according to outcome. They were treated by reassurance and amylobarbitone only. A group of 24 of these patients with good outcomes was isolated: these patients were thought to be best described as depressives with episodic anxiety. Such patients had no precipitant for their illness and had minor depressive features such as gloomy forebodings, inability to plan, fears of illness and death, and self reproach.

The distinction between depression and anxiety state is useful as a guide to treatment.[170] Of 126 patients admitted to psychiatric hospitals in Newcastle with "affective disorder", 45 were diagnosed as depressives and 66 as anxiety states. At discharge and at 6 months follow-up independent assessors found a significantly better outcome to ECT and to tricyclic drugs in depressives than in patients with anxiety states. Patients with anxiety states were also younger, their mean age being 35 compared to 51 for the depressives.

Phobic disorders

The clinical picture in phobic disorders has been reviewed elsewhere[330] and is outside the scope of this book. Free floating anxiety is not a common feature in phobic disorders except in the agoraphobic syndrome. Synonyms for this condition are phobic anxiety state or phobic anxiety depersonalisaton syndrome. This disorder usually affects young adults and is commonest in women. Sufferers have multiple fears of going out into public places, streets, shops, restaurants, trains and buses, and into open and closed spaces, and typically these phobias run a fluctuating course over some years.[330] The phobias are frequently accompanied by other non-phobic symptoms such as mild depression, depersonalisation, obsessions and free-floating anxiety.

When present, free-floating anxiety is of particular importance in this syndrome, since it augurs a poorer prognosis with treatments like desensitisation which are otherwise effective.[268,330] Whenever patients with this syndrome present for treatment it is necessary to enquire closely whether they experience non-situational anxiety at rest at home, when there is no contemplation of activity concerning the phobic situation. Particular questions need to be asked about panic attacks which may come on anywhere regardless of the patient's situation. Agoraphobia often begins during such panic attacks at which time the patient becomes afraid of re-entering whatever place he was in at the time, for fear of triggering further panics.

In agoraphobic patients with repeated panic attacks and a high level of background free-floating anxiety, the picture closely resembles an anxiety state and the distinction may become rather arbitrary. It is not known why some patients have great free-floating anxiety yet never develop phobias, while in others such anxiety is followed by crippling phobias which force the patient to become housebound. At one time

it was thought that differences in conditionability might explain this, but experiments on eyeblink conditioning do not support this idea.[339]

The panic attacks which occur in this syndrome are identical to those which characterise an anxiety state. Detailed descriptions of these will be given later.

The agoraphobic syndrome accounts for about 50–60 per cent of patients with phobic disorders met with in psychiatric practice. The next commonest phobic disorders include social phobias, where patients are afraid of specific social situations which trigger anxiety, e.g. they may shake and tremble when holding a cup in a restaurant or signing a cheque in the bank, or feel nauseated and be unable to swallow their food in public, or quiver in fear whenever anybody stares at them. These fears may become so pronounced that the patient gives up all social activities which trigger his discomfort.

Other common phobias in psychiatric practice are those of sickness and death. Patients become afraid that they have cancer, heart disease or venereal infection and interpret any trivial sensation as evidence of inexorable doom. Slight flatulence will be taken to mean cancer of the stomach, palpitations on running will be construed as grave coronary thrombosis, and endless negative investigations placate the patient only temporarily or not at all. Sometimes the patient is only reassured when he actually gets the disease he fears, as in one man described by Roger-son[410] who had a fear of having venereal disease. Negative tests failed to reassure him. Finally the patient actually contracted syphilis with a chancre large enough to see himself, and he was treated with anti-syphilitic treatment. The patient then lost all his fears of infection.

Other less common phobias are those of isolated situations like thunderstorms, heights, darkness, animals and so on. Almost any situation can become involved in a phobia but the commonest seen psychiatrically are those described above.

Obsessive compulsive disorders

These disorders should be clearly separated from obsessive or meticulous personality traits which do not handicap the patient, are acceptable to him, and are not a source of distress. Patients with obsessive-compulsive disorders commonly have pre-existing meticulous personality traits but exceptions do occur sufficiently often to justify the view that "the grouping of these particular traits together and the giving to them of the title 'obsessional' does not have a faultless theoretical basis".[191] They may occur at any age and affect men and women equally. Obsessions are "ideas which come to consciousness in spite of and contrary to the will of the patient, and which he is unable to suppress although he recognises them as abnormal and not characteristic of himself".[517] Compulsive rituals are obsessive ideas which are translated into action,

for example, obsessive fear of contamination may lead to compulsive handwashing. In many patients the obsessive idea produces intense anxiety which is then relieved by the compulsive ritual which acts as an anxiety reducer. The anxiety which precedes the compulsion has been referred to as the primary component[291] or stoeringspyschismus,[500] whilst the compulsion which terminates the anxiety temporarily has been called the secondary component[291] or abwehrpsychismus.[500] Typical as this division is, anxiety may not be evident in obsessive compulsive disorders in children or of very long standing, at which time the rituals may be carried out without any trace of preceding anxiety.

Even in cases where compulsions appear to be serving an anxiety reducing function, treatment can abolish the anxiety preceding a ritual while that ritual continues as strongly as ever.[333] Compulsive rituals thus not only serve to reduce anxiety, but are also maintained by other unknown factors.

Obsessive-compulsive disorders may be complicated by the presence of free-floating anxiety and phobic panic attacks not connected with obsessive ideas or compulsive actions. Phobic anxiety can also occur. The phobias may be of several varieties. First the phobia may itself be an obsessive fear of contamination by dirt, dust, germs or other items, a fear of injuring others or oneself with consequent avoidance of knives, broken glass and other sharp objects. Next, the fear may be of death or illness of any description, and the patient may have fixed hypochondriacal ideas which no reassuring investigations can dispel. Finally, obsessive compulsive patients often have phobias of the agoraphobic variety. Rarely patients may have such pronounced obsessions, free-floating anxiety and phobias mixed together that they straddle the categories of obsessive compulsive neurosis, anxiety state and phobic disorder.

Conversion hysteria

These are symptoms and signs, commonly of an apparently neurological nature, for which no organic cause can be found after intensive investigation. Unfortunately the diagnosis of conversion hysteria still rests largely on a negative criterion, the absence of physical disease, though there are positive criteria such as improvement of the disorder by suggestion, and anomalous preservation of some functions while related ones are disturbed, e.g. a patient with hysterical mutism may mouth words silently but be unable to whisper despite normal action of her vocal cords. Conversion hysteria is commonest in young adults especially women, and may involve any somatic system or consciousness, e.g. paralysis or anaesthesia of limbs, blindness, deafness, mutism, amnesia. Conversion symptoms are often associated with serious depression or with subsequent organic illness, and the diagnosis is not lightly to be made simply because physical disease is not apparent.

Generations of psychiatrists since Freud have been taught that "Even in its most severe symptoms no admixture of anxiety is found (with conversion hysteria)". This teaching has been associated with the idea that conversion symptoms represent the conversion of "psychic energy" associated with unacceptable anger into somatic symptoms, thus preventing the person from experiencing undesirable affects and their attendant anxiety. Conversion symptoms are thus thought to protect or defend the sufferer from feeling intense anxiety.

This concept has been criticised by several authors[73,539] and there is experimental evidence to suggest that conversion hysteria can be accompanied by free-floating anxiety and its physiological concomitants. Lader and Sartorious[272] found that 10 patients with chronic conversion symptoms rated themselves as more anxious than anxious phobic patients and had correspondingly higher autonomic activity, i.e. more spontaneous fluctuations in skin conductance level and less habituation of the galvanic skin response. Clinically, other investigators have also noted that an appreciable number of patients with hysterical symptoms had features of anxiety.[294,540] The latter authors commented that there was no evidence of belle indifference in their patients. Secondary gain from symptoms was less blatant than one might expect, and primary value to the patient of relief from anxiety or other painful affect was relatively ineffective, judging from the frequency of concomitant dysphoric affects.

Chronic conversion symptoms like those investigated by Lader and Sartorius may be different with respect to anxiety than those of acute onset. Levy (personal communication) found that 11 patients with acute conversion syndromes had little subjective anxiety and no signs of increased physiological arousal. In one of these patients, posthypnotic suggestion abolished the symptom for a few hours during which time subjective anxiety and physiological arousal appeared, only to subside again when the conversion symptom returned.

Organic confusional states (delirium)

In these conditions the clouding of consciousness, lowered awareness and disorientation may be accompanied by shifting affective changes including anxiety. When this occurs the patient becomes restless and agitated, with no obvious trigger for the anxiety. In certain varieties of confusional states such as delirium tremens, agitation and tremor can be so marked as to dominate the clinical picture. The diagnosis of a confusional state generally presents no problem even with marked free-floating anxiety, as cognitive changes usually make the condition immediately obvious.

Anxiety is sometimes a feature in early dementia when the patient still recognises that his powers are failing. It is not a prominent symptom in the later stages.

Epilepsy

Fear or anxiety can occur during seizures arising from the temporal lobe.[508,523] In such cases the anxiety may be part of the aura or of the seizure proper, and is incorporated into the march of the cortical discharge. The anxiety will be remembered if it is part of the aura but there will be no memory of anxiety during the seizure itself, which will only be recognised by an observer, not told by the patient. Accompanying events depend on the route taken by the march of the cortical discharge. Ictal anxiety is shortlived, usually lasting a few seconds or at most a few minutes. In contrast, on recovery from the seizure the patient may have an altered affective state for several hours or days with mild depression, anxiety, rarely even phobias,[330] but be free of these in the interictal phase.

The diagnosis of ictal anxiety will rest on recognition of its short-lived phasic character and its association with other ictal events, whilst the altered postictal state can be similarly linked to the events immediately preceding it. Chronic free-floating anxiety of anxiety states will not be mistaken for these phenomena.

Hyperdynamic beta adrenergic state

Most anxious patients generally complain of autonomic symptoms such as palpitations, and it is usually assumed that the autonomic symptoms are the result and not the cause of anxiety. In a small minority of cases, however, the anxiety does appear to follow the physiological state, and abolition of the physiological disorder relieves the anxiety. Frohlich et al.[139] were the first to describe this phenomenon in patients, which they dubbed hyperdynamic beta adrenergic state. They studied two female patients who complained of anxiety and palpitations. Both patients had tachycardia and hyperactive cardiac impulse which was shown to be due to increased adrenergic activity. Such activity was especially evoked by standing and in one case "affect varied from calm to near hysteria simply as a result of standing". This patient was forced to remain in bed for long periods because of disabling tachycardia. The other case was a woman school teacher who awakened feeling well, but within a few minutes after standing developed tachycardia and palpitation. Exertion heightened the heart rate and she had to instruct her classes sitting at a desk. At the end of the school day she would go home to bed, and only after a few hours' rest did her heart rate drop below 100.

Both cases thus had severe tachycardia in response to neurogenic and pharmacological stimuli with exaggerated emotional responses. These were reproduced in the supine position by intravenous isoprenaline (an adrenergic drug) and were prevented by beta adrenergic blockade.

The abnormality was postulated to be increased beta adrenergic

receptor activity which produced tachycardia and/or systolic hypertension or both. Anxiety was relieved by control of the tachycardia by the beta adrenergic blocker, propranolol, but not by placebo. Anxiety was thought to be dependent on the tachycardia and not the converse as it disappeared with control of the tachycardia.

Frohlich et al. extended these findings in a report on 14 patients.[140] These had a clinical picture suggestive of hyperdynamic beta adrenergic sensitivity and included 12 patients with hypertension of unknown cause. Most of these patients complained of disturbing palpitations, chest discomfort and rapid heart action associated with varying degrees of physical limitation. The 14 patients were compared with 13 essential hypertensive patients and 25 normotensive volunteers. Patients with cardiac symptoms had a significantly higher resting cardiac index and heart rate. Their heart rate increased significantly more with graded isoprenaline hydrochloride infusion, which indicated increased beta receptor sensitivity. In 9 of the 14 patients isoprenaline produced a "dramatic emotional outburst" which was promptly relieved by propranolol hydrochloride but not by placebo. Saline infusions did not produce these outbursts. Obviously anxious individuals with normal or only slightly increased heart rate before isoprenaline failed to show dramatic increase in heart rate and emotional response with the infusion. Frohlich et al. ascribed the syndrome of cardiac awareness, increased heart rate responsiveness to various stimuli, and hyperkinetic circulation to increased beta adrenergic receptor reactivity. They supported this conclusion by reducing symptoms and blood pressure in the 8 patients they treated with propranolol.

Frohlich et al. suggested that the criteria for the syndrome were: (1) response of heart rate to isoprenaline and coincidental reproduction of symptoms, even with precipitation of panic; (2) complaints of cardiac awareness and tachycardia at rest; (3) circulatory hyperkinesis; (4) specific benefit with beta adrenergic blockade. They believed that the syndrome did not represent a single disease since their patients included some who were normotensive or whose blood pressure was sustained, labile or episodic. The fact that most of their patients were hypertensive might simply reflect their investigative interests. Other patients of theirs presented with other conditions including anxiety neurosis. Their studies suggested the predominance of a specific neural influence in an abnormal situation.

Beta adrenergic stimulation might be the mechanism whereby cardiac symptoms are produced in certain anxious individuals. This is suggested in several studies which improved cardiac symptoms and anxiety by beta adrenergic blockade but did not try to reproduce symptoms by pharmacological beta adrenergic stimulation. Nordenfeldt[366] has shown that orthostatic effects can also occur in the ECG as a direct result of sympathetic stimulation of the heart. These ECG changes

were minimised by beta receptor blocking agents, even with the patient lying down. Three patients were described who after receiving beta adrenergic blocking drugs expressed relief at the slower heart rate and disappearance of unpleasant sensations in the chest. Besterman and Friedlander[35] also found that four patients with effort syndrome and tachycardia responded subjectively and objectively when treated by propranolol. In a controlled double blind trial in anxious patients, Granville-Grossman and Turner[163] noted that propranolol was more effective than a placebo. Heart rate was slowed and anxiety symptoms improved, especially autonomic ones (see also p. 78).

It is possible that beta adrenergic drugs may produce these calming effects not by their peripheral beta adrenergic blockade but by a direct central sedative effect. This would mean that patients who improve with propranolol need not necessarily have a primary higher sensitivity of beta adrenergic receptors, but that the disorder may be more central in origin.

At the present time it is not known what proportion of patients with chronic anxiety have a primary autonomic disorder, but the proportion is likely to be small. Very few anxious patients give the clearcut postural relationship elicited by Frohlich et al. and by Nordenfeldt but when it is present further investigation is certainly indicated.

Schizophrenia

Schizophrenia gives rise to disturbances of thought, volition and mood, and anxiety is one of the disorders of mood found occasionally in schizophrenia. The anxiety may be of variable duration and intensity and phobic anxiety is also sometimes seen. Usually anxiety in schizophrenia is a minor aspect of a clinical picture dominated by other phenomena typical of the psychosis. The term "pseudoneurotic schizophrenia" is sometimes applied in America to patients with persistent and severe mixed neurotic symptoms including anxiety. In the United Kingdom unless other schizophrenic phenomena are obvious such patients would usually be labelled anxiety states or agoraphobics, depending upon the dominant symptomatology.

ANXIETY STATES (ANXIETY NEUROSIS)

An anxiety state or anxiety neurosis is a cluster of symptoms based on anxiety, the source of which is not recognised by the patient.[352] The anxiety may be chronic and sustained, but more characteristically is episodic from a few minutes to hours or days. The chief symptoms are apprehension, inattention, palpitations, respiratory distress, dizziness, faintness, sweating, irritability, tremor, chest pains, feelings of impending disaster and fears of death (see also list of symptoms in Hamilton Scale, p. 99). These occur in the absence of other illness, and exist

independently of specific external situations. In between attacks the patient feels relieved but not completely well. There is disagreement about whether anxiety states are a discrete homogeneous clinical syndrome[37,411,502,532] and their features undoubtedly shade in many cases into several other forms of neurosis. However, until further component subgroups have been reliably demonstrated the global category will remain useful for descriptive purposes. Phobic disorders used to be subsumed under the heading "Anxiety State" until recent work showed these to be sufficiently distinctive to form a separate diagnosis. The same may apply in time to other patients who are currently included under the rubric of anxiety states.

Anxiety states are sometimes included under the general heading of "affective disorders", along with pathologies of mood like depressive illnesses and hypomania. Although anxiety states often resemble certain forms of depression, the different course and treatment require their separate classification.

Terminology

Numerous names have been given to conditions which are indistinguishable from anxiety states. The cardiovascular symptoms have led to several synonyms such as "muscular exhaustion of the heart".[185] "Irritable heart" was Da Costa's[86] term for a condition he described as a functional cardiac disorder, and subsequent authors spoke of Da Costa's Syndrome.[532] "Cardiac Neurosis"[439] was an equally popular label and vasomotor neurosis another, while in World War I "neurocirculatory asthenia" came into vogue[370] and subsequently became widely adopted.[77,137,228,406,520] Over the same period other writers supposed that the symptoms were brought on by exercise and so the term "effort syndrome" came into being[293] to describe "that condition of ill-health in which (those) symptoms and signs which are produced in normals by excessive exercise are called forth in patients by lesser amounts and in which no definite signs of structural disease are discovered".[162] The chief symptoms were dyspnoea, palpitations and fatigue, and patients were treated by graded exercise to try and increase their effort tolerance. The incidence of cardiac disease was only one per cent in this group.[162] The effort syndrome, irritable heart, soldier's heart and neurocirculatory asthenia were prominent in the medical literature of the time,[293,371,406] as sufferers made poor soldiers and had a high rate of invalidism out of the army, so that its early detection in recruits became a matter of some importance. The similarity of soldier's heart to anxiety states was not always recognised. As Wood[532] commented, in civilian life "the change of sex, plus the lack of khaki uniform, seems to have proved an effective disguise. 'Effort syndrome' in the male soldier becomes cardiac, respiratory or other neurosis in a female civilian." Wood noted further that the symptoms and signs

of the disorder closely resembled those of emotion, especially fear, rather than of effort.

The nervous symptoms of an anxiety state led to several other names. Neurasthenia or nervous exhaustion was an early term[27,189, 190,433] while Freud[135] introduced a label which is still often used today namely anxiety neurosis; French authors followed suit with "névrose d'angoisse".[184,188] Yet another synonym not used today was somatisation psychogenic reaction.[520]

Prevalence

Differing criteria of diagnosis make comparison of various authors rather difficult. Nevertheless most authors agree that anxiety states are fairly common (Table 3.1). In a normal population prevalence has

Table 3.1

Prevalence of anxiety states

Percentage	*Area*	*Source*
In total population:		
3·6	British urban	Kedward and Cooper[237]
2·0	„ rural	Gross[167]
2·0	Tennessee rural	Roth and Luton[412]
4·6	Swedish rural	Hagnell[171] (10 year period prevalence)
4·7	Boston	Cohen et al.[77]
In general medical practice:		
	Of patients with cardiovascular symptoms:	
10	Boston	White and Jones[521]
14	London	Wood[532]
	Of patients with psychiatric symptoms:	
27	London	Kedward and Cooper[237]
In psychiatric practice:		
6	Oslo	Eitinger[107]
7	Teheran	Davidian[90]
8	London	Hare[179]
15	Kuala Lumpur	Tan[484]
16	Hong Kong	Yap[534]
20	Chicago	Carmichael and Masserman[62]
25	London	Garmany[143]
27	Boston	Cobb[76]
	Of psychoneurotic patients:	
18	Teheran	Davidian[90]
19	New York	Hamilton et al.[174]
22	„ „	Hamilton and Wall[175]
43	Kuala Lumpur	Tan[484]
	Of patients in psychotherapy:	
40	Plymouth	Blair et al.[38]
44	London	Luff and Garrod[307]

been estimated as 2·0–4·7 per cent in Britain and the United States, while anxiety states form 10–14 per cent of patients in cardiology practices (Table 3.1) in the same countries. They make up a substantial proportion of patients who consult general practitioners, accounting for 27 per cent of those who saw their doctors for psychiatric problems in a London practice.[237] Among psychiatric outpatients anxiety states are diagnosed in 6–27 per cent of all cases, but other related conditions like phobic disorders swell some of these percentages. The figure of 8 per cent for Maudsley Hospital Outpatients[179] excludes phobics, and has remained constant over the past nine years. In two series of patients who received psychotherapy the incidence of anxiety states was much higher presumably through special selection for that treatment.[38,307]

Anxiety states are one of the commonest neurotic disorders. At the Maudsley Hospital the figure of 8 per cent of all outpatients is much higher than that for phobic disorders (3 per cent) and for obsessive-compulsive neuroses (1–2 per cent).

Sex incidence

Figures derived from general medical practice indicate two-thirds of patients with anxiety states to be women, but among psychiatric patients the sexes are equally distributed (Table 3.2). This discrepancy may be due to differences in diagnostic usage or in actual incidence but it is impossible to decide between these alternatives on the evidence available. In some series, e.g. Wheeler et al.,[520] it is clear that agoraphobics were included in the sample, and since agoraphobia is commoner in women

Table 3.2

Sex incidence of anxiety states

Per cent female	
In general population	
72	Hagnell[171]
In general medical practice	
67	Wood[532]
67	Wheeler et al.[520]
74	Kedward and Cooper[237]
In psychiatric practice	
13	Yap[534] (Chinese)
31	Tan[484] (mainly Chinese)
43	Miles et al.[352]
50	Hare[179]
53	Eitinger[107]
53	Yap[534] (Western expatriates)
57	Winokur and Holeman[527]
60	Luff and Garrod[307]
63	Davidian[90]

this may have overemphasised the incidence of women in the total group. On the other hand in Kedward and Cooper's study phobics were specifically excluded, yet the female preponderance of anxiety states remained. If the disparity is genuine it might suggest that women have milder forms of anxiety states as it is likely that the severer forms are more commonly referred to psychiatrists. Alternatively, or in addition, men may ignore minor degrees of this disorder and come for treatment only when they are severely incapacitated. However, no evidence for such a phenomenon has been described for phobic disorders.[224]

Age incidence

An anxiety state is mainly a disorder of young adult life; the mean age of onset of symptoms being around the mid-twenties (Table 3.3) with the great majority starting between the age of 16–40. In several series the mean duration of symptoms before treatment is about 5 years. Distribution of the age of onset closely follows that of the agoraphobic syndrome (Marks, unpublished data).

Anxiety which begins for the first time after the age of 40 is commonly part of a depressive syndrome rather than of an anxiety state.

Table 3.3

Age incidence of anxiety states

Mean age	
At onset of symptoms	
23	Miles et al.[352]
27	Wheeler et al.[520]
29	Marks (unpublished)
20–40	Hagnell[171]
At time of treatment	
27	Miles et al.[352]
28	Wood[532]
32	Wheeler et al.[520]
36	Garmany[143]

Genetic Aspects

The literature on this topic has been succinctly reviewed by Slater and Shields.[453] There is much evidence for genetic influences on phenomena related to anxiety. Selective breeding experiments with mammals show that emotional activity analogous to anxiety depends to some extent on multiple genetic factors.[49,106,362] Studies in man[273, 497,536] indicate that physiological responses such as habituation, number of spontaneous fluctuations in skin conductance, pulse and respiration rate, and EEG variables, are more alike in MZ than in DZ pairs. The same applies to the number of neurotic complaints checked in questionnaires.[449,536] The similarity of MZ pairs reared apart was

actually greater than those reared together, so that their environmental influences were unlikely to have been responsible for this concordance.

Evidence also points to a high incidence of anxiety states in the families of patients with anxiety neurosis. Three studies reviewed by Slater and Shields[453,54,77,310] found that 15 per cent of parents and siblings of anxiety neurotics were similarly affected, compared to only 0–5 per cent of relatives of control groups. Another study[453] found that about 50 per cent of MZ co-twins of anxiety neurotics had the same diagnosis, and 65 per cent had marked anxiety traits. In contrast, in DZ twins concordance for anxiety neurosis was only about 4 per cent, while marked anxiety traits were noted in only 13 per cent. Other twin studies reviewed by these authors also found MZ pairs to be more alike than DZ pairs with respect to neurosis. None of these studies excluded the effect of familial environment. However, Shields[449] described three pairs of MZ twins reared apart who were alike in that both twins showed marked tendencies to anxiety later in life. These findings are difficult to explain on purely environmental grounds.

Slater and Shields argue that anxiety states can best be understood with an interactional model. The constitutional tendency to become anxious might be a component of personality which is variable in degree and in that respect is normally distributed throughout the population, predisposing to conditions like anxiety states if it is marked. Whether an anxiety state develops will also depend on the amount of exposure to stress an individual encounters in his environment. Stress might precipitate an anxiety state which could continue irreversibly in some individuals after the stress has passed off.

Background

The little evidence that is available suggests that patients with anxiety states come from stable backgrounds. Miles et al.[352] found that the childhood home environment was "good" or "fair" in 75 per cent of his sample, and only 26 per cent had lost one or both parents before the patient was eight. 23 per cent of the siblings had emotional difficulties. More than half their patients were married, and none were divorced. Intelligence and education covered the normal range. In their earlier history patients did not give a history of undue physical illness.

Cultural aspects

Some evidence suggests that anxiety states may be commoner in certain cultural groups than in others. In a University Clinic in Kuala Lumpur significantly more Chinese than Malays or Indians presented with anxiety neurosis.[484] In Bangkok more Chinese than Thai women were found with neuroses in which anxiety featured.[479] It is not clear how much this reflects the marginal status of the Chinese in those

societies. The sex ratio may also differ across cultural groups. Yap[534] found a great preponderance of men to women in Chinese patients with anxiety states in Hong Kong, whereas Western expatriates there who had similar problems were as often women as men. However, this might reflect referral practices rather than prevalence.

Not only the prevalence but also the clinical features of anxiety states are culturally influenced. Amongst southern Chinese there is a strong belief that male genitals are essential for the preservation of life, and semen is highly valued. Thus, sexual excess is regarded as destructive of health. It is not surprising that among male Chinese with anxiety states 60 per cent complained of sexual symptoms, notably of imagined loss of semen.[484] In contrast, few male Malay patients had sexual complaints.

The same beliefs aid in the understanding of the phenomenon called Koro.[364] This is a term of Malay origin which describes a culture-bound syndrome of acute anxiety predominantly affecting emigré southern Chinese. It was described as early as 1834. The Chinese phrase for this condition is "shook yang"—literally "shrinking penis". The syndrome normally occurs sporadically but can be epidemic. It takes the form of an acute panic in which the patient fears his penis is shrinking into the abdomen with potentially lethal consequences. To prevent this the penis is grasped manually by the patient or his relatives and friends. Occasionally chopsticks or string are tied to the penis to prevent its retraction. Together with this acute fear comes palpitations, breathlessness, bodily pain, visual blurring, fainting, vomiting or nausea and paraesthesia. In the rare female cases there are complaints of retraction of the nipples of the breasts, and even of the vulva.

The response to anxiety and pain takes place within an elaborate cultural context in which the patient, his family and the community respond in socially patterned ways. For example, Zborowski[538] found that Jewish and Italian Americans respond emotionally and tend to exaggerate their pain experience, while Irish and "old Americans" in contrast are more stoical.

Worry is clearly not solely the prerogative of modern man. Anxiety about being bewitched was commonplace in mediaeval Europe and a detailed guide to recognize witchcraft was widely published.[474] One chapter of this book is devoted to demonstrating how witches deprive men of their "virile members", which suggests that even Koro-like syndromes may have occurred. The terror of being under a spell has been described by anthropologists observing many other pre-industrial societies. Australian aborigines who lived in primitive conditions in Northern Queensland completed a Cornell Medical Index translated into the vernacular. They had many complaints about fatigue, anger, insomnia, backache and respiratory trouble.[70]

Epidemics of acute anxiety

From time to time brief epidemics of acute anxiety affect various communities. These epidemics are short-lived and the affected are not left with any sequelae. Precipitating factors can usually be discerned in the background, and the form of the anxiety is culturally determined.

In Singapore one such epidemic took the form of Koro, and was described by Ngui.[364] In July 1967 there was an outbreak of swine fever in Singapore, and amid much publicity pigs were inoculated to control the outbreak. In October a few cases of Koro presented, and rumours spread that Koro could be caused by eating pork from infected or inoculated pigs. Over the next few days up to 100 cases of Koro a day presented at general hospitals and many more patients consulted their general practitioners. On the 7th day, at the height of the epidemic, a panel of experts appeared on television and radio, explaining to the

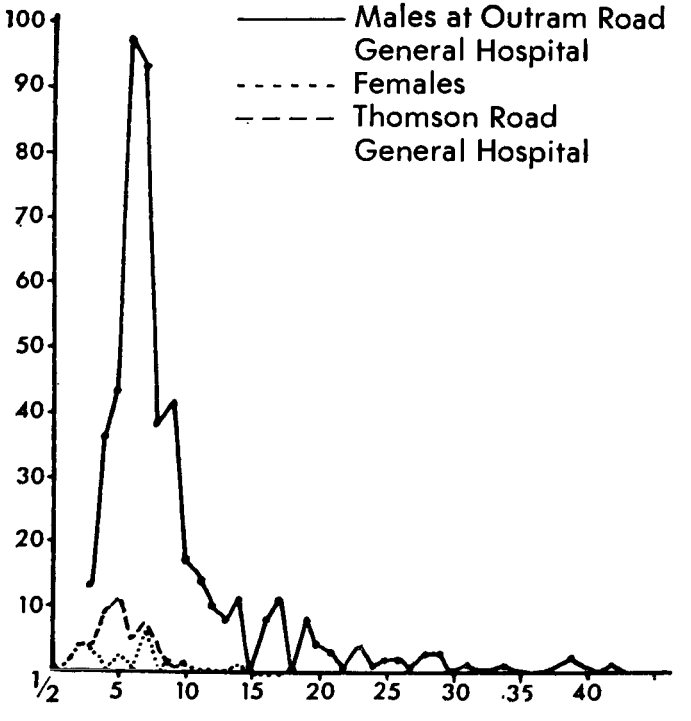


Fig. 3.1: Cases of Koro seen at two Singapore hospitals in July 1967. Ordinate is number of cases; abscissa, number of days from start of epidemic. (Reproduced from[364] by kind permission of the author and the editor of the Australian and New Zealand Journal of Psychiatry.)

public the psychological nature of Koro and the impossibility of penile retraction occurring. The incidence of Koro dropped sharply the next day and the epidemic ended shortly after (fig. 3.1). Of 232 cases which were interviewed, 94 per cent were southern Chinese, the remainder being from several groups. Only 3 per cent of the cases were females. 49 per cent of patients were aged 21–40 and 31 per cent aged 16–20. 77 per cent of the patients were single. Only one in five of the patients

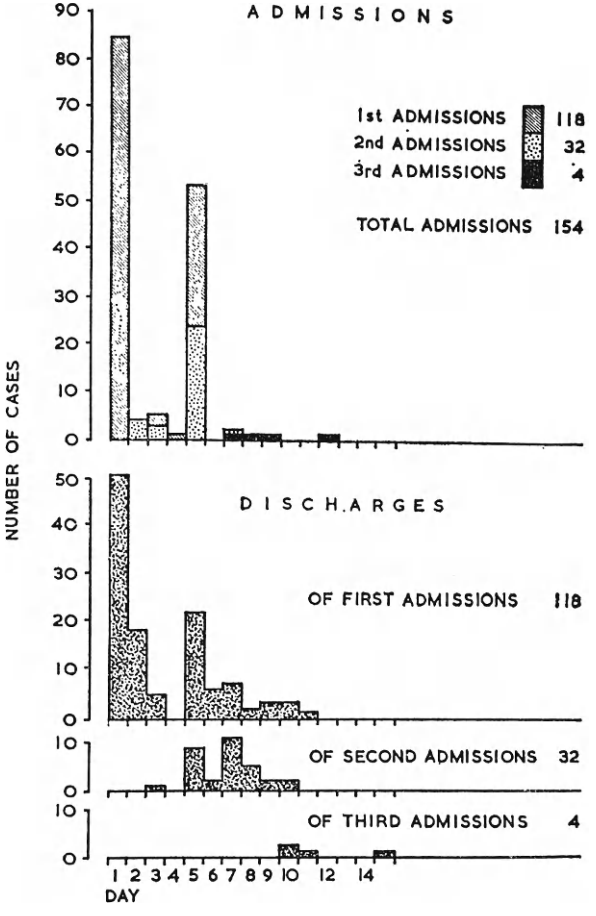


Fig. 3.2: Hospital admissions and discharges. (Note that all but 15 of the 154 admissions occurred on days 1 and 5, and that of these 15 all but 3 were re-admissions.) (Reproduced from [360] by kind permission of the authors and the editor of the British Medical Journal.)

had more than one episode of Koro. The condition appeared to be benign, with the majority recovering fully without serious consequences.

Koro is reminiscent of other forms of acute anxiety in different cultures. In Western societies occasional cases of panic are described in young men who suddenly think they are homosexual. This, however, does not become epidemic. Epidemics of anxiety symptoms such as overbreathing and faintness sometimes occur in young women, especially those like schoolgirls or nurses who are associated together in institutions.

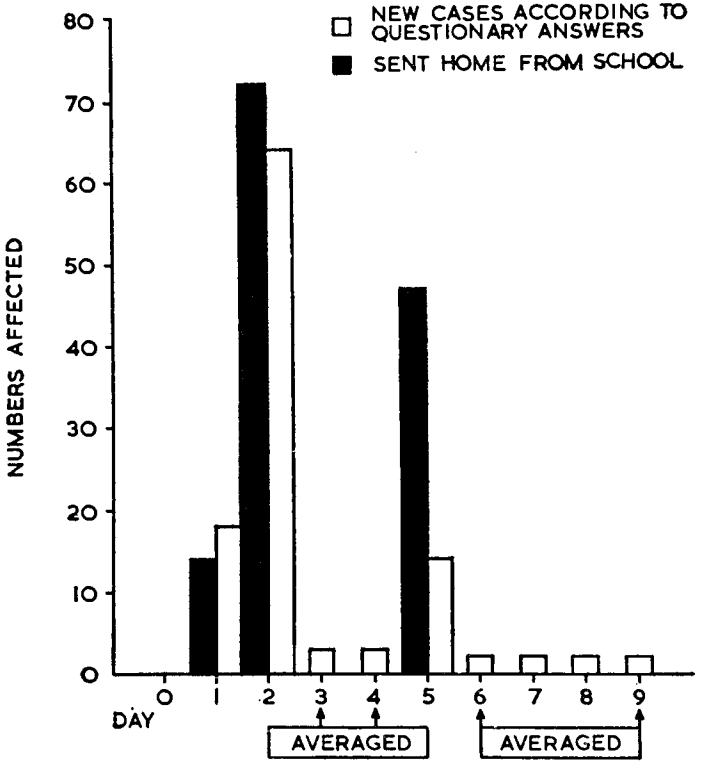


Fig. 3.3: Time course of the Portsmouth epidemic of vomiting and abdominal pain. (Reproduced from [309] by kind permission of the authors and the editor of the British Medical Journal.)

Two such epidemics were studied in detail in Britain. Both occurred in schools and lasted only a few days (figs. 3.2 and 3.3). The first epidemic[360] affected girls in a secondary modern school in Blackburn. Two-thirds of the total of 500 girls were affected, and one-third of the affected girls required inpatient care. Many had repeated episodes. The

precipitating circumstances were clear. Earlier in the year the town had received widespread adverse publicity during an epidemic of polio. Immediately before the epidemic of anxiety the schoolgirls went to a cathedral to attend a ceremony under Royal patronage. The ceremony was delayed by 3 hours due to late arrivals, and the girls waited in parade mainly outside the building. Twenty of them felt faint and had to break ranks to lie down. The next morning there was much chatter about fainting. At assembly in school there was one faint, followed shortly after by three girls saying they felt dizzy. When a fourth girl was asked to get a glass of water for the original fainter, she too said she felt faint. Over the next two periods more girls felt faint and were sat on chairs in a main corridor. A mistress thought that to prevent their falling from the chairs in a second faint they should lie on the floor. They lay thus in the corridor in full view at mid-morning break. The phenomenon now became epidemic. The chief symptoms were excitement and fear leading to overbreathing and its consequences—faintness, dizziness, paraesthesiae and tetany. The appearance of many girls was quite alarming. Each time school assembled more cases appeared. By day 12, however, its nature was realised and firm management prevented the problem spreading further.

The epidemic began among the 14-year-olds and spread to younger children. On the first day 25 per cent of the girls were affected, and, on day 5, 16 per cent developed symptoms. The cases occurred during break twice more frequently than at any other time. The symptoms slowly subsided over a few days in the affected subjects. Affected girls had higher neuroticism and extroversion scores on the EPI, and the highest scores were found in those girls who were the only members of their class to develop symptoms.

A similar pattern was noted in an epidemic of faintness in a Portsmouth girls' school.[309] This again lasted but a few days (fig. 3.3). The symptoms occurred exclusively during school hours. Once again affected girls had higher neuroticism scores than unaffected girls, but their extroversion scores were not high.

Clinical features

Anxiety states are characterised by the appearance of many symptoms but few signs. The chief complaints may be of episodic anxiety or attacks of panic, spells of choking, smothering or difficulty in breathing, palpitations with rapid heartbeat, pain in the chest, nervousness, dizziness, faintness, "get tired easily", "irritable with the children", or "believe I have heart trouble". The chief type of complaint may determine which kind of specialist the patient will see.

Discrete episodes of anxiety are characteristic of the disorder. The patient suddenly feels ill, anxious, weak, has palpitations, lightness and dizziness in the head (as opposed to true vertigo), feels a lump in the

throat and weakness of the legs, and has an illusion of walking on shifting ground. He feels as though he cannot breathe, or he may breathe rapidly to the point of hyperventilation which leads to paraesthesiae. He fears he may faint, or die, or scream out loud, or "lose control" or "go mad". His nervous panic may become so intense that he may be rooted to the same spot for some minutes until the intensity diminishes.

The seizure may last a few minutes or several hours. It may pass off leaving the patient feeling as fit as before until the next attack occurs the same day or week or even months later, or he may feel apprehensive and tremulous throughout the day (with the panic attacks being periodic exacerbations of this feeling). The attacks may occur only once in a few days, or come in successive waves every few minutes to become so troublesome that the patient is confined to bed. In more chronic forms the course is typically punctuated by remissions and relapses of varying duration.

The intensity of the nervousness varies from paralysing terror to mild tension, or the patient may not even be aware of subjective anxiety as such, but simply complain of autonomic symptoms. Anxiety may be continuous without punctuation by discrete attacks of panic. It may be mixed with mild feelings of depression, wishing to cry and even transient suicidal ideas, but serious suicidal urges are not a feature.

Breathing difficulties are common. The complaint may be "I can't take deep breaths", "I can't get enough air", "my breath keeps catching", and the patient may in fact show repeated catches in his breathing. The opposite problem of hyperventilation may be also be found. Choking and swallowing feelings are prominent, and may be intensified in crowds so that patients will have to open a window in crowded places.

Chest discomfort may include praecordial pain or aching, palpitations, epigastric pressure or feelings of gas around the heart. Desires to micturate or defaecate can reflect intense anxiety, and the patient may need to be constantly in reach of a toilet. Severe tension may also produce nausea and vomiting, and this can lead to secondary fears of vomiting when the patient is in public places with avoidance of such situations. Anorexia and loss of weight are not rare. Occasionally slight mucous diarrhoea can occur.

Troublesome faintness and dizziness may be triggered by walking or standing. The patient may feel so insecure as to hold on to a nearby chair or walk close to the walls of nearby buildings. Acute feelings of choking, palpitations and chest discomfort can accompany these and lead to fears of fainting, falling, having a heart attack or dying. These feelings may be intensified in certain situations and lead to their avoidance, thus giving rise to agoraphobic symptoms. Patients may tend to avoid hot crowded rooms or stores, and will stay clear of a cinema, theatre, hairdresser or church, of if they go there will sit near the end of the aisle to ensure that exit is possible with speed and dignity.

Crowded streets, buses and trains can become unendurable ordeals which evoke repeated attacks of panic, so that the patient may progressively restrict his activities until he is virtually confined to his home. Travel by motor-car is often possible, however, even when all other forms of transport are avoided and the patient is unable to walk alone in the streets. Phobic symptoms are often alleviated by the presence of reassuring adults, so that the patient may be able to accomplish accompanied what he cannot by himself. Sometimes he may need to be with someone even at home, and spouses may need to give up work and remain at home with the patient. When phobic avoidance is marked its clinical features become indistinguishable from severe agoraphobia.

Hypochondriacal fears are frequent. The patient may believe that heart disease or cancer is responsible for his symptoms and may entreat the doctor for repeated reassurance on this score, yet multiple investigations will not allay his fears.

General irritability is common. Patients have a low tolerance of frustration, lose their tempers easily, snap at their spouses and children. Fatigue develops readily, and the patient finds it hard to get through the day's work.

Depersonalisation and derealisation commonly occur in anxiety states. Patients complain of feeling unreal, strange, detached or far away from their surroundings, or may attribute the same quality to their environment. The feeling may come at the height of a panic, or at other times when there is no sensation of anxiety. It is more common than is generally appreciated as many patients find it difficult to describe their feelings of perceptual strangeness and may not volunteer these symptoms spontaneously.

The following patient illustrates many of the typical features found in anxiety states. In this case the anxiety began in a normal well-adjusted personality.

> A 35-year-old mathematician gave a history of episodic palpitations and faintness over the previous 15 years. There had been periods of remission of up to 5 years, but in the past year the symptoms had increased, and in the last few days the patient had stopped working because of his distress. His chief complaints were that at any time and without warning, he might suddenly feel he was about to faint and fall down, or tremble and experience palpitations, and if standing would cringe and clutch at the nearest wall or chair. If he was driving a car at the time he would pull up at the kerbside and wait for the feelings to pass off before he resumed his journey. If it occurred during sexual intercourse with his wife he would immediately separate from her. If it happened while he was lecturing his thoughts became distracted, he could not concentrate and he found it difficult to continue. He was becoming afraid of

walking alone in the street or of driving his car for fear that the episodes would be triggered by it, and was loathe to travel by public transport. Though he felt safer when accompanied, this did not abolish his symptoms. Between attacks the patient did not feel completely well, and a slight tremulousness persisted. The attacks could come on at any time of day or night. The patient felt that he lacked energy but was not depressed. He denied that he experienced fear, anxiety or panic during his attacks.

The patient had had a happy childhood without nervous symptoms, led an active social life when in remission, and had a contented marriage and vigorous professional life. There was no family history of psychiatric disorder.

During interview the patient was articulate and frank, though unduly humble. Thought content, memory and orientation were all normal. He had a persistent fine tremor of the head and hands, cold sweaty palms, and a persistent regular heartrate of 106 a minute at rest. While his blood pressure was being measured the patient suddenly became extremely anxious, was restless and sweaty, and would not lie down. He cringed when he stood up and sat down crying weakly "help, help". He tried to tear the sphygmomanometer cuff from his arms, saying it was painful. Blood pressure was 130/80 mins at this time, pulse rate remaining at 116/minute. After three to four minutes he calmed down again but wanted to remain sitting in an easy chair.

Over the next 18 months the patient gave up driving alone or travelling by public transport, so that he gave up his work. These agoraphobic symptoms improved after treatment by flooding so that the patient resumed travelling and working. However, the attacks of free-floating anxiety remained.

This patient illustrates the fluctuating nature of the disorder, that subjective feelings of anxiety need not be complained of during these episodes despite multiple physiological and behavioural concomitants of fear, that depression can be minimal or absent, that anxiety is largely non-situational though coloured by phobic elements, and that autonomic signs of anxiety may be prominent. It shows the marked overraction to mild stresses such as measurement of one's blood pressure and that the disorder can occur in well functioning personalities with stable backgrounds.

Anxiety states can also present as an exacerbation of life-long increased anxiety, as the following case illustrates:

A 52-year-old civil servant had suffered with excessive anxiety all his life. He recalled that as a child he had been timid and had avoided situations where physical harm could occur such as schoolboy fights and rough sports. He had on two occasions played truant

from school when the school bully had threatened him. His academic record at school had been indifferent and he did especially poorly in examinations when he became very anxious. In oral examinations he would usually stammer to a halt.

The patient's mother was described as highly strung and both his siblings had been treated by their general practitioners for anxiety attacks precipitated by marital crises. As a young man, the patient had been very shy of social occasions and of girls but he had fought against his shyness by making himself do public speaking. He married at age 28. His wife had always been sympathetic towards his anxiety symptoms but regretted that he had not been able to achieve his full potential because of them. He was working as an administrative assistant but was studying part-time to take a degree and to become a teacher.

The patient described how any alterations in routine threw him into a panic and he would worry for days in advance over minor difficulties at work. He had visited his general practitioner many times over the previous 25 years and had found barbiturates to help him over exacerbations of his anxiety. However, he thought that the use of drugs was a weakness in him. The present episode had been precipitated three months earlier when he had been given additional responsibilities at work and also as examinations became imminent.

At interview the patient gave a very good account of himself. His symptoms were "all-pervasive feelings of anxiety", "tension in the neck" and "palpitations, dry mouth and sweating". On physical examination the expected signs of sympathetic overactivity were present.

Treatment consisted of small doses of diazepam (1 mg. six times a day) and supportive and re-educative psychotherapy in which the patient learned to take a realistic view of his capabilities and shortcomings. He attained a precarious equilibrium which he has maintained for four years. Exacerbations of anxiety are treated with sedatives for a limited period.

Systematic observations of the frequency of each complaint in anxiety states have been made by Wheeler, White, Reed and Cohen[520] and by Miles et al.[352] Wheeler et al. studied 173 patients suffering from "neuro-circulatory asthenia" who were identified in a cardiology practice. Their controls were 50 men and 11 women from a large industrial plant and 41 healthy postpartum women from the Boston Lying-in Hospital. The patients of Miles et al. suffered from "anxiety neurosis" and came from the inpatient wards of the Massachusetts General Hospital. Forty-three were men and 33 were women. Fifty of these were selected for detailed study of symptoms. Detailed analysis

of symptoms in patients from the two studies is seen in Table 3.4. The five commonest symptoms found by Wheeler et al. were: palpitations, tires early, breathlessness, nervousness and chest pain. The five commonest complaints found by Miles et al. were nervousness, palpitations, acute anxiety at home, apprehensiveness and fatigue.

Table 3.4

Percentage of patients with anxiety neurosis who showed particular symptoms

All figures refer to patients of Wheeler et al.[520] except figures in parenthesis which refer to 50 patients of Miles et al.[352]

	Patients	Controls
Palpitation	97 (90)	9
Tires easily	95 (78)	19
Breathlessness	90 (75)	13
Nervousness	88 (99)	27
Chest pain	85 (–)	10
Sighing	79 (20)	16
Dizziness	78 (55)	16
Faintness	70 (20)	12
Apprehension	61 (80)	3
Headache	58 (65)	26
Paraesthesia	58 (25)	7
Weakness	56 (65)	3
Trembling	54 (70)	17
Breath unsatisfactory	53 (75)	4
Insomnia	53 (48)	4
Unhappiness	50 (–)	2
Shakiness	47 (70)	16
Fatigue	45 (76)	6
Sweating	45 (62)	33
Fear of death	42 (–)	2
Smothering	40 (28)	4
Syncope	37 (–)	11
Flushes	36 (–)	–
Yawning	35 (–)	14
Pain radiating to left arm	30 (–)	2
Vascular throbbing	29 (–)	1
Dry mouth	25 (–)	1
Nervous chill	24 (–)	–
Frequency	19 (–)	2
Nightmares	18 (40)	9
Vomiting and diarrhoea	14 (–)	0
Anorexia	12 (28)	3
Panting	8 (–)	–

Patients with anxiety states have similar symptoms to the average anxious person, but the symptoms are more intense. Hamilton[176] devised a 14-item rating scale for anxiety which differentiated 42 patients with anxiety states from 53 dermatological patients who had

anxiety. The profiles of the two groups were parallel, suggesting that the patterning of the symptoms was the same in each group, even though patients with anxiety states had the more severe anxiety.

The threshold for anxiety is lowered in patients with anxiety states, i.e. stimuli which produce only slight or no anxiety in a normal person lead to much anxiety in patients with anxiety states.

Physiological changes

Despite the earlier description of irritable heart for this syndrome, and despite the cases described by Frohlich and his colleagues, in fact there is generally no sign of overreactivity to normal sympathetic stimulation (e.g. by injection of adrenaline) nor does the condition result from hyperadrenalism or hypersensitivity of the peripheral autonomic apparatus.[532] There is no characteristic ECG abnormality associated with anxiety states.[228]

A number of abnormalities have been reported in patients with anxiety states in response to standard exercise or stress (reviewed by [77,388]).

Stimuli and stresses which produce abnormal responses or unusual responses at lower stimulus level include pain, cold, muscular effort, CO_2, noise, flash and anticipation. Abnormal responses to these situations were noted in patient's pulse, minute respiration/volume, ventilatory efficiency, increase in blood lactate concentration, work performance, oxygen consumption and wincing and withdrawal reactions. On the other hand 24 hour urinary excretion of 17 ketosteroids does not differ from normal. It is not clear whether any of the abnormalities demonstrated so far apply specifically to patients with anxiety neurosis or whether they are the general signs of poor health, chronic illness, or poor state of physical training.

Recent investigations[242,388] demonstrated that infusions of sodium lactate produced anxiety in patients with anxiety neurosis much more than they did in controls, and that glucose and saline infusions caused no anxiety (see also p. 141). This work confirms that patients with anxiety neurosis react abnormally to many stresses of a psychological, physiological and biochemical kind but we remain ignorant of the basic disturbance distinguishing anxiety states from normals which leads to this abnormal reaction.

Other workers recently demonstrated abnormalities in the skin conductance and forearm blood flow of patients with anxiety states. This is dealt with in detail in Chapter Eight.

Differential diagnosis

The commonest and most difficult problem is the differentiation of anxiety states from *depressive disorders*. So difficult can this be that many suggest the two conditions cannot usefully be distinguished. In

depressive disorders there may be marked anxiety with all its psychological and physiological concomitants. However, there is also pronounced depressive mood, hopelessness about the future, feelings of guilt and unworthiness, desires to cry and suicidal ideas. In addition, there may be a past history of depressive episodes, or of mania, and a family history of the same. Where the depressive and anxiety components appear present to equal degree in a patient, the clinical practice is justifiable whereby antidepressive measures are resorted to first and only after their failure are sedatives employed.

In patients with marked anxiety and *alcoholism*, doubts may arise whether the alcoholism is primary or secondary. In the latter case there is usually a clear history of alcohol being employed to alleviate pre-existing anxiety or phobias and, where there are multiple phobias, removal of the patient from the phobic situations should result in reduction in alcohol intake, thus clarifying the diagnosis. Primary alcoholism would be suspected where anxiety appears to follow withdrawal rather than precede it, or to follow excessive alcohol intake.

Acute anxiety states could be confused with a few physical disorders.[444] Tachycardia can occur both in anxiety states and in *paroxysmal tachycardia*. During paroxysmal tachycardia patients can experience great anxiety and extreme exhaustion. With very fast rates there may be sweating, pallor and faintness. In anxiety states the rate is usually below 140 per minute, while in paroxysmal tachycardia the rate is usually between 140–220. Diagnosis of the latter depends upon the history of repeated attacks of tachycardia of extremely abrupt onset and offset, usually without cause but sometimes related to postural changes, and upon the electrocardiogram.

Thyrotoxicosis can mimic an anxiety state when physical signs are minimal and the complaints are mainly of palpitations, tiredness, anxiety and tremor. However, the tremor is fine, not coarse, and the palms are warm and pink, not cold and clammy as in anxiety. Tachycardia is usually present but the pulse rate does not slow to normal levels during sleep. Diagnosis can be confirmed by finding an elevated protein bound iodine, an increased uptake of radio-iodine, or a raised level of serum tri-iodothyronine.

Rarely a *phaeochromocytoma* might mimic an anxiety state. Here patients can have attacks of sweating, palpitations, nervousness, coldness and pallor. However, they may also complain of angina and abdominal pains, and all these complaints are associated with very high blood pressure. The hypertension may be sustained, though it usually fluctuates or is paroxysmal. During hypertensive phases the urine will contain large amounts of catecholamines and vanillyl mandelic acid.

Course and Prognosis

Anxiety states may be acute or chronic. Acute forms can follow extreme stress such as near fatal accident or injury and last but a few days or weeks. No referral at all to a doctor may result or the patient may see his general practitioner or attend psychiatric outpatients. Short-lived anxiety states can be indistinguishable from depressive disorders, so that it is common clinical practice to treat acute anxiety states with antidepressives on the premise that they are depressive episodes. The long term outcome of such cases is unclear, as most prognostic studies have concerned more severe chronic forms which have required inpatient treatment.

There is no evidence that patients with anxiety states develop diseases said to be caused by anxiety any more than other people, even though they all have high anxiety. For example, in a 20-year follow up of 173 patients, Wheeler et al.[520] found that they were not predisposed to develop hypertension, heart disease, peptic ulcer, diabetes, asthma, thyrotoxicosis, ulcerative colitis, hysteria or schizophrenia. In that study fewer deaths had occurred than were to be expected. In another study,[352] a two to twelve year follow-up of 62 patients with anxiety neurosis found no case of unrecognised medical or surgical disease which was later found to be associated with the symptoms, and no patient later became psychotic.

A careful review of the literature on outcome of anxiety states was made by Greer.[165] He confined his account to studies which: (a) had followed up patients with anxiety states for more than one year from discharge from treatment; (b) had ascertained outcome in more than 20 patients, representing at least 75 per cent of the original sample; and (c) had obtained follow-up information at least in part from psychiatric interviews. Reports based entirely on evidence from mailed questionnaires were excluded.

Six investigations were found which met these requirements (Table 3.5), all of which were retrospective. The diagnostic criteria were not always explicit. The data supplied suggested that they conformed to the clinical picture described earlier. The proportion of neuroses diagnosed as anxiety states in these studies varied from 6–40 per cent.

Methods used to determine outcome differed in these studies. Some were based on verbal assessment.[38,107,118,520] These included an evaluation of symptoms and their incapacitating effect. Wheeler et al. also assessed family and social life. Miles et al.[352] and Greer and Cawley[166] used rating scales to measure symptomatic outcome and social functioning. From Table 3.5 it can be seen that 41–50 per cent of cases were recovered or much improved at 1–20 year follow-up in the different studies. Thus the outcome of anxiety states appears to be satisfactory in roughly half of cases in these studies. None of the studies found a

Table 3.5

Systematic follow-up studies of anxiety neurosis

Author and Source	Treatment	Follow up interval (years)	Final Sample n	Outcome (%) Recovered	Much Improved	Slightly Improved	No change
Wheeler et al.[520] Outpts. Cardiac Clinic, Boston, U.S.	Reassurance sedatives	20	60	12	35	53	
Miles et al.[352] Inpts. Mass. Gen. Hosp., Boston, U.S.	Psychotherapy Mean 3.7 session	2–12	62	8	50	21	21
Eitinger[107] Inpts. Univ. Psychiat. Clinic, Oslo	Drugs E.C.T. Supportive	10	29	41		35	24
Blair et al.[38] Outpts. Plymouth, U.K.	Psychotherapy Mean 7 sessions	1–6	81	59		32	9
Ernst[118] Outpts. Univ. Psychiat. Clinic, Zurich	Psychotherapy 2/3 5 sessions 1/4 5–32 " rest hypnosis analysis	24	31	13	32	35	19
Greer and Cawley[186] Inpts. Maudsley Hosp. London	Supportive, physical or psychotherapy	5	37	27	30	19	24

high incidence of serious physical or other psychiatric illness at follow-up. One report not meeting Greer's criteria found a much poorer outcome of anxiety states in the three years' follow-up: Kedward and Cooper[237] followed up patients who had consulted general practitioners in London and found only 18 per cent to be recovered or much improved.

Firm prognostic variables did not emerge from these studies, though in another report[37] patients who had been ill for less than a year showed the most short-term improvement on placebo or barbiturates.

SUMMARY

Anxiety occurs in many clinical states, especially affective disorders, the agoraphobic syndrome and obsessive-compulsive disorders. In each syndrome anxiety is part of a distinctive pattern.

Where anxiety dominates the clinical picture in the absence of other gross disorders the term "anxiety state" is used. Many synonyms exist for this condition, whose prevalence is variously estimated in recent studies at 2–5 per cent of the total population and 7–16 per cent of psychiatric patients. In psychiatric practice men and women are about equally affected. The disorder mainly affects young adults, and family incidence is high. Certain cultural groups are prone to anxiety states, e.g. southern Chinese, and cultural factors colour its manifestations, e.g. Koro. Epidemics of acute anxiety affect some communities but are short lived.

Clinical features include fluctuating episodic anxiety and panic, breathing and swallowing difficulties, palpitations, dizziness, irritability and faintness. The disorder may be acute and transient especially after extreme stress. Acute anxiety attacks may be indistinguishable from depressive episodes. Chronic forms can fluctuate and persist for many decades. Chronic anxiety states do not carry a high risk of serious physical or other psychiatric illness. In different series from 41–59 per cent of cases were recovered or much improved at 1–20 year follow-up intervals.

Chapter Four

MANAGEMENT OF CLINICAL ANXIETY

The clinician's first problem in management is to determine the kind and source of anxiety of which a patient complains. A detailed psychiatric history is needed in all patients with acute anxiety. Review of a patient's life style will reveal how he dealt with past crises, and whether a current crisis exists. Interviews with relatives and friends may reveal hidden problems which the patient might be denying. A psychiatric social worker can help identify these.

In a few patients the anxiety may be one feature of organic illness of cerebral or systemic nature. Hyperthyroidism can be confused with an anxiety state, and if suspected can be confirmed by appropriate laboratory tests. Elderly patients readily develop anxiety with infections or other systemic illness. Menière's syndrome may produce dizziness and fear of falling which simulates acute anxiety, but the latter state usually has other symptoms as well. Depersonalisation may raise the suspicion of temporal lobe disturbance, but in the latter the episode is transient and set in an orderly march of events. Phaeochromocytoma is a rare cause of paroxysmal anxiety and hypertension.

A more difficult distinction is between an anxiety state and a depressive illness. Feelings of gloom, hopelessness and retardation with insomnia and anorexia may help the identification of depression. When in doubt a trial of antidepressive drugs is worthwhile. In many patients acute anxiety may be triggered by sudden environmental stress. This possibility should be carefully explored. When anxiety repeatedly occurs in certain situations and not in others a phobic disorder is suggested.

When clearcut sources of anxiety are identifiable treatment should be directed towards removing them. Organic syndromes require appropriate treatment. A depressive illness needs to be treated in its own right, and the anxiety which accompanies it can be expected to remit concurrently with or soon after the depression. Phobic disorders should respond to one of the various techniques now available for the reduction of morbid fear. Obsessive-compulsive disorders can improve with several new psychological techniques.[394]

Most patients with an acute anxiety attack can be managed as outpatients. Inpatient treatment is rarely indicated except for evaluation or tiding the patient over a social crisis. He may need to be off work for a few days, or a housewife might need to have temporary help in

the home. Sedative drugs can help to lower the level of anxiety. Drugs given by mouth are usually sufficient, and intravenous or intramuscular administration of sedatives are rarely necessary except in the most intense panic attacks. Both barbiturates and benzodiazepine sedatives carry some risk of addiction, so that it is advisable not to continue with high dosage for longer than a few days. With barbiturates addiction is a real danger at doses over 500 mg/day. Insomnia can be helped by hypnotics such as nitrazepam. Abreaction by intravenous drugs is not indicated, except possibly for acute traumatic neuroses of the kind found in shell-shocked soldiers. In such cases intravenous barbiturates sometimes result in dramatic relief after the patient expresses intense emotion, regardless of the relevance of that emotion to his traumatic experiences.[432]

Psychiatric social workers can help the patient make economic, occupational and domestic readjustments when these are indicated. The patient will require empathy and reassurance, with emphasis on his need to deal adequately with any problems he may have. A posture of coping rather than of invalidism is to be encouraged. Simple explanation of the nature of anxiety symptoms is often helpful. A patient who hyperventilates with resultant paraesthesiae and dizziness can be taught the mechanism and its prevention by inhalation into a paper bag. Explanations that they are not going mad are very helpful, especially if patients' symptoms are bizarre, as may occur with depersonalisation. One of our patients became extremely aware of her feet during panic attacks, and felt as though she was just a brain with feet. Others fear that their breathing may stop, and feel easier simply by knowing that this is a manifestation of anxiety.

In acute anxiety states environmental triggers can often be identified and the patient helped to cope with them by a psychotherapeutic approach. A patient deserted by his spouse may need considerable support until he has adjusted to a new style of living and developed fresh personal relationships. Dynamic discussion of events leading to his desertion can lessen the chances of a similar pattern repeating in the future. A dependent woman whose mother is dying will benefit from ventilation of her relationship to her mother and the problems her death will cause. The grief reaction can be anticipated and the patient helped to work through it when it finally occurs. A man who is perturbed about his sexual orientation after a homosexual seduction will need assessment of his adjustment and reassurance and guidance about the various life styles open to him. A student in the throes of examination anxiety will gain from review of his position and may require specifically antiphobic measures such as desensitisation or flooding, though milder cases might only need sedative drugs as a palliative.

The clinician needs always to be alert to the various possible meanings of the complaints an anxious patient brings to him. A patient may give a headache or tension as the reason for consultation, yet after a few

minutes' sympathetic hearing may mention interpersonal troubles which appear to be more important. The initial complaint can *sometimes* be a face-saving device whereby a patient tests out whether to confide more private difficulties to the psychiatrist. With all patients, including those with anxiety, psychiatrists need to be alert to the different possibilities which might be causing their distress. The therapist needs to be sensitive, empathic, and willing to listen to the patient's messages. The patient needs a supportive relationship, and in selected cases dynamic interpretation of the patient's relationships can be helpful in the context of brief therapy. Where the patient's disorder is clearly part of a repetitive maladaptive pattern of behaviour, more intensive dynamic psychotherapy may be indicated. In certain patients specific methods like assertive training or role play manoeuvres can be useful.

When anxiety persists, patients should be taught how to prevent phobias from developing to the situations in which their panic strikes. They need to "ride out" the panics and remain in the situation in which it began until it passes off. If it starts while he is driving a car the patient should pull over to the kerbside and wait for it to pass off before driving away again. If panic begins in a busy shop the patient should wait in a corner, preferably sitting down, until it has gone, rather than rush out for fresh air. If it develops on a bus or train journey, that journey should be completed. The principle is that patients should never escape from a situation in the middle of an acute anxiety attack. The majority of acute panics pass off within a few minutes and they rarely persist beyond an hour.

Probably most patients with acute anxiety states recover without intensive treatment. An unknown number progress to become chronic anxiety states whose therapy can pose great difficulties. Repeated reassurances may calm these patients for a few minutes or hours, after which the complaints resume in full force. Many psychological methods have been claimed to be of value for the relief of chronic free-floating anxiety, though none of these claims rest on firm evidence.

In the following section more specific measures for the relief of chronic free-floating anxiety are considered. Conditions like phobias and obsessive-compulsive disorders are outside the scope of this book, and have been reviewed elsewhere.[330,394,504] Sedative drugs remain the mainstay of the treatment of anxiety because they are fairly effective as palliatives, are not time-consuming to administer, and do not require the use of techniques outside the experience of most doctors. For these reasons drug therapy is dealt with in some detail in Chapter Five.

RELAXATIONAL METHODS

Relaxation techniques have been in vogue for at least a generation. Most of these involve muscular exercises designed to relax the patient

and induce mental calmness. Jacobson[212] pioneered this work and details of his technique are to be found in Wolpe,[530] Rachman[393] and Marks.[330] In the absence of controls it is difficult to assess its value for anxiety states.[270a] Jacobson's relaxation was later incorporated by Wolpe[530] into his desensitisation procedure for the treatment of phobic disorders. Recent workers have cast doubt on the contribution of muscular relaxation to the efficacy of this method.[29,81,345,378] Though muscular exercises can undoubtedly produce muscular relaxation in many patients, this by no means necessarily leads to mental relaxation. Very anxious patients sometimes say "my muscles are relaxed but I don't feel any calmer". More often very anxious patients are unable even to achieve muscular relaxation despite intensive practice. Some patients find it helpful to listen periodically to a tape recording of relaxation instructions which they can play at home whenever necessary. It is not clear how much of the relief is actually due to the muscular relaxation, how much to the suggestions of mental calmness which might accompany this, and how much to the reassuring voice of the therapist giving instructions on the tape. Whatever the mechanism, the ritual of muscular relaxation can be helpful to induce mental calmness in some patients, and the latter is accompanied by a significant decrease in spontaneous fluctuations of skin conductance.[346]

Recently EMG feedback training has been helpful in teaching patients to relax tense muscles. Budzynski et al.[56] used EMG feedback from the frontalis muscle for the relief of tension headaches. The technique awaits extension to and evaluation in the treatment of free floating anxiety.

Hypnosis, too, can lead to mental calmness in some anxious patients. This effect lasts for a variable time. The mechanism of action of hypnosis is still a mystery two centuries after Mesmer first publicised the phenomenon. In many experiments[18] the effects of hypnosis are indistinguishable from those of simple suggestion, or from those induced merely by sitting quietly in a chair.

Autogenic training is another method of relaxation which has been widely used on the continent of Europe.[279,441] In this technique emphasis is not on muscular relaxation but on prolonged concentration on mental images of different parts of the body. Eventually this leads to muscular relaxation and mental calmness. The temperature of different parts of the body can be raised in this way. As with Jacobson's method and hypnosis, some patients find the method of benefit. Whether it is more valuable for anxiety states than is simple suggestion is unknown as controlled studies have not been carried out.

Related techniques are those of meditation. Similar effects appear to result from methods as different as zen, yoga, transcendental and Catholic mystic meditation. Subjects report being more calm and stable for up to weeks afterwards. Physiological effects can be detected

during meditation, as they can during autogenic training. Breathing slows and the alpha rhythm becomes more prominent in the EEG while the eyes are open. The reverse has also been reported. With the help of feedback displays of their EEG, subjects can learn to produce prominent alpha rhythms with their eyes open and some have said they felt tranquil when they achieved this state[52,226] although another study did not confirm this.[420] The bulk of these studies have been with normal volunteers, and some of these suggest that more anxious subjects have greater difficulty in achieving either meditation or alpha control. The therapeutic value of these methods in anxiety states awaits serious study. It is possible that precisely those anxious patients who need to benefit from meditation or its analogues are unable to achieve the necessary mental state. No one knows the criteria necessary for successful meditation, nor whether training can help initially unsuitable candidates. This field holds intriguing possibilities, but decades of rigorous research will probably be needed before firm guidelines emerge for the practising clinician.

FLOODING-TYPE METHODS

Rather different psychological techniques to the foregoing are flooding and its analogues. In these methods anxiety is deliberately provoked in the patient for periods up to an hour or more in an attempt to habituate the patient to the experience of anxiety. Stampfl and Levis[475] publicised the technique of implosion, which implies a bursting from within. During it an intense anxiety reaction is reputedly followed by collapse of the symptoms because of extinction of the anxiety which supports them.[200] The treatment consists of the patient listening for long periods to the therapist's description of his anxieties and hypothesized psychodynamic conflicts underlying them e.g. a woman, worried about her hirsute appearance and the teasing it induced, would hear the therapist shouting "moustachio" at her repeatedly and a description of all her worries in exaggerated fashion. A spider phobic would be asked to imagine herself in a room full of spiders which crawl up her legs and arms while she screams helplessly.

Little work in this area concerns anxiety states. Flooding or implosion has mainly been studied in the treatment of phobic volunteers and patients. In volunteers conflicting results have been obtained with implosion in fantasy. Some workers report great improvement with the method (e.g.[20,201]), while others have not found it of benefit.[350] In phobic patients flooding is an effective way to reduce phobic anxiety,[42,332,504] and in fact is more effective than other psychological procedures such as desensitisation. Its mechanism of action is not clear, but flooding appears to have more than one component. The induction of anxiety which is irrelevant to the phobia is therapeutic e.g. asking an agoraphobic to imagine herself being mauled by a tiger. The

therapeutic effect of irrelevant anxiety is proportional to the amount of anxiety shown during treatment.[504] This effect can be construed as a form of abreaction, since the experience of different intense emotions can be anxiety-reducing, e.g. anger or sexual arousal. Alternatively, this effect might result from the patient's learning to cope with anxiety or unpleasantness in general, regardless of its relevance to the phobic problem.

The flooding of patients with anxiety relevant to their phobias is also therapeutic. However, this effect is not proportional to the intensity of anxiety experienced during treatment, and is thus unlikely to be abreactive in nature.[504] This effect might be one of simple extinction, in that the conditioned stimulus (imagined phobic scenes) is continued for long periods without the patient avoiding it, until habituation occurs. The fact that the patient is kept in continuous contact with the phobic material might also suggest that response prevention is responsible. This method is known to produce extinction of conditioned avoidance responses in rats.[25] However, Shearman[447] has shown that such extinction can be obtained in rats by prolongation of the conditioned stimulus alone (a tone in his study), regardless of the occurrence of the avoidance response, and provided that avoidance does not terminate the conditioned stimulus.

The importance of continued contact with the anxiety-provoking situation is emphasised by the work of Watson et al.[503] They found that specific phobics lost their fears rapidly when exposed continuously to the real phobic object for up to $2\frac{1}{2}$ hours at a time. Their impression was that anxiety was not necessary for improvement, but in fact might simply be an unfortunate byproduct of exposure to the real phobic object. If this conjecture is correct, the way might be open to making treatment more pleasant with the aid of drugs during exposure.

Analogous to flooding are some aspects of paradoxical intention or "logotherapy". This was publicised by Frankl.[132] The patient is asked to cease fleeing or fighting his symptoms, and instead is asked to exaggerate them, after which he is no longer haunted by the symptoms. The technique depends upon observations that anticipatory anxiety brings about precisely what the patient had feared, while excessive intention or self-observation of one's own functioning may make this functioning impossible. Anxiety or compulsions may be increased by the endeavour to avoid or fight them.

In similar vein was Malleson's[318] rationale for use of a flooding procedure. "Fear or panic is always integrally bound up with the wish to escape. So long as that wish persists, reciprocally the fear persists." Earlier physicians also recognised this principle. John Hunter[208] described a patient who was impotent each time he tried to make love to his mistress. As soon as the patient was told not to engage in intercourse his potency returned.

Paradoxical intention and flooding are reminiscent as well of Japanese morita therapy.[252] In the treatment of patients with severe anxiety and fear of death, "The patient will always entertain a premonitory fear that the seizure (of anxiety) might attack him any moment and his sphere of activity is usually very much limited because of this anxiety.

". . . he should be told that it is important not to upset the regular pace of his life even if he had a premonitory fear that the seizure might attack him, by accepting such fear as it is calmly and passively. When he does not have the fit, the patient should be made to go out all by himself even if he has an anticipatory fear or is suffering from anxiety. He should ride the bus or the street car if that is necessary and should attempt to enlarge his sphere of activity in any way possible. If he takes advantage of his disease and leads a life like that of a patient by capitalising on his condition, he will never be cured."

Similarly, in the treatment of intrusive thoughts "the only solution is to accept the desultory thoughts as something inevitable and to keep on reading without repelling them, but tolerating them as they are. If this stage of self-resignation is achieved, there will no longer be any antagonistic ideas . . ."

These elements too are found in meditational methods. Describing the states of zen training, Maupin wrote:[347] "There is an initial phase in which concentration, difficult at first, eventually becomes more successful. Relaxation and a kind of pleasant 'self-immersion' begin to follow. At this point internal distractions, often of an anxiety-arousing kind, come to the fore . . . the only way to render this disturbance inoperative is to 'look at it equably and at last grow weary of looking'."

It is not easy to extrapolate from this work to the treatment of anxiety states in which there are no situational phobias. No controlled studies are yet available on the value of flooding or its congeners in anxiety states. Because prolonged irrelevant anxiety can reduce phobic anxiety it might also reduce non-situational anxiety, though for how long is a matter for study. Others have suggested the possible value of induction of prolonged panic attacks by infusions of lactate (Bonn, personal communication), i.e. biochemical as opposed to psychologically induced flooding. At the time of writing, there is no firm evidence for the value of flooding or its analogues in the treatment of anxiety states.

The sad conclusion is that no psychological technique is clearly of lasting benefit for the relief of chronic free-floating anxiety. Claims abound but their proof is lacking. Many psychological treatments might be useful in acute anxiety states, but evaluaton here is also unsatisfactory.

LEUCOTOMY

Leucotomy is sometimes recommended as a useful treatment for chronic tension states. The subject has been reviewed by Schurr.[442]

Many thousands of patients of diverse kinds had a "standard" leucotomy between 1936 and the early 1960s. It gradually emerged that most benefit was obtained in the relief of anxiety and depression. However, the "standard" operation had side-effects so serious that they became known as the post-leucotomy syndrome. This was characterised by intellectual retardation, emotional blunting, loss of self-control and apathy. These sequelae highlighted the need for alternative surgical procedures.

In post-mortem material the area of damage common to successful cases lay in the inferomedial quadrant of the white matter of the frontal lobes, where projection fibres are carried from the anterior frontal cortex to the thalamus and elsewhere. Operations were devised to isolate or ablate this or related areas. These operations became known as modified leucotomies and came to replace the "standard" procedure in the 1960s. They were designed to produce the minimum cerebral damage necessary for improvement with the fewest unwanted effects. In time the optimum procedure seemed to be the subcortical division of white matter parallel to the roof of the orbit.[249] Recently the destruction of white matter was limited still further by the stereotactic implantation of rods of yttrium-90 under the cortex of area 13 on the inferior surface of the frontal lobes.[250]

No prospective controlled studies have been carried out on modified leucotomies in anxious patients. Two retrospective controlled studies [331,483] showed that free-floating anxiety was reduced significantly more after *modified* leucotomy than after nonsurgical treatment, and that this difference persisted to 5 years follow-up. Furthermore, this benefit was obtained without appreciable personality change. These studies were of patients who had not only marked free-floating anxiety but also severe agoraphobia[331] or obsessive-compulsive disorders.[483] The patients had been seriously and chronically ill for many years, and leucotomy had been resorted to only when all other treatments had failed. Although the leucotomy groups did better than the control groups, residual symptoms were the rule, and the group as a whole retained some of their former handicaps, though these were less than in the unoperated cases.

Schurr[442] summarised the chief indications for leucotomy. The most likely problems to be relieved are tension, fear and anxiety, and operation should only be considered when other treatments have been ineffective.

The previous personality of a patient is an important factor. Those with a long history of dependence on others or maladjustment to their environment usually do badly. Previous aggressiveness might be aggravated by leucotomy. Where the patient's environment is not supportive post-operative rehabilitation will be difficult. Patients with coronary artery insufficiency, arteriosclerosis or vascular hypertension

fare badly with modified leucotomy. Schurr pointed out that leucotomy alone was not sufficient treatment. Postoperative care and rehabilitation are almost as important as the operation itself.

In conclusion, modified leucotomy has a small part to play in the treatment of selected patients who are severely disabled by free-floating anxiety of long standing.

Chapter Five

DRUG TREATMENT OF ANXIETY

INTRODUCTION

Drugs primarily used for the treatment of anxiety are referred to by a variety of terms. The older term "sedative" means a drug with the property of allaying anxiety and inducing calm. However, it has come to suggest the production of feelings of heaviness, drowsiness and slowness which occur rather readily with the earlier compounds used in the control of anxiety, namely, the barbiturates. These soporific effects are unwanted by the patient and the term "sedative" has taken on a pejorative meaning. "Anxiolytic" is used frequently especially on the Continent of Europe. However, it has a mixed etymological derivation and implies an unwarranted specificity of action. All anxiolytics have hypnotic actions at dosage levels above those controlling anxiety and all hypnotics given in low dosage are effective to some extent in alleviating anxiety. Finally, the term "minor tranquilliser" has even less to commend it: such compounds are not minor in that their effects are appreciable and useful; nor do they possess much in common with the major tranquillisers such as the phenothiazines.

In a review nearly 10 years ago Weatherall[506] concluded ". . . in anxious patients the most successful if not the only successful drugs are barbiturates. They are clearly effective, and, unlike all the newer drugs, their toxicity is not gross and is well known". How far is this statement still true today? In this chapter the evidence for the effectiveness of the various drugs in anxiety states is reviewed and in the final section (p. 79) recommendations for drug treatment are suggested.

TECHNIQUES FOR ASSESSING SEDATIVE DRUG EFFECTS

The difficulties in evaluating anti-anxiety drugs have recently been reiterated.[202,529] The problem of choosing or developing sensitive measures of changes in anxiety is a central one: as clinical anxiety is a subjective symptom, the validating criterion remains the patient's verbal report. In Chapter Six, various instruments for self-rating of anxiety and of associated symptoms are outlined and the use of linear rating scales advocated despite their *ad hoc* nature. An example of the changes in severity of symptoms produced by the sedative diazepam as assessed by one patient using linear scales is shown in fig. 5.1.

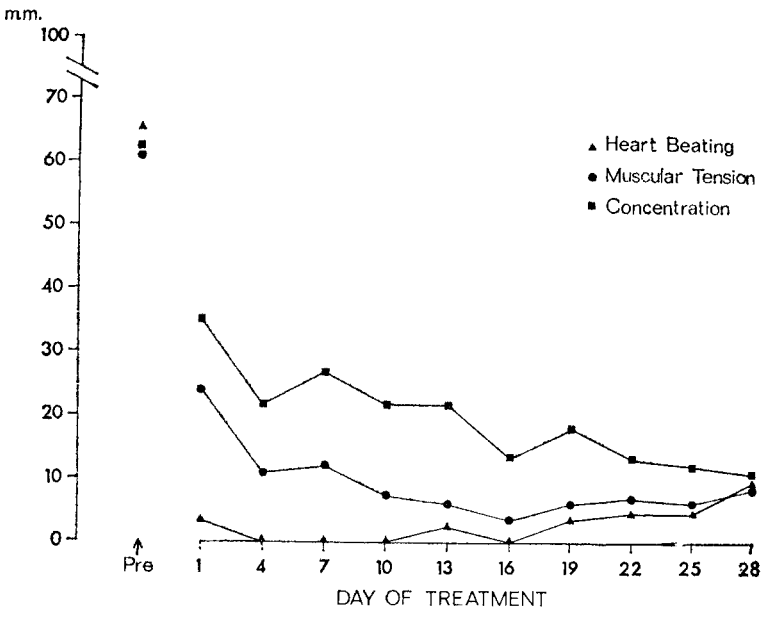


Fig. 5.1: Effect of diazepam 2 mg. three times a day on self-ratings of three symptoms. Note drop in severity as compared with pre-drug ratings.

Observer rating scales are also discussed in Chapter Six. The use of such scales requires training but sensitive measurement of anxiety changes with treatment can be attained. It should be emphasised that instruments assessing trait anxiety (anxiousness) or anxiety-proneness under stress are not usually appropriate for measuring alterations in levels of state anxiety.

It is worthwhile to use both subjective and objective measures. In general the two instruments correlate quite highly but discrepancies are often illuminating. For example, placebo effects show more clearly with self-assessment than with observer ratings (see fig. 5.2).

A wide range of physiological and behavioural techniques are available for the objective assessment of sedative drug effects. Many of these techniques are essentially those discussed in the chapter on the psychophysiology of anxiety and those psychological tests known to be affected by anxiety (see Chapter Seven). The underlying rationale is that anxiety is a state of overactivity or overarousal and that sedative drugs counteract that abnormal state. However, because of the inverted U-shaped relationship between arousal and performance, overarousal may impair performance on some tests and augment it on others (see p. 112). Consequently, the action of sedatives would be to improve results on those tests impaired by anxiety but to worsen performance on those

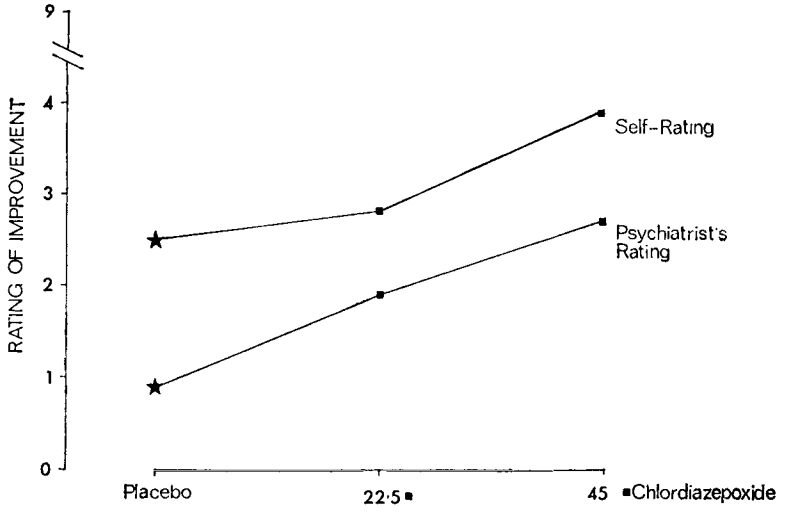


Fig. 5.2: Improvement in bodily symptoms of anxiety in 30 anxious patients treated with placebo or chlordiazepoxide, 22·5 or 45 mg/day. Note that improvement is consistently more marked with the patients' self-ratings than with the psychiatrist's assessments. A double-blind procedure was used and ratings were made on a 9-point scale in both cases. Data from.[273]

tests improved by overarousal. Furthermore, even in tests impaired by anxiety and subsequently improved by sedative treatment, higher doses of sedatives would eventually impair performance. In too many studies, single dose levels only of drugs have been used and a change in performance in either direction, impairment or improvement, explained by assuming a pre-drug position on the descending or ascending limb of the curve respectively (see fig. 5.3).

Despite these limitations numerous techniques are available and will be outlined.

Physiological

Many physiological indices have been used including autonomic measures, the electromyogram and the electroencephalogram. Using quantitative techniques it has been shown that sedatives decrease the mean energy content of the EEG and increase its variability.[155,387]

In one series of experiments, attempts were made to develop physiological indices of sedative drug action.[273] In the first set of studies, single doses of cyclobarbitone were given to volunteer subjects and compared with placebo. By this means, tests sensitive to depressant drug action could be calibrated. In the next study, a group of patients

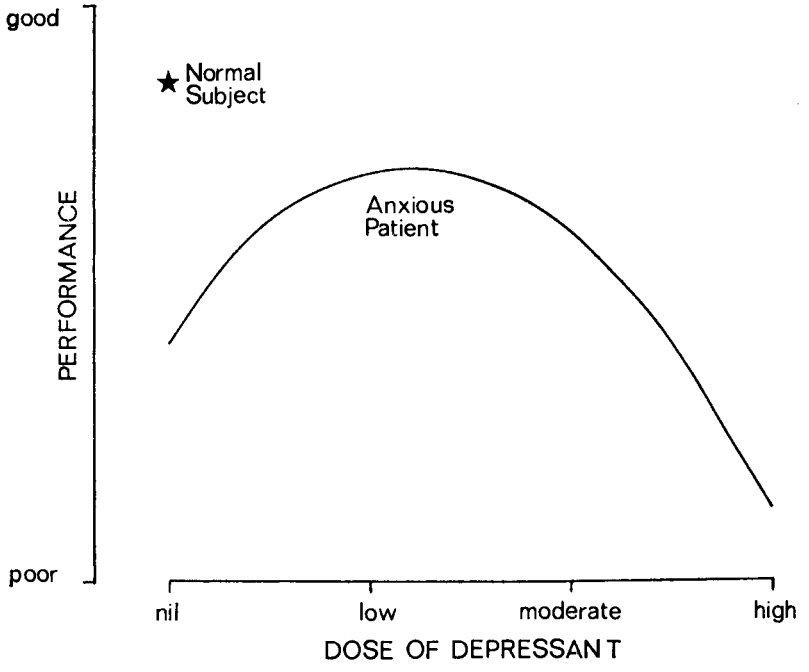


Fig. 5.3: Theoretical relationship between anxiety, dose of depressant drug and behavioural performance. Anxiety lowers performance as compared with calm normals. A low dose of drug improves performance which falls away as dosage is increased. Note that several dose levels would be necessary to derive such a curve.

with anxiety states was compared with normal subjects matched for age and sex. The effects of amylobarbitone sodium 200 mg/day were measured. Finally, chlordiazepoxide, 22·5 mg/day and 45 mg/day, was compared to amylobarbitone sodium, 150 mg/day and 300 mg/day, and to placebo in the treatment of anxious patients. The physiological measure which proved most useful was palmar skin conductance (sweat-gland activity). The number of spontaneous fluctuations in this measure appeared to be the most sensitive variable enabling an estimate of the relative potencies of the two drugs to be calculated. One mg of chlordiazepoxide was equivalent to about 7 mg of the barbiturate.

In a double-blind, controlled evaluation of chlordiazepoxide against placebo using a flexible dosage schedule, forearm blood flow provided a useful estimate of sedative drug effect. Indeed, out of a great many physiological and psychometric measures, only "observer rating of global improvement" proved appreciably more sensitive in distinguishing the active drug's effects from those of the inert preparation.[241]

A physiological system which appears to be particularly sensitive to depressant drugs is that which controls eye movements. The time-courses of barbiturates have been monitored by quantifying the degree of disturbance induced by them in eye movements involved in scanning a moving target.[367]

Behavioural tests can be listed in terms of the level of psychological functioning which they assess:

Sensory

Assessment of this function is usually by measurement of the various sensory thresholds, auditory, olfactory, tactile and visual. More complex tests include vibration threshold and two-point discrimination.

Perceptual

A commonly used test is tachistoscopic perception and discrimination in which stimuli are exposed to view for brief intervals; because of persistence of vision this interval should be longer than 100 ms. Numbers, letters or geometrical patterns are the most commonly used stimuli and discrimination between such stimuli as the size of circles can be undertaken.[254] This test has been used also to assess sedatives in patients.[390] In our experience the exposure of 7 numbers at a time for 600 ms yields an error rate of about 30 per cent on which drug effects can be estimated.

Another test is the critical flicker fusion test in which the subject is required to discriminate between a rapidly flickering light and a continuous image. The time courses of action of single doses of sedatives have been mapped out using this technique.[34]

Psychomotor

There have been many tests of this sort devised because the equipment required is relatively simple and inexpensive, easily quantifiable data is obtained, and the tests are gratifyingly sensitive to sedative drug effects. However, several different psychomotor functions exist and can be estimated.[355] In one large scale study over 200 tests were administered to thousands of subjects in order to evaluate this.[129] After correlation and factor analysis it was found that no general factor of physical efficiency emerged. However, several specific factors each related to at least one test did appear. These factors included manual dexterity, finger dexterity, wrist/finger speed (simple tapping test), arm/hand steadiness (holding a stylus steadily without touching the sides of a hole), and a disc dotting test in which the subject has to aim at dots passing rapidly behind an aperture. Another factor is control precision which may be assessed by means of the pursuit rotor task where the subject is required to keep a stylus on a rotating target.

Reaction time estimations also fall into this category and a variety

of different procedures are available. The simplest is when the subject presses or releases a key immediately a tone, click, flash of light, etc. is presented. More complex reaction times are estimated when the subject has to discriminate between two or more stimuli. Other parameters which can be manipulated include the provision of a warning signal, the presence of a distracting background noise and altering motivation by, for example, payment by results.

Real-life functions can also be assessed. Handwriting can be used as an estimate of sedative drug effect, the length of the words being the most sensitive measure.[285] Another aspect is athletic performance which is known to be diminished by depressant drugs.[454]

A very important real-life skill is that of driving since there is little doubt that patients on sedative drugs may be appreciably impaired with respect to this skill.[187,363] Several methods of study are available and include: (1) controlled experiments on certain relevant isolated components of behaviour, reaction time being the most obvious; (2) studies in mock driving apparatus of the sort used by driving schools in preliminary lessons; (3) controlled experiments on driving test grounds; and (4) statistical evidence from the analysis of accidents and accident statistics. In one study using a simulated automobile driving apparatus, 100 mg of quinalbarbitone sodium produced a definite decrease in performance in normal subjects; meprobamate produced less marked deterioration.[302]

Conceptual and higher mental activities

Simple arithmetic tests may be used to assess numerical performance but the relationship between time and number of errors has to be carefully examined as some drugs in appropriate dosage will produce a larger number of problems completed but with a greatly increased number of errors. Memory functions can be assessed by the speed of learning related words and by the length of the digit span. Nonsense syllables may be learned and immediate or delayed recall assessed. Associative productivity can be assessed using free association techniques, the enumeration of items beginning with a chosen letter and the number of uses for common objects such as a brick. Digit and symbol substitution tests are also sensitive to sedative drug effects.

Responses under stress conditions

The rationale for using stressful procedures lies in the suggestion that some psychiatric illnesses represent abnormal responses to life stresses. Consequently it is argued that it is more relevant to assess the clinical, physiological, and psychological status of the patient during the performance of difficult or impossible tasks when performance may deteriorate and pathological responses occur. In one procedure insoluble tasks are presented after the patient has completed a

series of soluble problems. His behaviour in tackling the insoluble problems is assessed and the effect of sedative drugs on that behaviour evaluated. Another example is the Stroop test where the subject is required to call out the names of colours printed in a different colour; for example the word "red" is printed in blue and the subject has to call out "red".

One example of this type of study was that carried out by Wing[525] in which patients with anxiety states were requested to call out the colours of a series of strips of paper passing very rapidly behind an aperture while their own voices were played back to them after a delay of 0·2 seconds. Under such conditions many patients showed marked physiological responses and their performance very often deteriorated.

Batteries of tests

It can be seen that a wide variety of tests are available for the study of sedative drug actions on human physiological and psychological functions. Because of this many studies have employed a series of tests each designed to assess a different function. As wide a variety of such functions as possible is assessed. For example, in a current project, outpatients with anxiety states are being assessed on the following tests before and during treatment with several different sedatives:

Simple auditory reaction time (32 trials).

Simple arithmetic—the number of the following type of sum completed in two minutes:

$$\begin{array}{r} 8432 \\ +7691 \\ +2469 \\ \hline \end{array}$$

Three *attention tasks*—the subject is required to scan a series of numbers printed on paper and (1) to cross out all of one number (2's), (2) every time any number occurs twice, and (3) every time one number e.g. 4 follows an 8 or 9. Two scores are obtained for each task, the time taken and the number of errors.

Tachistoscopic perception—the identification of fifty 7-digit numbers exposed for 600 ms; score is number of errors.

Digit symbol substitution test—the standard sub-scale of the Wechsler Adult Intelligence Scale; the number correct in 90 sec. is the score.

Card sorting—the subject is required to sort cards with one to eight dots on them into various categories; an estimate of motor time and of central decision time is obtained.

In addition *electroencephalographic measures* are taken and the patient is rated clinically for anxiety levels on the Hamilton Scale. The patient carries out a self-assessment every three days, using a linear scale for each of his major symptoms. The completed form is posted back immediately to avoid biasing the next set of ratings.

CLINICAL TRIALS

It is outside the scope of this book to examine in detail the requirements for the scientific evaluation of sedative compounds. However, there are certain considerations which are especially germane to the assessment of sedative drugs. The simplest experimental design is to allocate patients at random to the treatments to be compared, active or placebo. However, with many objective tests the variability in scores between the patients is several times that for one person tested on successive occasions. As a result very large numbers of patients are required to compare with adequate precision groups each given one treatment. One way out of this difficulty is to test the patients before treatment as well as on the treatment, and then to measure the change with treatment either by simple subtraction or by the use of sophisticated covariance techniques. The alternative is to use the patient as his own control with a "cross-over" design in which the order of treatment administration is balanced across subjects. A placebo control or "wash-out" period may be interposed between the active treatment periods to attempt to minimise "carry-over effects", where the effects of the current treatment are influenced by the comparison with the effects of the preceding one. The latter type of design is not really appropriate for the assessment of sedative drug action on acute anxiety states which pursue a fluctuating course and may remit. It is difficult to predict whether an acutely anxious patient will go on to a chronic anxiety state or will recover completely. If recovery occurs while one drug is being administered then it is pointless to continue the patient with the next drug in his pre-assigned sequence. However, in patients with chronic anxiety states cross-over designs are appropriate and are very "economic" in use in terms of numbers of patients required.

Some patients suffer from recurrent attacks of anxiety and the drug treatments to be compared could be prescribed for limited periods on an *ad hoc* basis during these separate episodes.[202]

Non-pharmacological Factors

These so-called non-specific factors are particularly important with sedative drugs and may often be greater than the specific pharmacodynamic action of these sedative compounds. The effects may be grouped into four categories:

1. The placebo effect.
2. The effects relating to the psychiatrist prescribing the drugs and his associates, such as nurses and social workers.
3. Effects associated with the characteristics of the patients receiving the drugs.
4. The effects associated with the situation or environment in which the drug is prescribed.

Placebo effects have been examined in several studies and have been found to be important in the response of anxious patients. In one study it was found that outpatients with anxiety neuroses responded more favourably to a series of three dissimilar placebo capsules each given for two weeks than to one type of placebo continued for six weeks.[398] However, the concept of the placebo reactor—the patient who consistently responds to inactive medication—is less strongly held than formerly. It appears more likely that there is a patient-situation interaction, some patients responding to placebo in one situation but not in another.

The influence of the prescribing physician has been well studied. In general, psychiatrists who believe in the effectiveness of sedative compounds obtain superior results to those whose opinion of the drugs is less favourable. This was clearly shown in the study of Uhlenhuth and his collaborators.[494] They found no differences between meprobamate (1600 mg/day), phenobarbitone (65 mg/day) and placebo each given double-blind in a balanced cross-over design for two weeks to 52 anxious outpatients. The patients had been treated by one of two psychiatrists, one with expectations that the medications would be beneficial, the other with neutral attitudes. When the data for the two groups of patients were analysed separately it was found that the drugs were no more effective than placebo in the "neutral" psychiatrist's practice, whereas the active agents were equally effective but superior to placebo in the "positive" psychiatrist's group.

The many problems in outpatient assessment of sedative drugs have been pointed out. There is no guarantee that the patients have actually taken their prescribed tablets despite returning to the clinic with empty tablet bottles. Periods on placebo may lead to the patient dropping out from the trial or the therapist becoming disconcerted when confronted by a patient suffering from severe symptoms of anxiety.[236]

The interaction of sedative drug treatment and other therapies is a complex topic. For example, one very detailed and careful study has examined the interaction of psychotherapy and drug treatment in 180 male veteran patients. The five treatments, given for 8 weeks, were meprobamate, 1600 mg/day, chlorpromazine, 100 mg/day, phenobarbitone, 130 mg/day, placebo and no drug, each combined with once-a-week psychotherapy. Criteria of change included various symptom scales, the Taylor Manifest Anxiety Scale and Hostility scores. The data from the groups showed no advantages for drug treatments. Indeed, the patients on the barbiturate were slowed down in their recovery. This phenomenon was particularly noticeable in assessments related to the psychotherapy situation such as the interview relationship.[305]

In a similar study, Lorr and his colleagues[304] divided 150 male out-patients into a psychotherapy group and a no-psychotherapy group. Within each group a third were given chlordiazepoxide up to 60 mg/day,

a third placebo and a third no medication. The prescribing physician was not the same person as the psychotherapist. Many assessments of the patients' symptoms, interview relationship, etc. were made. Patients on chlordiazepoxide were rated as significantly more improved than the placebo group but the proportions improving were 74 per cent in the drug group and 62 per cent in the placebo group so the drug effect was not marked. From the patients' self-reports it appeared that groups receiving psychotherapy responded no differently than groups not receiving psychotherapy. However, it should be pointed out that the psychotherapy was only given once weekly on four occasions. Anxiety was lessened in all the groups except the no-medication, no-psychotherapy group. Chlordiazepoxide did not hinder the interview relationship and possibly facilitated it.

An interesting study has examined the effects of meprobamate, chlordiazepoxide and diazepam on "normal" subjects. 120 male college students were allocated on the basis of their scores on the Taylor Manifest Anxiety Scale to a high anxiety group (scores over 20; upper 20 percentile of population) and a low anxiety group with scores below 7 (lower 20 percentile). Of the former group 54 per cent had in the past sought psychiatric assistance; only 7 per cent of the low anxiety group had done so. Meprobamate 1200 mg/day, chlordiazepoxide, 15 and 30 mg/day, diazepam, 6 mg and 15 mg/day, and a placebo were each given for a week to 10 subjects in each group. Changes in the Scheier and Cattell Anxiety Questionnaire were used as measures of drug effect. Over all subjects no differences between any of the active medications and placebo were found. However, in the High-Anxiety group a significant reduction in anxiety was found with the smaller doses of chlordiazepoxide and diazepam; conversely, in the Low Anxiety group the smaller dose of chloridazepoxide produced an increase in anxiety scores.[21]

SEDATIVE DRUGS

There are now many sedatives available for the treatment of patients with anxiety states. The problems of deciding which, if any, is the most effective are great. Furthermore, some patients respond better to one drug than to another so that the composition of patient groups used in the assessment of sedative drugs is important.

Despite these and other factors, a consensus of findings regarding sedative drugs can be discerned in the voluminous psychopharmacological literature (Table 5.1). In the following sections, each of the more important drugs is briefly discussed and illustrated by outlining a few trials mostly of a controlled nature. The trials were chosen because the patients involved were suffering primarily from anxiety states and not symptomatic anxiety occurring in the context of other psychiatric conditions.

Table 5.1

Drugs used in treatment of anxiety states

Type of Drug	*Examples*	*Trade name*	*Dosage range* (mg/day)	*Comments*
Barbiturates	Amylobarbitone	Amytal	120–180	Effective in severe anxiety
	Nealbarbitone	Censedal	180–360	
	Pentobarbitone	Nembutal	50–200	
	Phenobarbitone	Luminal	45–90	Some tendency to produce depression
Substituted Diols	Meprobamate	Equanil	800–1600	Not as effective as benzodiazepines
		Miltown		
	Tybamate	Benvil	750–1000	Effective compound
Benzodiazepines	Chlordiazepoxide	Librium	15–30	Safety in overdosage; less drowsiness than with barbiturates: diazepam probably most effective sedative.
	Diazepam	Valium	6–40	
	Oxazepam	Serenid-D	45–90	
	Medazepam	Nobrium	15–30	

BARBITURATES

The barbiturates have been in clinical use since 1903 when barbitone was introduced. Phenobarbitone was introduced nine years later and amylobarbitone in 1923. These compounds have long been standard remedies for the treatment of anxiety states and they still often act as the prototypal drugs against which newer sedatives can be assessed. Consequently, it is important to examine the evidence that these drugs themselves are effective in the treatment of anxiety.

Two members of the barbiturate group have been most extensively used for the treatment of anxiety, phenobarbitone and amylobarbitone ("amobarbital" in the U.S.A.). The latter achieved great popularity as a sedative and is believed to have some euphoriant actions as well. On the other hand, phenobarbitone has a reputation for inducing depressive effects and behavioural difficulties in some patients.

In the study of Reynolds and her co-workers,[397] phenobarbitone, 45 mg and 90 mg/day, amylobarbitone, 180 and 360 mg/day, and nealbarbitone, 360 and 720 mg/day, each given for a month were compared with placebo in 19 chronically anxious outpatients in an incomplete block cross-over design. Each patient acted as his own control but only a few received all of the seven possible treatments, most leaving the study before the end. Assessments included a symptom questionnaire, a mood questionnaire and measurements of visual reaction time. The higher dose of nealbarbitone produced a marked decrease in symptoms; the larger dose of phenobarbitone produced similar but less marked changes. Prolongation in visual reaction times was also induced by the

two drugs. The other treatments did not differ significantly from placebo. The possibility that symptom control in anxious patients cannot be divorced from psychomotor impairment when barbiturates are used is raised by this trial.

Evaluation of phenobarbitone has been carried out in general practice conditions. In acute anxiety states treated with phenobarbitone and placebo on a three-week cross-over basis, the failure rate with the drug was only 12 per cent as compared with 41 per cent with the placebo. In the second part of the study, 58 patients with chronic anxiety states were assessed. Two-week periods of drug and placebo tablets were alternated over a total period of eight weeks. The active treatment proved much superior: complete relief in 61 per cent, partial relief in 35 per cent and no relief in 14 per cent in the final week of the trial. The most representative figures for placebo were complete relief in 14 per cent, partial in 9 per cent and nil in 77 per cent. A flexible dosage schedule was used, 90 mg/day being the commonest.[148]

Using a sequential analysis method, Davison[94] compared amylobarbitone 200 mg/day with placebo. From the preferences derived from the patients' self-assessments it was apparent that the barbiturate was superior to placebo. Acceptable significance levels were reached after 17 patients with anxiety states had been treated.

Similarly, in brief courses of treatment lasting a week, amylobarbitone sodium, 200 mg/day, was significantly superior to placebo in the treatment of 20 patients with anxiety states. In addition, physiological effects of the barbiturate were apparent, including diminution of sweat-gland activity.[273]

Amylobarbitone 300 mg/day, benactyzine 6 mg/day, chlorpromazine 150 mg/day, meprobamate 2400 mg/day, and "sedaltine" (a polypharmaceutical preparation containing rauwolfia, carbromal and bromvaletone) were compared with placebo in the treatment of outpatients with anxiety and tension. Each patient served as his own control and was given the six treatments for successive two-week periods using a Latin Square balanced design. Self-rating of overall drug effect was used as the method of assessment. Of the 75 patients with adequate data, 24 defaulted before the end of the trial but the rate of defaulting appeared random. Statistical analysis showed that only the barbiturate proved of any benefit, all the other compounds being no more effective than placebo. Examination of the individual data reveals essentially normal uni-modal distributions for all the compounds except amylobarbitone, with the mean response at about the zero (no change) point. The distribution of scores with the barbiturate is bimodal with patients tending to show either no response at all or quite an appreciable one.[396]

A sustained release form of pentobarbitone has been compared with meprobamate in the treatment of patients with anxiety. Both with

respect to therapeutic effects and paucity of unwanted effects it proved superior.[1]

It appears that the barbiturates, amylobarbitone in particular, are effective anxiety-allaying compounds, at least in an appreciable proportion of patients with anxiety states. However, unwanted effects such as drowsiness and objectively assessed impairment of psychological functioning are very prone to occur. The patient swings all too easily from inadequate symptom control, presumably at low plasma levels, to sleepiness and sopor at higher plasma levels. Nevertheless, for the acutely anxious patient in a panic attack, an intramuscular injection of amylobarbitone sodium in doses of 100–200 mg remains a very effective treatment. Some patients with less pronounced anxiety states respond very well to 200–300 mg/day of the drug given in small divided doses and may prefer it to the newer drugs. Care must be taken that the patient does not insidiously increase his dose as dependence becomes a distinct possibility at total daily dosage levels of 400 mg and above. A patient stabilised on barbiturates should not have his drug discontinued abruptly because of the risk of withdrawal fits.

Intravenous amylobarbitone can be given to "abreact" patients of previously normal personality who have developed symptoms following traumatic experiences during wartime or catastrophes. The dose is usually 200–500 mg given at a rate of less than 100 mg/min. The patient often relives his experiences very vividly during the abreaction.

MEPROBAMATE AND RELATED COMPOUNDS

Meprobamate was a development of mephenesin, a compound discovered in 1946 to have muscle relaxant properties of brief duration. Attempts to prolong this action led to the synthesis of meprobamate and its introduction for the treatment of anxiety. It possesses muscle relaxant properties by virtue of its action on the spinal cord, and was vigorously promoted as a drug different in many respects from the barbiturates.[30] However, the evidence for these claims is not strong as the barbiturates also have many actions including effects on the spinal cord. Controlled clinical trials have not been particularly encouraging.

A detailed and critical review of the effectiveness of meprobamate in the treatment of anxiety, published in 1958, commented sadly on the plethora of uncontrolled studies which claimed marked therapeutic effects. The conclusions of Laties and Weiss[280] are:

> "There is no good evidence that meprobamate can be distinguished from a placebo in treating anxiety in psychiatric outpatients" . . .
>
> "There is evidence that meprobamate is better than a placebo in treating anxiety in hospitalized neurotic and psychotic patients" . . .
>
> "There is no good evidence that meprobamate is any better than a barbiturate in assuaging anxiety" . . .

"There is some evidence that it may not be as good" . . .(as barbiturates).

In one study few if any effects, therapeutic or unwanted, could be attributed to meprobamate as compared with placebo. Ratings included psychiatrists' and self-assessments and the MMPI.[78]

Meprobamate 3200 mg/day was administered to 24 mainly anxious patients for 21 day courses alternating with placebo.[203] Eleven patients improved only on the drug, 3 only on placebo, 3 on both, and 7 on neither, an unimpressive therapeutic effect.

In detailed comparison of meprobamate and placebo, each given to separate groups of anxious patients, no significant differences were found. A detailed analysis of the data suggested that meprobamate did not produce the effects expected of an anti-anxiety compound. Patients scoring highly on pretreatment ratings showed less improvement with meprobamate than with placebo; the mildly ill patients did derive some small benefit from the active drug as improvement was somewhat greater on the active medication than on placebo.[311]

In a trial in which 114 anxious patients participated, meprobamate, 1600 mg/day, produced significantly more improvement than did placebo. This difference was found for global measures of change and direct improvement criteria such as questionnaires. Cattell's IPAT anxiety scales were generally unsuccessful in distinguishing between the active and inactive medications.[401]

A detailed evaluation of meprobamate, 1600 mg/day, as compared with placebo given for three weeks to anxious patients has been carried out. An objective test battery was given including driving-simulator, vision tests, attention span and muscular persistence. The drug slowed reaction time (by only about 4 per cent) but had few other behavioural effects. Clinically patients appeared more rested, less tense and more active on the drug than on placebo.[495]

In another study 40 anxious outpatients were treated with either meprobamate 1600 mg/day or placebo for four weeks. General improvement with the drug failed to reach a significantly higher level than improvement with placebo. Examining individual symptoms, meprobamate was superior to placebo in alleviating anxiety, tension and phobic symptoms. Insomnia, anorexia and somatic symptoms were not significantly improved.[197]

Meprobamate 1600 mg/day was compared with phenobarbitone 120 mg/day and placebo in a very extensive evaluation. Each drug was given to a group of about 30 anxious patients over four weeks. "Drop-outs", i.e., patients failing to complete the four weeks, were due to treatment failure in the placebo group but to treatment success in the drug groups. Clinical overall improvement was significantly greater in the drug groups than in the placebo-treated patients for several ratings. No marked differences between the active drug groups were found but

the trend was in favour of meprobamate. Side effects were commonest with meprobamate.[399]

An examination of the effects of meprobamate, 1600 mg daily, and phenobarbitone sodium, 60 mg daily, as compared with placebo has been carried out in two different clinic populations, namely, from Medical and Psychiatric Clinics. In each clinic patients received one of the drugs and placebo each for two weeks. No direct comparison of the two active compounds was carried out. Both drugs showed superior therapeutic effects to placebo but these were only consistently significant with meprobamate. Meprobamate appeared effective in the moderately to mildly anxious neurotic patient; phenobarbitone was effective in the highly anxious but not the mildly anxious. No differences were found in the results from the two clinics.[400]

In extensive double-blind trials, meprobamate proved superior to placebo but in doses of 1600–2000 mg/day it showed no marked differences in effectiveness as compared with amylobarbitone sodium (260–325 mg/day).[516]

Meprobamate enjoyed an early popularity such that it became one of the most widely prescribed of all drugs. However, it became apparent that its advantages relative to barbiturates were largely illusory: as instanced above its therapeutic superiority over the barbiturates was never convincingly established and, indeed, in several controlled comparisons, it appeared significantly inferior. The unwanted effects of meprobamate are as troublesome as those of the barbiturates, the danger of dependence is a problem and overdoses, accidental or intentional, are potentially lethal and require expert management.

Compounds similar to meprobamate but with more pronounced central relaxant effects have been tried in the treatment of anxiety states. Both phenaglycodol[542] and chlormezanone were found to be inferior to meprobamate.[71]

Tybamate

This drug is related chemically to meprobamate and has been introduced relatively recently. It appears to be more efficacious with fewer unwanted effects than meprobamate.

In a large-scale collaborative study of American private-practice patients, tybamate produced more significant improvement than placebo only after four weeks. It appeared to be primarily effective not against free anxiety but against the somatic concomitants of anxiety. The tybamate-placebo differences were most clearly seen in the symptomatically more ill patients.[402]

Tybamate was superior to placebo in another study and the drug countered exaggerated reflexes[59].

In a large-scale evaluation, tybamate was markedly superior to placebo and side effects were minimal.[445]

In an early report, tybamate compared very favourably with chlordiazepoxide and placebo in the treatment of anxiety symptoms. the drugs being given in flexible dosage schedules. Tybamate provided greater relief of all symptoms—agitation, anorexia, insomnia, psychosomatic complaints, apathy, anxiety, loss of concentration, crying and headache—than chlordiazepoxide which in turn was better than placebo. Unwanted effects, mainly drowsiness, were least frequent with tybamate. Analysis of the pre-treatment symptom levels of the three groups showed the patients receiving tybamate to be more ill than the others[473]. Although one might expect this to have biased the results against tybamate this is not necessarily so: sometimes in psychiatry the more ill patients have the better prognosis and this may occur with anxiety symptoms also.[263]

In another study, the benefits of tybamate as compared with placebo were not marked: 12 patients had better symptomatic relief of anxiety on tybamate (1400 mg/day) than on placebo; 4 were helped more by placebo and in 15 no difference was detectable.[45]

As part of an extensive evaluation of tybamate, Vazuka and McLaughlin[498] administered it in doses of 750 mg/day and compared it with meprobamate 1200 mg/day, and chlordiazepoxide 30 mg/day. 52 anxious patients participated in the trial, each receiving all three drugs in succession for periods of two weeks. Placebos were given for a week between active treatments to act as a "wash-out" procedure. There was little difference between the drugs with respect to therapeutic response with tybamate perhaps being marginally the most effective. The incidence of unwanted effects, mainly drowsiness, was tybamate, 23 per cent; chlordiazepoxide, 39 per cent; and meprobamate, 48 per cent. It must be remembered that fixed single dose levels of each drug were given but, despite this, tybamate appeared the most effective with least side effects.

In summary, tybamate appears to be a distinct improvement on meprobamate and a useful alternative to the benzodiazepines.

BENZODIAZEPINES

The first of these compounds, chlordiazepoxide, was synthesised in 1947 and was found to have the unusual ability to tame aggressive animals. Selected on this basis it was administered to a group of chronic schizophrenic patients and, although having little effect on psychotic symptoms, it appeared to combat anxiety. Extensive evaluation in patients with symptoms of anxiety was then carried out and the drug was introduced in 1960.

Other benzodiazepines such as diazepam and oxazepam have since been marketed. Many other similar compounds have been synthesized and their effects assessed in animals; several have reached the stage of preliminary evaluation in man.[476]

Chlordiazepoxide

From a series of early studies, chlordiazepoxide was regarded as "moderately effective in the symptomatic treatment of psychiatric conditions with prominent symptoms of anxiety, tension, associated psychophysiologic complaints, phobic reactions, and some obsessive-compulsive symptoms".[359]

A large number of anxious patients were used in the study of Azima, Arthurs and Silver.[17] 75 were given chlordiazepoxide at an average daily dosage of 70 mg; the control group of 75 received placebo. 46 per cent of the drug-treated group showed appreciable improvement in the three weeks of the study. Only 8 per cent of the placebo group showed such improvement. Unwanted effects in the drug groups were mild except for one patient who developed ataxia.

McNair and his associates[311] compared chlordiazepoxide in flexible dosage with placebo in two groups of anxious patients assessed over an 8-week period. The group on the active drug showed a much greater therapeutic response which was maximal after 6 weeks of treatment. Significant differences were found for the following scales: confusion, anger, fatigue, vigour, friendliness and somatic distress. Chlordiazepoxide appeared to be especially effective in the more anxious patients.

A direct comparison of chlordiazepoxide (up to 40 mg/day), meprobamate (up to 1600 mg/day) and phenobarbitone (up to 200 mg/day) has been carried out. Each treatment was given for two weeks in sequence to 36 patients with anxiety symptoms. More of the patients (18) experienced symptomatic relief while on meprobamate than on chlordiazepoxide (6) or on the barbiturate (2). Meprobamate also proved superior on the physician's evaluations and some objective tests. The majority of the patients, however, tended to be mildly ill and chlordiazepoxide appeared more effective in those patients who were more severely ill.[99]

A two-stage evaluation of chlordiazepoxide was carried out by Jenner and his associates. In the first study, the drug in doses of 60 mg/day, proved effective in the management of anxious patients. Side effects were limited to slight drowsiness and ataxia. The latter was of a subjective nature and mainly found in elderly patients.[217]

In the second study, chlordiazepoxide 60 mg/day was compared to amylobarbitone 180 mg/day in a total of 92 anxious patients. Each treatment was given for two weeks in a cross-over design. The patients showed a highly significant preference for the benzodiazepine. The authors admit: "It is possible that the dose of methaminodiazepoxide* used in this study was too high and that of amylobarbitone too low for a fair comparison" and conclude fairly that "in the doses used

*The original name for chlordiazepoxide.

methaminodiazepoxide is more likely to be effective than amylobarbitone".[218]

Using flexible dosages and a cross-over design, Gore and McComisky[158] compared chlordiazepoxide, amylobarbitone and placebo each given for two weeks. For the psychiatrist's assessments both drugs were superior to placebo and chlordiazepoxide better than the barbiturate. The trend with the patients' self-ratings was similar but did not quite reach acceptable levels of significance. No preponderance of unwanted effects was seen with any one treatment.

In a study involving a wide range of patients with anxiety and psychosomatic disorders, it was reported that, while chlordiazepoxide was effective in the treatment of anxiety and hyperkinetic states, it did not alleviate depressive symptoms.[436]

The essentially negative findings of some other studies have been attributed to insufficient dosage.[315]

Diazepam

In an uncontrolled evaluation of diazepam, the degree and rate of improvement was highest in acute cases and dropped steadily with chronicity of illness. Initial improvement appeared within 3 to 15 days and maximum benefit was attained in one to seven weeks. The effectiveness of diazepam was compared to that of chlordiazepoxide on a double-blind cross-over trial: diazepam was more effective.[7]

A double-blind, cross-over trial with diazepam, 15 mg/day, and placebo has been carried out using sequential analytic techniques. Diazepam reached the 0·05 level of significance with respect to superiority over placebo after 21 patients had completed the trial: 14 felt better on the drug, 3 on placebo, and in 4 there was no difference. The active drug's effects were usually rapid in onset.[300]

In a similar study, diazepam, 15 mg/day, was compared with chlordiazepoxide, 30 mg/day, and with placebo, each given to over 30 anxious patients. The active medications were significantly superior to placebo and diazepam was superior to chlordiazepoxide at the doses used.[88]

In another double-blind study, diazepam was compared with phenobarbitone and placebo using a flexible dosage schedule. Both drugs were superior to placebo with respect to overall psychopathology. Diazepam was superior to phenobarbitone in the treatment of anxiety and tension, only 14 per cent of patients failing to respond to diazepam as compared with 43 per cent on the barbiturate.[537]

In a double-blind cross-over study using fixed dosages of diazepam (22·5 mg/day) and amylobarbitone (150 mg/day), a marked superiority of the former drug was apparent.[61]

Oxazepam

Oxazepam, one of the metabolites of diazepam, is a more recent introduction. In general, its properties appear very similar to those of chlordiazepoxide.

Oxazepam was evaluated in a series of studies by Tobin and his associates.[490] After pilot investigations to establish the dosage range, it was administered in doses of up to 60 mg/day to anxious patients. Chlordiazepoxide, 30 mg/day, and placebo were the control medications. Oxazepam was as effective as chlordiazepoxide and both were superior to placebo. In a further direct comparison of oxazepam and chlordiazepoxide, the improvement rating of target symptoms showed no significant difference between the two compounds.

Using a sequential design oxazepam was evaluated with respect to placebo in 24 anxious patients[85]. A very clear preference for the active compound was apparent. The Minnesota Multiphasic Personality Inventory was rather more sensitive to the effects of oxazepam (60–120 mg daily) as compared with placebo than were behavioural and clinical ratings. The therapeutic effects were not marked but neither were reported side-effects such as drowsiness.[213]

Prazepam

Prazepam, a new benzodiazepine derivative, has been assessed by comparison with chlordiazepoxide and placebo. It compared favourably, 96 per cent of patients receiving it showing good to excellent response; the percentages for chloriazepoxide and placebo were 65 and 19 respectively.[105] Medazepam is another new derivative.

MAJOR TRANQUILLISERS

Major tranquillisers such as the phenothiazines are infrequently administered to patients with anxiety states and then only if sedatives such as chlordiazepoxide have proved ineffective. The unwanted effects of phenothiazines, even in low dosages, are disturbing to anxious patients and may increase somatic symptoms, e.g. dry mouth, dizziness and blurred vision. The extrapyramidal effects such as restlessness and mild akathisia (evocatively termed in German, "innere Unruhe") are extremely upsetting.

Robin[407] compared pecazine (mepazine) in doses of 75–150 mg/day with amylobarbitone sodium, 200–400 mg/day, in two closely matched groups of patients with anxiety states. Therapeutic effects were much greater in the barbiturate-treated patients. Twice as many new symptoms including side effects were reported in the pecazine-treated patients as in the other groups.

A comparison of fluphenazine hydrochloride (2 mg/day), chlordiazepoxide (40 mg/day) and placebo has been carried out with patients suffering from reactive anxiety states. A rigid "all-or-none" criterion

of efficacy was utilised to analyse the evaluative data: the per cent effectiveness of the phenothiazine was 52·6 and of the benzodiazepine 54·3. However, the placebo was effective in 43·0 per cent of the trials, so that the additional benefits accruing from the active drugs were not marked.[24]

Diazepam (30–100 mg/day) compared favourably with chlorpromazine (125–450 mg/day) and trifluoperazine (5–8 mg/day) in the treatment of anxiety symptoms. Most of the 60 patients suffered from anxiety states. After two weeks, trifluoperazine was distinctly inferior to the other drugs and as the trial proceeded diazepam tended to become superior to chlorpromazine. As might be expected unwanted effects were more common with the phenothiazines.[455]

In a mixed group of patients, diazepam was comparable with but probably superior to chlorpromazine and placebo in the treatment of the symptom of anxiety.[181]

Oxypertine, a non-phenothiazine major tranquilliser, has also been found to be relatively ineffective in anxious patients.[408,493]

MISCELLANEOUS

Among other compounds, benactyzine did not appear very effective.[182] Doxepin, a tricylic compound, has shown sedative properties superior to those of chlordiazepoxide as well as possessing definite antidepressive properties.[157,221]

BETA-ADRENERGIC BLOCKING AGENTS

In Chapter Three an account was given of the syndrome of the beta-adrenergic hyperdynamic syndrome. Although it is doubtful whether this syndrome is really separate from the anxiety states, the existence of patients with the symptoms of excessive sweating, cold extremities, palpitations and diarrhoea demonstrates the overactivity of the sympathetic nervous system. The effects mediated through beta-receptors include vasodilatation of coronary and muscle blood vessels, tachycardia and increased force of contraction of the heart.[491] Symptoms such as palpitations appear to be particularly related to beta-receptor over-activity.

Consequently, attempts have been made to treat anxiety symptoms with beta-adrenergic blocking agents such as propranolol. In one study, eight patients with thyrotoxicosis were compared with eight anxiety states with respect to heart rate changes following an intravenous infusion of saline, amylobarbitone sodium, 62·5 mg, and propranolol, 5 mg, each given over the course of one minute on successive days. Neither saline nor the barbiturate had any effect on the heart rate but mean drops of about 25 beats/min occurred in both groups following the beta-blocker. The authors concluded that the "results suggest that

in both conditions the stimulation of beta-adrenergic receptors is important in the production of the tachycardia."[492]

In a second study, Granville-Grossman and Turner[163] carried out a double-blind comparison of propranolol, 20 mg four times daily, and placebo, each given for one week to anxious outpatients using a cross-over design. A sequential design was used, the criterion being the psychiatrist's overall assessment. After 15 patients the superiority of the active drug reached significant levels. Relief of symptoms by propranolol was significant only for autonomic symptoms such as palpitations, sweating and diarrhoea. No significant drug effects were found for other physical symptoms, e.g. headache and tremulousness, or for mental symptoms such as worry, fear and irritability.

However, propranolol may have central effects as it is depressant in mice and it is uncertain whether this effect is mediated through beta-receptors.[361] Another blocking agent, I.N.P.E.A., is devoid of central effects yet it is also effective against autonomic symptoms of anxiety.[98]

A comparative trial of propranolol, 30 mg three times a day, and chlordiazepoxide, 10 mg three times a day, in the treatment of anxious patients in general practice has been carried out.[519] Propranolol was as effective as the benzodiazepine in the treatment of symptoms of anxiety but was less effective in combating depression and sleep disturbance.

In spite of studies such as those outlined above, surprisingly little interest has been shown in the use of beta-blocking agents in the treatment of anxiety. In our experience there are some patients with pronounced somatic complaints of anxiety who respond well to propranolol, up to 120 mg a day. If sedatives prove ineffective or if the symptoms are very specific, e.g., palpitations, propranolol should be tried. It should not be used in patients with cardiac failure or in asthmatics.

THERAPEUTIC REGIMES

From an overall view it appears that meprobamate is no more effective than the barbiturates and is probably less effective in the more severely anxious patients. The benzodiazepines, however, are rather more useful than the barbiturates for the treatment of anxiety states. Even in those controlled studies in which no statistically significant superiority for the benzodiazepines has been shown, the trend is usually in favour of the newer drugs.

The usefulness of any drug is a function of both its wanted and unwanted (main and side-) effects. In this respect the balance markedly favours the benzodiazepines. They are somewhat less likely to induce the commoner unwanted effects of sedatives such as drowsiness, a feeling of heaviness, and a sense of impaired mental functioning. However, the most decided advantage of the benzodiazepines is their safety

in overdosage. Death due to overdosage, intentional or accidental, has not been reported in any well-authenticated account. For example, in one extensive series of 121 cases, 55 overdoses were of chlordiazepoxide alone and the remainder in combination with other drugs, mainly barbiturates. The lowest total dosage of the benzodiazepine was 60 mg, the highest 1000 mg. In all cases of chlordiazepoxide poisoning alone, the patient could be wakened from sleep and all the symptoms disappeared within 24 hours except for two patients where they lasted for twice this period. No specific form of treatment was deemed necessary.[151]

Although the benzodiazepines have been in use for a relatively short period and evaluation must be tentative, it appears that they are much less likely than the barbiturates to induce states of physical and psychological dependence. However, such dependence can occur especially when high dosages have been used; withdrawal syndromes have been described.

On balance, on medical grounds, the benzodiazepines are a real advance on the barbiturates although they are by no means cure-alls for anxiety states. As is usual with newer drugs they are more expensive than barbiturates but not prohibitively so.

It is difficult to come to any firm decision regarding the relative effectiveness of the several benzodiazepines. Diazepam is probably the most useful in general, with chlordiazepoxide and oxazepam a little less effective. Barbiturates still have a place in the treatment of acute, severe anxiety states especially if admission to hospital has been necessary. The feelings of drowsiness are then less important than if the patient were still working or at home.

Whichever drug is administered, flexibility in prescribing is essential but far too infrequently attained in practice. Even with drugs with relatively long metabolic half-lives like diazepam, the increase in plasma levels (and hence cerebral levels) following a moderately large dose may be sufficient to induce feelings of drowsiness. Smaller doses given more frequently are always worth trying. For example, one of our patients (in a responsible position) experienced unacceptable drowsiness for about 45 minutes following each of the three 2 mg doses of diazepam initially prescribed. However, his symptoms were well controlled without any unwanted effects when the regimen was changed to 1 mg *six* times a day. Patients should be instructed to take their tablets after meals whenever possible as the ensuing plasma levels are lower and more uniform than if the drug is taken on an empty stomach.

Patients of average and superior intelligence are very able to judge for themselves their optimum dosage schedules providing they are seen frequently, say weekly, during this initial period of adjustment. Furthermore, they can often predict when a time of unusual stress is imminent and can increase their dosage accordingly. As mentioned above, the tendency for patients to spiral their dosage upwards is much less for the benzodiazepines than for the barbiturates.

Nevertheless, even with great flexibility in dosage resulting from resourcefulness on the part of both patient and physician, poor response to one sedative may result or unwanted effects be troublesome. There should be no hesitation in changing to another compound even of a similar nature, e.g. from diazepam to chlordiazepoxide. Why some patients respond adequately to one congener and less so to another has not been satisfactorily explained. However, many of these compounds have complex metabolic pathways with a range of clinically active metabolites. It is possible that an individual patient's particular enzymic pathways could lead to a more useful range of active metabolites from one compound than from a congener. Hence, different patients with different metabolic enzymic preponderances would respond differently to various drugs.

Chapter Six

THE MEASUREMENT OF ANXIETY

Many inventories and scales have been used to measure various aspects of psychological functioning including levels of anxiety. Rating scales and similar devices such as symptom inventories attempt to increase the precision with which psychopathology, abnormal behaviour and personality variables are recorded. Symptoms or aspects of personality can be evaluated more precisely than by global, general assessments so that sophisticated statistical techniques can be used in their development and analysis. High reliability is possible when the scale is expertly constructed and refined, and when it is used by properly trained personnel.

Many difficulties are encountered in producing a satisfactory rating scale.[303,528] Firstly, the conditions under which the rating is to be performed must be decided—whether the patient will merely be observed, or whether an interview with a psychiatrist, psychologist or social worker will be undertaken. An important consideration is whether the patient will rate *himself* for anxiety or whether outward signs of anxiety are to be rated by an *observer* such as a nurse or relative. The subject might rate only one scale or rate several denoting various aspects of anxiety such as muscular tension or subjective dread. The reliability of the scale must be established by determining inter-rater consistency, by test-retest correlations if appropriate, and by examining the uniformity between sub-scales of the instrument. The scale should be sensitive to changes in anxiety: here a distinction must be made between on the one hand scales which are primarily diagnostic instruments and insensitive to changes in severity of symptoms, and on the other scales which reflect changes in symptom severity but which do not yield diagnostic profiles.

The most important attribute of a rating scale is validity. Does the scale really "measure" anxiety? The establishment of validity is complex but the items in a scale should appear to be consistent, and certain key items should show close relationships. With self-ratings, recourse may be had to external validating criteria such as marked overt anxiety with tremor, hyperhidrosis, etc.; internal validating criteria such as the patient's verbal reports of "anxiety", "tension" and "nervousness" may be used with observer ratings. All depends on an impression of consistency between well-established indices of anxiety and the test instrument.

Other problems include the mechanics of scale-construction. A few intervals with anchoring points such as "absent", "mild", "moderate" and "severe" can be used or linear scales labelled only at the extremes may be utilised. Scales are most useful when they transcend cultural boundaries, i.e. they should be applicable to both semi-literate peasants and blasé, urban sophisticates.

There are particular problems with respect to anxiety scales. Firstly, instructions to the subject should indicate whether a given scale refers to "trait" or to "state" anxiety, i.e. whether one is interested in the subject's habitual mode of responding or feeling ("trait"), or in how he feels at that particular moment ("state"). Secondly, the scale may be designed to assess anxiety as one symptom among many occurring in any particular psychiatric illness or as the particular syndrome of the anxiety state. Finally, "free-floating" anxiety should be distinguished from "phobic" anxiety and assessed separately.

Inventories are one of the most used means of assessing facets of anxiety and related areas of clinical and personality function. To some extent inventories can be regarded as verbal surrogates for behaviour samples. Most are self-report questionnaires, scales or card sorts. In a typical inventory the subject answers a list of up to 500 questions with a simple "yes" or "no" or sometimes "I cannot say". It is obvious that the utility of an inventory depends on its constituent statements. These items are chosen intuitively for their relevance to personality or clinical problems. After empirical testing, the most useful items are winnowed from the large initial number of statements.

In this chapter some of the more commonly used instruments for the assessment of anxiety as a personality trait, as a symptom, and as a syndrome will be described.

The Minnesota Multiphasic Personality Inventory[87,186]

The Minnesota Multiphasic Personality Inventory (MMPI) is probably the most widely used of all inventories, especially in North America. It was originally developed as a clinical instrument to measure the characteristic traits of disabling psychological disorders. It consists of 550 statements which the patient answers "true" or "false". The statements are presented either on individual cards or listed on forms. The statements cover many areas from physical health to neurological disorders and political and social attitudes. Two examples of statements are "I believe I am being plotted against" and "I am worried about sex matters".

The 550 statements fall into nine groups, some of which are clinical, e.g. "depression", "hysteria", "schizophrenia" and "paranoid", and some of which are personality factors, e.g. "ego strength". There are also four groups of items which check for carelessness, malingering and similar problems. Each group of items has been worked out empirically

on groups of patients diagnosed as depressive, hysteric, paranoid, etc., and the scores on these items are also known for control populations. The test results are plotted as a profile which can be compared with that obtained in normal people and with different types of patients (see fig. 6.1). Computerised methods of analysis have been developed.[507]

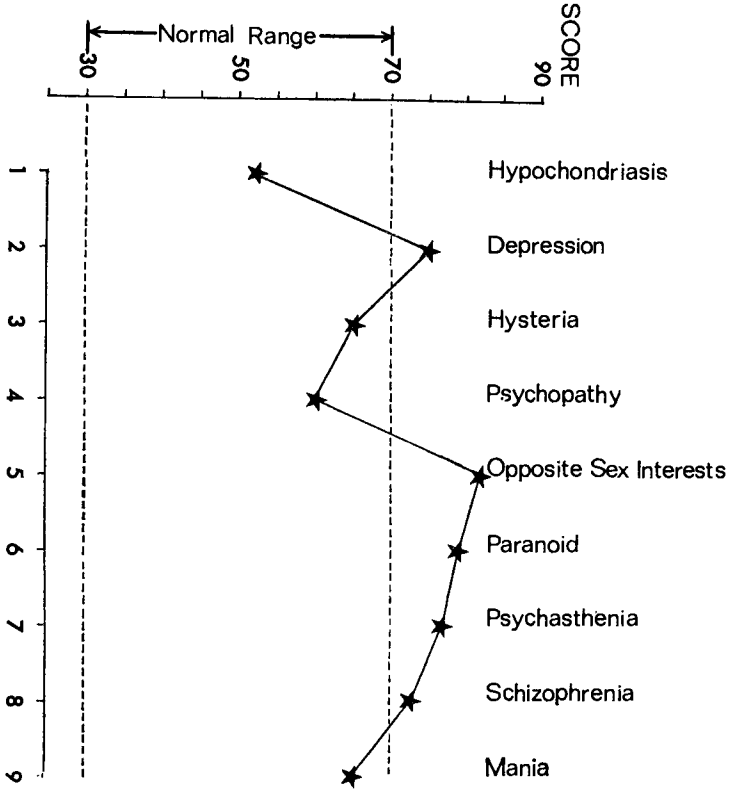


Fig. 6.1: MMPI profile of a patient suffering from an anxiety state with social phobias.

The disadvantages of the MMPI are that it is cumbersome and time-consuming, and that the original grouping of items was made intuitively and may not reflect the most natural groups which occur in practice. Moreover, the MMPI does not assess personality function within the normal range of adjustment; and it is illogical to use psychiatric patients as criterion groups for normal personality dimensions. It is also unsatisfactory to mix together clinical groups like "depression" with personality factors such as "ego strength". However, the MMPI is widely used clinically as a legitimate aid to diagnosis rather than as

an estimate of personality traits; the profile changes, if any, in a patient after a given treatment may also be followed.[48]

The MMPI has been used in attempts to predict breakdown under stress. For example, simple dichotomy of MMPI profiles into normal and abnormal was carried out in one study on 516 Air Force officers going into active service flying duties: 97 profiles were abnormal.[219] On follow-up, 5·3 per cent of the total 516 had developed psychiatric symptoms (usually chronic anxiety) of such severity that they had been withdrawn from flying duties. A higher proportion, 14·4 per cent, of the 97 aircrew with previously abnormal MMPI scores had succumbed. This is still a fairly low proportion, so the abnormal MMPI could not have been used as a screening procedure without much needless wastage of aircrew.

In view of the generally accepted importance of anxiety both in clinical practice and as a personality variable, it is surprising that there is no single MMPI scale to assess anxiety. From a consideration of profile configurations of anxiety patients Welsh[513] developed an anxiety index, AI:

$$AI = \frac{(Hs + D + Hy)}{3} + ((D + Pt) - (Hs - Hy)),$$ where Hs is the Hostility (Paranoid) score; D, Depression, Hy, Hysteria; and Pt, Psychasthenia. This weighted combination of four scales has been found to relate only moderately to clinical anxiety[281,481] and also to correlate closely with the Pt scale itself. Very little further development of this index has occurred. Welsh[513] also asked 10 clinicians to pick out of the MMPI pool of items those which were related to anxiety. Thirty-one items were selected to form an anxiety scale which correlated very highly with the AI. However, this scale, although developed in a similar way to the Taylor scale described in the next section, has hardly been used.

The Taylor Manifest Anxiety Scale[486]

This is the most widely used of all the self-report scales of trait anxiety. In the late 1950s a flood of articles appeared in which the MAS was used. In some universities in the U.S.A. enrolment as a psychology student seemed to be followed inexorably by the administration of this test; if one happened to fall into an extreme group, usually the upper and lower ten percentiles, a whole range of tests—cognitive, psychomotor, conditioning—would follow. Several hundred papers have been published in which the Taylor Scale was the main or sole measure of anxiety. It is therefore essential to examine in some detail its premises, conceptual basis, content and drawbacks.

The Scale arose out of the need to test ideas about anxiety as a drive state (p. 112). Janet Taylor, working in Spence's laboratory, was concerned to develop a pencil and paper test which would distinguish

habitually anxious from habitually calm subjects. To quote from Janet Taylor Spence and Kenneth W. Spence:[458]

> "The rationale underlying the development of the scale was based, first, on the experimental evidence . . . concerning acquired fear or anxiety which provides firm support for the hypothesis that conditioned anxiety-provoking stimuli evoke internal emotional responses which, in turn, increase drive level. Second, it was based on the observation that many of the symptoms exhibited or reported by individuals diagnosed clinically as suffering from anxiety reactions are similar to the overt behaviors elicited by the conditioned, as well as the unconditioned, stimulus in experimental studies of acquired fear. Thus it seemed reasonable to assume that acquired anxiety or fear as it is described by the experimentalist had properties in common with overtly observable or manifest anxiety as it is described by the clinical psychologist or psychiatrist. In order to obtain a convenient and objective device for rating subjects, a series of items judged by clinical psychologists to describe both the physiological reactions reported by individuals suffering from anxiety reactions and the accompanying subjective reports of worry, self-doubt, anxiety, etc., were chosen from the Minnesota Multiphasic Inventory (MMPI) to form the Manifest Anxiety Scale . . ."

The theoretical bases of the scale are less important than the practical assembling of its constituent items. In practice, *clinical* psychologists were asked to select items from the MMPI to describe physiological and psychological aspects of anxiety. The MMPI is a *personality* inventory so that the items refer to habitual modes of response (i.e., traits) rather than to the state at the time of the subject's reporting. Many items selected were not even specific to anxiety but referred to emotionality in general, e.g. "I am a high-strung person", "I cry easily". Others are very general physical statements, e.g. "I feel hungry almost all the time", "I do not tire quickly".

The original Taylor MAS consisted of 50 items (together with 175 buffer items) to make up the scale as it is most generally used in adults. The 50 questions are shown in Table 6.1. A short form with 20 items has also been described[28] and a children's version has been developed.[64] Factor analysis of the adult form administered to 220 students revealed no single common factor but 5 individual factors.[369] They were: A—self-consciousness, lack of self-confidence, constant worrying; B—fear of blushing, cold hands, sweating; C—loss of sleep, worry, feeling of insurmountable inadequacy; E—restlessness, motor tension, heart pounding, out of breath. The complex nature of these factors suggests that in normal subjects the Scale is sampling several interrelated but nonetheless distinct variables.

Table 6.1

Taylor MAS questionnaire (modified)

(Completed for maximum anxiety score)

We want to know whether you would agree or disagree with the following statements. Please answer each statement by putting a circle around the "TRUE" or the "FALSE" following the statement. Work quickly and do not ponder too long about the exact shade of meaning of each sentence. Put a circle around the "?" only if you find it impossible to decide whether you agree or disagree with the statement. There are no right or wrong answers, and no trick questions. *Please remember to answer all the questions.*

1.	I do not tire quickly	**True**	?	**False**
2.	I often feel sick	**True**	?	False
3.	I am about as nervous as other people	True	?	**False**
4.	I have very few headaches	True	?	**False**
5.	I work under a great deal of strain	**True**	?	False
6.	I cannot keep my mind on one thing	**True**	?	False
7.	I worry over money and business	**True**	?	False
8.	I frequently notice my hand shakes when I try to do something	**True**	?	False
9.	I blush more than others	**True**	?	False
10.	I have diarrhoea ("the runs") once a month or more	**True**	?	False
11.	I worry quite a bit over possible troubles	**True**	?	False
12.	I practically never blush	True	?	**False**
13.	I am often afraid that I am going to blush	**True**	?	False
14.	I have nightmares every few nights	**True**	?	False
15.	My hands and feet are usually warm enough	True	?	**False**
16.	I sweat very easily even on cool days	**True**	?	False
17.	When embarrassed I often break out in a sweat which is very annoying	**True**	?	False
18.	I do not often notice my heart pounding and I am seldom short of breath	True	?	**False**
19.	I feel hungry almost all the time	**True**	?	False
20.	Often my bowels don't move for several days at a time	**True**	?	False
21.	I have a great deal of stomach trouble	**True**	?	False
22.	At times I lose sleep over worry	**True**	?	False
23.	My sleep is restless and disturbed	**True**	?	False
24.	I often dream about things I don't like to tell other people	**True**	?	False
25.	I am easily embarrassed	**True**	?	False
26.	My feelings are hurt easier than most people	**True**	?	False
27.	I often find myself worrying about something	**True**	?	False
28.	I wish I could be as happy as others	**True**	?	False
29.	I am usually calm and not easily upset	True	?	**False**
30.	I cry easily	**True**	?	False
31.	I feel anxious about something or someone almost all of the time	**True**	?	False
32.	I am happy most of the time	True	?	**False**
33.	It makes me nervous to have to wait	**True**	?	False
34.	At times I am so restless that I cannot sit in a chair for very long	**True**	?	False
35.	Sometimes I become so excited that I find it hard to get to sleep	**True**	?	False
36.	I have often felt that I faced so many difficulties I could not overcome them	**True**	?	False

37.	At times I have been worried beyond reason about something that really did not matter	**True**	?	False
38.	I do not have as many fears as my friends	True	?	**False**
39.	I have been afraid of things or people that I know could not hurt me	**True**	?	False
40.	I certainly feel useless at times	**True**	?	False
41.	I find it hard to keep my mind on a task or job	**True**	?	False
42.	I am more self-conscious than most people	**True**	?	False
43.	I am the kind of person who takes things hard	**True**	?	False
44.	I am a very nervous person	**True**	?	False
45.	Life is often a strain for me	**True**	?	False
46.	At times I think I am no good at all	**True**	?	False
47.	I am not at all confident of myself	**True**	?	False
48.	At times I feel that I am going to crack up	**True**	?	False
49.	I don't like to face a difficulty or make an important decision	**True**	?	False
50.	I am very confident of myself	True	?	**False**

Many criticisms have been levelled at the Taylor MAS as a measure of anxiety.[234] Brackbill and Little[44] found a correlation of 0·81 between the MAS and the Psychasthenia Scale of the MMPI in a large sample of college students and a correlation of 0·92 in 106 male neuropsychiatric patients: the value of a separate anxiety scale is thus questionable. Furthermore, although the scale can select groups of subjects who will also differ with respect to some other psychological factor such as "conditionability" (i.e. the scale has "concurrent validity"), it is poor at discriminating between groups of subjects selected independently for differing levels of trait or state anxiety ("criterion validity").

Several attempts have been made to validate the MAS. A correlation of 0·34 ($p < 0·01$) was found between MAS scores and psychiatrists' ratings of overt anxiety in 90 psychiatric patients; patients with anxiety states had significantly higher scores than other subgroups.[451] A mean correlation of 0·83 was reported between global ratings for clinical anxiety of 64 neuropsychiatric patients. The ratings were made independently by four psychologists who all observed the patients in the same interview. The correlation with the MAS was 0·60; the correlation between the MAS and reports of physiological concomitants of anxiety was only a little higher, +0·68.[58] Similarly Lauterbach[281] described a significant correlation of 0·44 between MAS scores and psychologists' ratings in 44 male patients of mixed diagnoses. In another study, no difference in mean MAS scores was found between patients with anxiety states and non-anxious patients so that the authors concluded that it was premature to assume that anxiety was being measured.[342] In both this study and that of Sampson and Bindra,[422] significantly higher scores were obtained from mixed psychiatric patient groups than from normal subjects. In the latter study and in that of Rubin and Townsend[413] anxious patients were not discriminated from non-anxious neurotic patients. In 93 patients with tuberculosis who were rated for manifest

anxiety by two nurses, no significant difference in MAS scores was found between patients in the upper and lower anxiety rating groups.[243] An item analysis by Buss[57] showed that only 14 items in the MAS discriminated significantly between patients rated high on anxiety by four clinical psychologists and those rated low.

From these and many similar studies, certain conclusions can be drawn. It is unlikely that the MAS simply samples manifest anxiety in the subject. Because of its high correlation with certain scales of emotionality or neuroticism (e.g. the N-scale of the Eysenck Personality Inventory), it is probable that it assesses a more general tendency to respond emotionally. The scale assesses the subject's awareness of, estimate of, and willingness to report emotional feelings and especially their physiological concomitants. It estimates habitual response rather than feelings at the time of completion of the scale, and general emotional responsiveness rather than specific anxiety-proneness.[426]

Noteworthy about the scale is its widespread acceptance and usage. Cautiously introduced by Taylor before it had been properly validated, it rapidly became popular and was used as the basis for a wide range of studies on anxiety. It gave the appearance of a simple test which separated out groups of subjects with different psychological performance capabilities. Its long usage should not be allowed to obscure the fact that it is an imperfect instrument which is poorly validated and with the construct it purports to measure diffusely defined. The Manifest Anxiety Scale is not a good measure of manifest state anxiety and better scales, such as the Hamilton Anxiety Scale, are available for this purpose.

The 16 Personality Factor Questionnaire[67,69]

This was developed by Cattell at the Institute for Personality and Aptitude Testing and is sometimes called the IPAT Scale.

Cattell's approach has been essentially that of the factor analyst manipulating data.[66] Several hundred measures on large samples of normal subjects have been amassed. The measures were derived from each of three possible media of personality observation—*L-data* (essentially life-history behaviour ratings), *Q-data* (questionnaire and interview information) and *T-data* (objective, laboratory test variables). By factor-analytic techniques, the Q-data were found to contain a factor labelled "QII" which appeared to be related to anxiety. Similarly, T-data were found to yield a clear anxiety factor, indexed as UI24. Next, over 250 subjects underwent tests lasting 5 to 6 hours in order to gather Q-data and T-data simultaneously. The new QII and UI24 factors were found to align very closely suggesting that anxiety was an unitary entity with respect to questionnaire and test variables.

Cattell has adduced evidence that the factors which he has identified are trait factors and not state factors. Obviously, a single estimation

in an individual of an anxiety factor could not distinguish between the two. However, repeated estimations over 2 weeks to 3 years have yielded factors stable enough to suggest that a trait is involved.

The basic work on personality has been extended to the clinical field with interesting findings. Neurotics, defined by psychiatric examination, were found to differ greatly from normals with respect to many factors but UI24, the anxiety factor, was not a good discriminator. This suggests that if one groups all neurotic syndromes together neurotics are not primarily distinguished by high anxiety levels. A scale of neuroticism constructed to distinguish neurotics from normals correlated at only modest levels with the anxiety scale. Cattell[67] remarked that these findings "support those who have criticised such anxiety scales as that of Taylor . . . for defining good anxiety items as those which maximally distinguish neurotics from normals".

Although Cattell's criticism of the Taylor scale is valid, his own work too has an important weakness in that all "neurotics" are grouped together as though they formed a unitary syndrome group. However, there is much evidence to the contrary (see p. 108).

Sub-tests of the complete instrument, the 16 PF questionnaire,[68] have been formed into an instrument for the assessment of trait anxiety, the IPAT Anxiety Scale.[65]

The MPI (Maudsley Personality Inventory) and EPI (Eysenck Personality Inventory)[120,123]

The MPI was one of the most widely used inventories in Britain and has been revised and renamed the EPI. There are two alternative forms of 48 questions and each question has to be answered "yes" or "no". These questions were selected from 250 questions after an analysis of answers in terms of extraversion and neuroticism scores. It is claimed that these represent fundamental dimensions of personality but in fact these two dimensions can be broken down into further categories depending upon the method of analysis employed.[124] The range of scores is known for groups of normal subjects and for patients with certain abnormalities. The scores remain reasonably stable from one occasion to the next and the test is easy to give and score. Some of the questions relating to the neuroticism questions are listed in Table 6.2.

The MPI has been helpful in following changes in some patients. It is dubious, however, whether the N score is superior for this purpose to similar instruments like the Cornell Medical Index or the Taylor Manifest Anxiety scale, with which the N score correlates highly, or whether the E score is more valuable than other measures of sociability.

An example of a study in which the MPI has been useful comes from Levinson and Meyer[288] who studied the changes in two groups of neurotic patients after modified leucotomy. Fig. 6.2 shows the change in scores before and after leucotomy. After operation the patients became

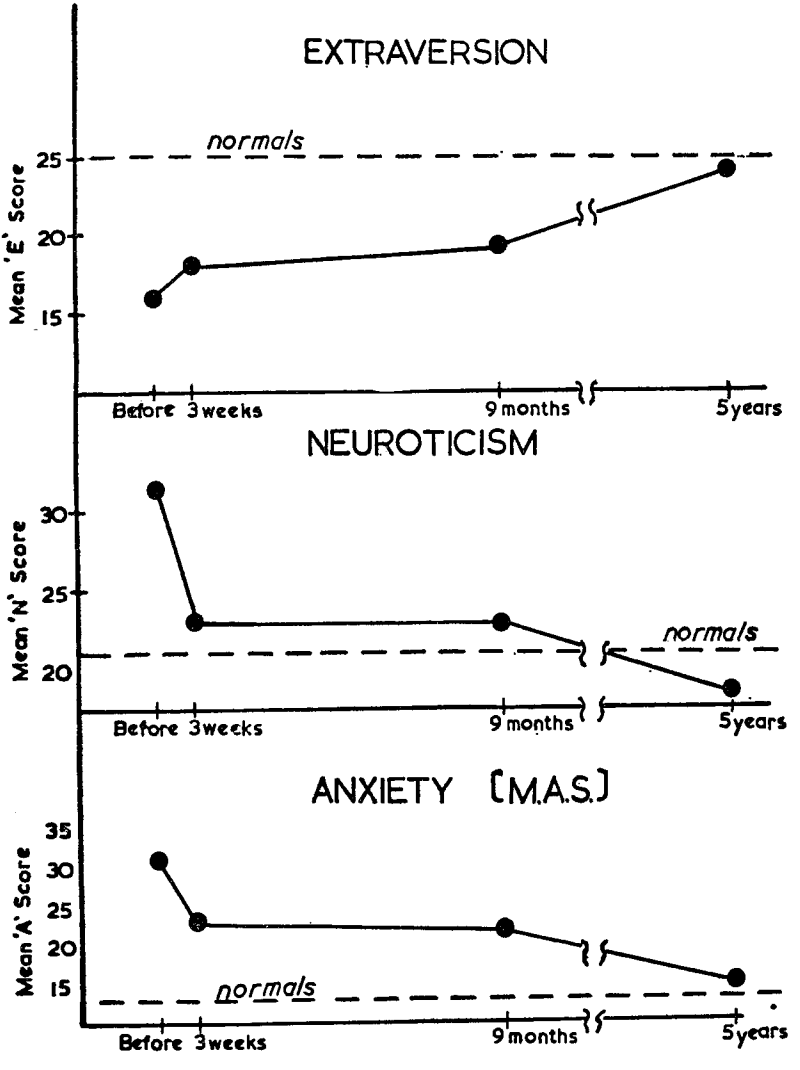


Fig. 6.2: Effect of leucotomy in 207 patients. Note change in scores of "extraversion" and "neuroticism" on the Maudsley Personality Inventory and in scores on the Taylor Manifest Anxiety Scale (based on data of Levinson and Meyer).[288] (Reproduced from [329a] by kind permission of the editor of the Postgraduate Medical Journal.)

Table 6.2

Selected questions from the Eysenck Personality Inventory

(Reproduced from [123] by kind permission of the authors and the University of London Press)

14. Do you often worry about things you should not have done or said?
16. Are your feelings rather easily hurt?
26. Would you call yourself tense or "highly-strung"?
33. Do you get palpitations or thumping in your heart?
35. Do you get attacks of shaking or trembling?
38. Are you an irritable person?
40. Do you worry about awful things that might happen?
45. Are you troubled by aches and pains?
47. Would you call yourself a nervous person?
57. Do you suffer from sleeplessness?

more "extroverted" (i.e. sociable) and less "neurotic" (i.e. had few complaints), and this change corresponded with the overall condition assessed clinically. It is noteworthy that the change in the Taylor scale (marked "Anxiety" MAS) runs parallel to that in the N score.

The MPI has also been useful in showing how the partners in a marriage come to resemble one another more as the years go by[255] and in studying psychiatric morbidity in a new town.[180]

Eysenck and coworkers have produced a vast amount of research based on his inventory to relate anxiety and personality. He did not divide individuals into groups or personality types, but instead arrayed them along the two continua of extroversion and neuroticism. These two dimensions originated out of his studies of psychiatric patients but were later validated in normal subjects. In the latter, judges nominated individuals as highly extroverted or highly introverted, and as stable or emotionally labile. These judgments were shown to agree very well with the subject's scores on extroversion and neuroticism.

Eysenck found that patients with anxiety states scored highly on neuroticism and introversion and he classified them, together with obsessive-compulsives and reactive depressives, as "dysthymics". Hysterics and psychopaths were regarded as high on neuroticism and high on extroversion. Eysenck's dimensions were more global than those of Cattell, and he made bold predictions relating E and N with cortical excitation and inhibition.

One obvious criticism of this approach is that it only explains one unknown (personality structure) in terms of another (cortical activity) and the latter represents Pavlovian neuromythology rather than contemporary neurophysiology.

In a more recent theoretical exposition, Eysenck[121] attempted to place his personality hypotheses onto a more firm biological footing by adducing evidence from many sources, genetical, psychophysiological, and endocrinological. However, the hypotheses have not been adequately validated.

One of the most cogent criticisms of Eysenck's bi-dimensional theory for normal personality function is that it was originally derived from psychiatric patients who were vaguely labelled as "neurotic" or "psychotic". The use of such criterion groups is highly suspect as they are inevitably heterogeneous; furthermore, the assumption that hysterics are extreme extroverts and that "dysthymics" are extreme introverts is unsupported by more than anecdotal evidence, the personality of psychiatric patients can be distorted by their illness, and there is no firm evidence that pre-morbid personality is related to the illness contracted. Indeed, in one series of 20 anxious patients studied by Lader and Wing,[273] only 50 per cent had introverted pre-morbid personalities. A repeated finding has been that hysterics are no more extroverted than normals.[209] One must conclude that Eysenck was misled by the over-simplifications of clinical observers from Galen to Kretschmer and Jung.

Adcock[5] has compared the concepts of Cattell and Eysenck; he equates Cattell's Anxiety factor with Eysenck's neuroticism or emotional reactivity.

The State-Trait Anxiety Inventory[469]

This is a brief self-report measure of both state and trait anxiety. The "A-state scale" consists of 20 statements that pertain to the subject's feelings at a particular moment in time. Half the statements concern apprehension, worry or tension, while the rest concern the absence of such feelings (e.g. "I feel calm", "I feel content"). Subjects rate each statement (e.g. "I feel tense") on a 4 point scale ("not at all" to "very much so"). The "A-trait scale" comprises 20 statements which refer to how the subjects generally feel. Each statement (e.g. "I lack self-confidence") is rated on a 4 point scale from "almost never" to "almost always".

Scores on the "A-state scale" increase in response to stress, decrease after relaxation training and correlate with scores on the Zuckerman MAACL "Today" Form (see below).[471]

Assimilation Scales[2,314]

These scales form an inventory which list a number of topics which "a person may at times feel *unsettled* about". These are rated on a 4 point scale. Scores on this instrument showed a correlation of 0·32 with clinical ratings of anxiety and 0·52 with the MAS.

Freeman Manifest Anxiety Test[134]

This is structured like an attitude inventory. It is made up of general statements to agree or disagree with, e.g. "Looking down from a high building is usually frightening". Some of the items have to be scored "yes" or "no", others are multiple choice items or "forced-choice pairs".

S-R Inventory of Anxiousness[114]

In this inventory to measure anxiety proneness there are descriptions of 11 anxiety-provoking situations. Subjects indicate on a 5-point scale the intensity with which they experience each of the 14 response tendencies in the 11 basic situations. Questions in the inventory are designed for college students. It is time consuming and a shorter form was suggested by Perkins.[377]

Activity Preference Questionnaire[308]

This is said to be a measure of anxiety-proneness which is relatively difficult for the subject to fake and which does not have the preponderance of the psychiatric or somatic symptom items of many other inventories. A set was drawn up of brief descriptions of experiences or events which most people would regard as unpleasant: some were frightening or embarrassing (e.g. "making a parachute jump", "finding you've forgotten your billfold after eating dinner in a restaurant"); others were onerous but not frightening (e.g. "having to walk 5 miles along a highway for gas", "spending an evening with some boring people"). Test items were constructed by pairing a frightening with an onerous experience having the same average unpleasantness. The subject has to choose which of each pair of alternatives was the lesser evil. The "anxiety" score was the number of endorsements of the non-frightening (onerous) alterative.

The questionnaire score is reliable but it is not clear what it is measuring. It has little correlation with the MAS, Welsh's Anxiety Index or the anxiety factor of the IPAT Scales, and but a low correlation with the S-R Inventory. Patients with depression, anxiety states, and acute schizophrenia had high scores on this measure.

Multiple Affect Adjective Check List (MAACL)

Zuckerman et al.[541] developed a multiple adjective check list for the assessment of affective states (MAACL). The subject checks only those items that describe how he feels rather than indicating the intensity of specific feelings. Three affective dimensions are covered—anxiety, hostility and depression. Of the 132 adjectives that comprise the MAACL, 21 adjectives can be scored on the anxiety key, 28 on the hostility key and 40 on the depression key. The remaining items serve as buffer items from which additional scales may be eventually derived. "State anxiety" is measured when the subject responds as he feels "today", and "trait anxiety" when he responds according to how he feels "generally".

FEAR SURVEY SCHEDULES

These inventories list different situations which people rate for the amount of fear they experience when confronted by those situations,

e.g. dogs, buses, thunderstorms. The schedule thus measures phobic anxiety, and scores of particular items can be used in the same way as the clinical phobia scale (p. 96). When many situations are listed the total score is a measure of anxiety proneness in general.

Several studies of fear survey schedules report significant correlations between total scores on the schedules and other measures of "anxiety" such as the Taylor Manifest Anxiety Scale, the neuroticism score of the Eysenck Personality Inventory, the emotionality scale of Bendig's inventory and Welsh's anxiety scale.[144,168,178,277] Manosevitz and Lanyon[328] failed to find a significant relationship in men between fear survey schedule scores and the Taylor Manifest Anxiety Scale. Though several groupings of fears have been suggested, on the whole the range of fears covered in survey schedules so far is too small and the relationship of the fears to other phenomena too ill-defined to allow of meaningful conclusions from these groupings.

Hall was probably the first to survey fears in a normal population.[172] Few studies of fears in adults appeared subsequently until the last decade, since when many surveys have been made. In 1956 Akutagawa constructed a reliable fear inventory which formed the basis for many later studies.[144,168,178,277,328,415,524,531] Marks and Herst[334] constructed yet another fear inventory to assess the fears present in a phobic population and this has also been used by Julier.[224] A fear inventory for children was reported by Scherer and Nakamura.[437] Yet other inventories exist to screen for problems like stage-fright,[373] examination anxiety[9,113,326,430] and stress during simulated combat.[244]

Another measure of fear is avoidance behaviour, and many simple situations have been devised to measure particular forms of avoidance, e.g. of snakes[277] or of dogs.[403,404] Most fear survey schedules measure self-reports of fear without relating these to actual avoidance of the frightening situations. The relationship between such self-reports and avoidance behaviour was studied by Geer[144] who found that the more women reported fear, the more they avoided dogs; men showed no avoidance of dogs even when they reported intense fear. Lanyon and Manosevitz[279a] also noted that women's self-reports of fear of spiders correlated significantly with subsequent avoidance of spiders in a test situation. They concluded that self-reports of fear are valid, if gross, indicators of fear in an actual situation. Further observations relating the self-reports of snake phobias to their avoidance behaviour are described by Lang.[276]

CLINICAL RATING SCALES

For the measurement of states of clinical anxiety very simple line scales have proved to be reliable and useful indices and predictors of clinical change. Some of the scales used have had 5 points, but more points are permissible. Such scales were devised by Miles et al.[352] and Hamburg

et al.,[173] the former being modified by Gelder and Marks.[146] These scales can be constructed to measure any particular aspect of anxiety in which one is interested, e.g. phobic (situational) anxiety, general (free-floating, non-situational) anxiety, phasic acute attacks of panic, and so on.[146,504] Examples are given in Tables 6.3 to 6.6. Reliability between observers and between observers and patients varies from 0·82 to 0·97 for the phobia scale and from 0·56 to 0·94 for the general anxiety scale in various studies.[146,348] Changes in the phobia scales were excellent indicators of clinical change while ratings of general anxiety and panic attacks at start of treatment were good predictors of clinical and physiological changes during treatment.[147,268,332]

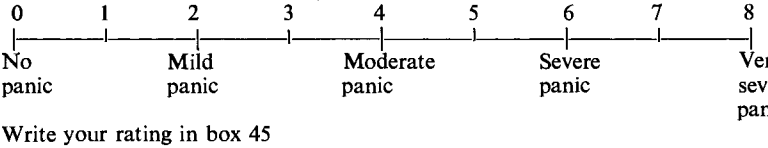
For clinical purposes such simple scales are at least as useful as more complicated inventories like the EPI, Cornell or Tavistock Inventory. They are also much quicker to use and easier to score, so that for clinical assessment of state anxiety they are still greatly preferable to any inventories or questionnaires so far devised. Furthermore, they can be used to assess anxiety in any context such as a depressive or schizophrenic illness or in normal subjects in an anxiety-provoking situation.

Table 6.3

Free floating panic scale for observer rating

Panic

Rate the attacks of panic, anxiety or palpitations which the patient has had for no obvious reason during the previous 3 days. Rater take note of frequency, intensity and duration. (Do NOT include persistent background tension, or specific phobias.)



Write your rating in box 45

Box 45

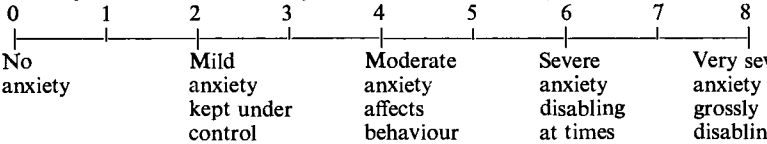
Table 6.4

Free floating anxiety scale for observer rating

Anxious mood

Rater—take note of persistent anxious mood, subjective tension, physical manifestations, poor concentration and motor restlessness.

Base your assessment on the patient's state during the previous 3 days.



Write your rating in box 48

Box 48

Table 6.5

Free floating panic scale for patient rating

Have you suffered from *acute attacks* of panic, anxiety, or palpitations for no obvious reason during the past 3 days? (Do NOT include persistent background tension or your specific phobias.)

Use this scale

0	1	2	3	4	5	6	7	8
Not at all		A little: mild panic, or a few attacks		To some extent: moderate panic, several attacks		Markedly: severe panic, or frequent attacks		Very much indeed: very severe panic, or very frequent attacks

Please write your rating in box 46

Box 46

Table 6.6

Free floating anxiety scale for patient rating

Have you suffered from sweating, trembling, palpitations or breathlessness during the past 3 days? If so, how severe and persistent have these symptoms been?

Use this scale

0	1	2	3	4	5	6	7	8
I have not suffered from these symptoms		Mild symptoms which occurred occasionally		Moderately severe symptoms, often pressnt		Severe symptoms, frequently present		Very severe symptoms, hardly ever absent

Please write your rating in box 49

Box 49

Lader and Wing[273] have also used simple linear scales in the assessment of anxiety symptoms. The patient was asked to describe his symptoms *in his own words*, e.g. "thumping of the heart", "feeling something bad will happen", etc. These symptoms were entered alongside a horizontal 100 mm line (Table 6.7), and the subject was instructed to rate his symptom from "absent" at one end of the line to "very severe" at the other. The rating was for the appropriate time interval, e.g. over the past week, past day or at the present time. The line can be measured to the nearest millimeter; the arcsin transformation may be appropriate to normalise the data.[6] The scales of Lader and Wing[273] differed from those of Gelder and Marks[146] only in the omission of intermediate anchoring points. Such scales are very easy for the patient to understand and have proved sensitive to drug effects.[273] The individual patient's symptoms can be fairly easily categorised into one of the groupings used by Hamilton (see below) or into one of four main groupings—somatic symptoms, psychological symptoms, phobic symptoms and depression.

Table 6.7

PATIENT RECORD FORM

Patient No.	C/14
Name	XXXX
Week No.	3

TO BE FILLED IN ON 24th March, 1971

On the day stated above, please complete this form in the evening before going to bed. Having completed it, please place it in the envelope provided. Do not compare notes with anyone else. Post the envelope the next morning.

Underneath, you will find a list of symptoms with a line beside each. At one end of the line is written "Very Severe"; in the middle—"Moderate", and at the other end—"Absent". Show how much each symptom has troubled you during the day which has just passed by putting a mark in the appropriate place on the corresponding line, e.g. if the symptom has been very severe, put a mark at the right-hand end; if it has troubled you only a little, put a mark somewhere towards the left, and so on. Do this for each symptom in the list and then put the form away in the envelope.

SYMPTOMS

Muscular tension	ABSENT	MODERATE	VERY SEVERE
Concentration	ABSENT	MODERATE	VERY SEVERE
Head congestion	ABSENT	MODERATE	VERY SEVERE
Heart beating	ABSENT	MODERATE	VERY SEVERE
Loss of appetite	ABSENT	MODERATE	VERY SEVERE
Insomnia	ABSENT	MODERATE	VERY SEVERE
	ABSENT	MODERATE	VERY SEVERE
	ABSENT	MODERATE	VERY SEVERE

Hamilton Anxiety Scale[176]

This scale "is intended for use with patients already diagnosed as suffering from neurotic anxiety states, not for assessing anxiety in patients suffering from other disorders".[176] Twelve groups of symptoms are used, culled from clinical experience, and together with the patient's behaviour at interview make up the 13 variables of the scale. The symptom headings are shown in Table 6.9. Each of the variables is defined in a series of brief statements to which the interviewer refers.

Table 6.8

Example of completed modified Hamilton Rating Scale of Anxiety
The ticks show which symptoms were present.

NAME: XXX
NO: C/14/3
DOCTOR: MHL
DATE: 21st March 1971

Item No.	Symptom		
1.	*Anxious mood* √Worries √Anticipation of the worst Apprehension (fearful anticipation) Irritability	absent	very severe
2.	*Tension* Feelings of tension √Fatiguability √Inability to relax Startle response Moved to tears easily Trembling √Feelings of restlessness	absent	very severe
3.	*Fears* Of Dark Strangers √Being left alone Large animals, etc. √Traffic Crowds	absent	very severe
4.	*Insomnia* √Difficulty in falling asleep √Broken sleep Unsatisfying sleep and fatigue on waking Dreams Nightmares Night terrors	absent	very severe

Table 6.8—*continued*

Item No.	Symptom		
5.	*Intellectual (cognitive)* Difficulty in concentration √Poor memory	absent	very severe
6.	*Depressed mood* √Loss of interest Lack of pleasure in hobbies Depression Early waking Diurnal swing	absent	very severe
7.	*General somatic (muscular)* Muscular pains and aches Muscular stiffness Muscular twitchings Clonic jerks Grinding of teeth Unsteady voice	absent	very severe
8.	*General somatic (sensory)* Tinnitus Blurring of vision √Hot and cold flushes Feelings of weakness Pricking sensations	absent	very severe
9.	*Cardiovascular symptoms* √Tachycardia √Palpitations Pain in chest √Throbbing of vessels √Fainting feelings Missing beat	absent	very severe
10.	*Respiratory symptoms* Pressure or constriction in chest √Choking feelings √Sighings Dyspnoea	absent	very severe
11.	*Gastro-intestinal symptoms* Difficulty in swallowing Wind Dyspepsia: pain before and after meals burning sensations fullness	absent	very severe

Table 6.8—*continued*

Item No.	Symptom	
11.	*Gastro-intestinal symptoms—cont.*	
	waterbrash	
	nausea	
	vomiting	
	sinking feelings	
	Borborygmi	
	"Working" in abdomen	
	Looseness of bowels	
	Loss of weight	
	Constipation	
12.	*Genito-urinary symptoms*	absent very severe
	Frequency of micturition	
	Urgency of micturition	
	Amenorrhea	
	Menorrhagia	
	Development of frigidity	
	Ejaculatio praecox	
	Loss of erection	
	Impotence	
13.	*Autonomic symptoms*	absent very severe
	√Dry mouth	
	√Flushing	
	√Pallor	
	√Tendency to sweat	
	Giddiness	
	√Tension headache	
	Raising of hair	
14.	*Behaviour at interview*	absent very severe
	√Tense, not relaxed	
	√Fidgeting & restlessness:	
	hands	
	√picking fingers	
15.	*Behaviour physiological*	absent very severe
	√Tremor of hands	
	√Furrowed brow	
	Strained face	
	Facial pallor	
	√Swallowing	
	Belching	
	√Sweating	
	Eye-lid twitching	

Additional comments:

Assessments of each variable are made on a five-point scale: 0, none; 1, mild; 2, moderate; 3, severe; 4, very severe, grossly disabling.

The ratings of the 13 variables for the first group of patients studied were correlated and factor-analysed. Two main factors were apparent (Table 6.9): first, there was a general factor of anxiety; secondly, a bipolar factor of psychic symptoms as opposed to somatic symptoms emerged. This pattern has been confirmed more recently using data from a further 115 patients.[177]

The Hamilton Scale is very useful for rating patients with anxiety states and can be used by psychiatrists or clinical psychologists. Adequate training and standardisation of raters is essential. A refinement which one of us (M.H.L.) has found worthwhile is to rate the patients along a 100 mm linear scale instead of into one of five categories. This increases the flexibility and precision of the assessment. An example of this modified scale is given in Table 6.8.

Table 6.9

Saturations for factors from Hamilton Scale

	General factor	*Bipolar factor*
Anxious mood	0·43	0·75
Tension	0·60	0·26
Fears	0·29	0·37
Insomnia	0·79	0·32
Intellectual (cognitive)	0·56	0·07
Depressed mood	0·38	0·52
Somatic symptoms	0·48	−0·31
Cardiovascular symptoms	0·34	−0·62
Respiratory symptoms	0·31	−0·54
Gastro-intestinal symptoms	0·41	0·00
Genito-urinary symptoms	0·43	−0·34
Autonomic symptoms	0·56	−0·10
Behaviour at interview	0·37	0·22

Psychiatric Outpatient Mood Scales (POMS)[312]

There are several scales in this instrument which is designed to assess mood in psychiatric outpatients. One of the scales is "Tension Anxiety" and it can be used to rate state anxiety.[270] Each adjective is rated on a 4-point intensity scale—"not at all" (0), "a little" (1), "quite a bit" (2), and "extremely" (3). The adjectives and their weightings on the Tension-Anxiety factor are set out in Table 6.10.

Thus, if a patient rates himself "a little tense", "quite a bit nervous", "not at all on edge" and etc., his T-A score will be the sum of $(1 \times 0{\cdot}52)$ plus $(2 \times 0{\cdot}56)$ plus $(0 \times 0{\cdot}41)$, etc., giving a single score.

Cornell Medical Index[50]

This instrument is not usually regarded as a personality inventory nor was it designed to measure anxiety, but is a better correlate of clinical

Table 6.10

Factor T: Tension-Anxiety, from POMS

Adjective	*Weighting*
Tense	0·52
Nervous	0·56
On edge	0·41
Shaky	0·55
Restless	0·56
Not relaxed	0·41
Anxious	0·40
Uneasy	0·30

anxiety than the inventories discussed so far. The CMI is a list of 195 questions about physical and mental health which was designed as a rapid scan of patients' complaints before they saw a doctor. Most of the items (sections A–L) concern physical symptoms, but about a quarter (sections M–R) (see Table 6.11) deal with psychological problems. The total score is a measure of the number of complaints the patient has. The score on sections M–R correlates highly with the neuroticism score of the MPI and with the Taylor MAS scale. The CMI has been useful in identifying patients with multiple complaints who are likely to seek medical help and it has been used extensively in epidemiological and clinical work (e.g.[51,210,255,448]). The range of scores for normal subjects and for groups of patients with different abnormalities are available. The scores are stable from one occasion to the next. The CMI takes no account of the tendency for patients to show a response set, i.e. to answer "yes" or "no" repeatedly to any questions regardless of their content. The questionnaire also gives no indication about the normal aspects of a patient's personality.

Table 6.11

M–R Scales of Cornell Medical Index

(Reproduced by kind permission of Cornell University Medical College)

M

145.	Do you sweat or tremble a lot during examinations or questioning?	Yes	No
146.	Do you get nervous and shaky when approached by a superior?..	Yes	No
147.	Does your work fall to pieces when the boss or a superior is watching you?.....	Yes	No
148.	Does your thinking get completely mixed up when you have to do things quickly?.....	Yes	No
149.	Must you do things very slowly in order to do them without mistakes?.....	Yes	No
150.	Do you always get directions and orders wrong?.....	Yes	No
151.	Do strange people or places make you afraid?.....	Yes	No
152.	Are you scared to be alone when there are no friends near you?	Yes	No
153.	Is it always hard for you to make up your mind?.....	Yes	No
154.	Do you wish you always had someone at your side to advise you?	Yes	No
155.	Are you considered a clumsy person?.....	Yes	No
156.	Does it bother you to eat anywhere except in your own home?..	Yes	No

N

157. Do you feel alone and sad at a party? ..... Yes No
158. Do you usually feel unhappy and depressed? ..... Yes No
159. Do you often cry? ..... Yes No
160. Are you always miserable and blue? ..... Yes No
161. Does life look entirely hopeless? ..... Yes No
162. Do you often wish you were dead and away from it all? ..... Yes No

O

163. Does worrying continually get you down? ..... Yes No
164. Does worrying run in your family? ..... Yes No
165. Does every little thing get on your nerves and wear you out? .. Yes No
166. Are you considered a nervous person? ..... Yes No
167. Does nervousness run in your family? ..... Yes No
168. Did you ever have a nervous breakdown? ..... Yes No
169. Did anyone in your family ever have a nervous breakdown? .. Yes No
170. Were you ever a patient in a *mental* hospital (for your nerves)? Yes No
171. Was anyone in your family ever a patient in a *mental* hospital (for their nerves)? ..... Yes No

P

172. Are you extremely shy or sensitive? ..... Yes No
173. Do you come from a shy or sensitive family? ..... Yes No
174. Are your feelings easily hurt? ..... Yes No
175. Does criticism always upset you? ..... Yes No
176. Are you considered a touchy person? ..... Yes No
177. Do people usually misunderstand you? ..... Yes No

Q

178. Do you have to be on your guard even with friends? ..... Yes No
179. Do you always do things on sudden impulse? ..... Yes No
180. Are you easily upset or irritated? ..... Yes No
181. Do you go to pieces if you don't constantly control yourself? Yes No
182. Do little annoyances get on your nerves and make you angry? Yes No
183. Does it make you angry to have anyone tell you what to do? Yes No
184. Do people often annoy and irritate you? ..... Yes No
185. Do you flare up in anger if you can't have what you want right away? ..... Yes No
186. Do you often get into a violent rage? ..... Yes No

R

187. Do you often shake or tremble? ..... Yes No
188. Are you constantly keyed up and jittery? ..... Yes No
189. Do sudden noises make you jump or shake badly? ..... Yes No
190. Do you tremble or feel weak whenever someone shouts at you? Yes No
191. Do you become scared at sudden movements or noises at night? Yes No
192. Are you often awakened out of your sleep by frightening dreams? Yes No
193. Do frightening thoughts keep coming back in your mind? .... Yes No
194. Do you often become suddenly scared for no good reason? .... Yes No
195. Do you often break out in a cold sweat? ..... Yes No

Middlesex Hospital Questionnaire (MHQ)[82,83,84]

This is a 48 question inventory designed to measure neurotic symptoms in an English population. It covers 6 areas—free-floating anxiety, obsessions, phobias, somatic anxiety, depression and hysteria—to yield a profile of 6 scores. The questions constituting the scales for free-floating anxiety and somatic anxiety are listed in Table 6.12. The questionnaire differentiates between normals and neurotic and depressive patients. Its constituent items overlap with other inventories such as the MPI, the Cornell Medical Index and the Tavistock Self-Assessment Inventory. The MHQ is useful as a rapid screening test and is more relevant than most to a clinical neurotic population. However, to follow clinical changes over time, say for depression or phobias, more detailed and specialised scales are necessary.

Table 6.12

Middlesex Hospital Questionnaire

(Reproduced from Crown and Crisp[82] by kind permission of the authors and the editor of the British Journal of Psychiatry)

Questions forming free-floating anxiety scale

1. Do you often feel upset for no obvious reason? Yes..2.. No..0..
7. Have you felt as though you might faint? Frequently..2.. Occasionally..1.. Never..0..
13. Do you feel uneasy and restless? Frequently..2.. Sometimes..1.. Never..0..
19. Do you sometimes feel really panicky? No..0.. Yes..2..
25. Would you say you were a worrying person? Very..2.. Fairly..1.. Not at all..0..
31. Do you often feel "strung-up" inside? Yes..2.. No..0..
37. Have you ever had the feeling you are "going to pieces"? Yes..2.. No..0..
43. Do you have bad dreams which upset you when you wake up? Never..0.. Sometimes..1.. Frequently..2..

Questions forming somatic symptoms scale

4. Are you troubled by dizziness or shortness of breath? Never..0.. Often..2.. Sometimes..1..
10. Do you often feel sick or have indigestion? Yes..2.. No..0..
16. Do you sometimes feel tingling or prickling sensation in your body, arms or legs? Rarely..1.. Frequently..2.. Never..0..
22. Has your appetite got less recently? No..0.. Yes..2..
28. Do you feel unduly tired and exhausted? Often..2.. Sometimes..1.. Never..0..
34. Can you get off to sleep alright at the moment? No..2.. Yes..0..
40. Do you often suffer from excessive sweating or fluttering of the heart? No..0.. Yes..2..
46. Has your sexual interest altered? Less..2.. The same or greater..0..

Tavistock Self-Assessment Inventory[102,103]

This is a series of statements about neurotic symptoms which subjects check "yes" or "no" as it applies to them. It was used originally to

survey the symptoms of neurotic psychiatric outpatients. Some of its component dimensions have been elicited by factor analysis[329] and are similar to those of the MPI and the Cornell Medical Index (see below).

OTHER MEASURES

Some other commonly used rating and diagnostic instruments have been investigated for use as estimates of trait or state anxiety. Eighteen possible signs of anxiety were derived from the TAT (Tell-a-Tale Test) given to 20 students who were also rated for anxiety.[299] Three of the TAT measures correlated significantly with the anxiety rating but not at a very useful level. In another study,[443] it was claimed that TAT protocols revealed more intense castration-anxiety in homosexual males than in heterosexual males. In a detailed study,[109] some indicators of anxiety were derived from the Rorschach test. They discriminated between neurotics and normals and also correlated significantly with other ratings of anxiety.

Wessman and Ricks[515] developed a set of self-report "Personal Feeling Scales" which defined dimensions such as tranquillity vs. anxiety and elation vs. depression. For the tranquillity–anxiety measure subjects check "how calm or troubled you feel" on a single ten-item cumulative scale.

Nowlis and Green[368] collected a large number of adjectives that could be used to complete the sentence "I feel . . .". On the basis of factor analytic studies they derived scales for measuring 12 different mood dimensions. The anxiety factor was defined by the adjectives "clutched up", "fearful" and "jittery". In subsequent research each of these three adjectives is rated on a 4-point scale.

Relationships between scales

Many inventories contain similar questions, e.g. the Taylor Manifest Anxiety Scale is derived from part of the MMPI while the Maudsley and Eysenck Personality Inventories, the Cornell Medical Index and the Tavistock Self-Assessment Inventory share many items. An example of the way different questionnaires have similar correlates comes from a study of 62 phobic patients by Marks.[329] A principal components analysis was made of 21 clinical and 5 questionnaire variables measured both at the start of treatment and at its completion 3 to 6 months later. The salient feature which emerged was a *complaints* factor (1st order) with identical structure both at the start and the end of treatment (Table 6.13). The items which made up the factor were four questionnaire scores (Tavistock phobic and social anxiety scores, N score of the EPI and the Cornell score) plus sexual maladjustment. All the questionnaire scores correlated highly significantly with one another (mean $r = 0{\cdot}58$). This stable factor shows that patients who score highly on

one of the four questionnaires also tend to score highly on the other three and that such patients also tend to be sexually maladjusted.

The answers to individual questions from the questionnaires were subjected to principal components and to item analyses. From the Tavistock Inventory two components were found—agoraphobia and social timidity—which strongly resembled factors found in a mixed psychiatric outpatients population by Dixon et al.[102,103] From the Cornell Medical Index four stable components were extracted—depression, exhaustion, paranoid irritability and social anxiety. It was of particular interest that answers to certain questions from the Neuroticism, Cornell and Tavistock questionnaires predicted outcome better than did the total questionnaire scores. This suggested that the predictive value of the questionnaires was due to particular components rather than to any "dimensions" they were measuring as a whole.

Table 6.13

Complaints factor—1st Order. (From [329])

(Principal components analysis, oblique rotation, based on 26 variables: n = 62)

	Factor loadings (×100) when forms completed at:	
	Start of treatment	End of treatment
1. Tavistock social anxiety section (total scores)	79	99
2. Neuroticism—EPI (total scores)	79	75
3. Cornell—sections G, I, J and L–R (total scores)	71	86
4. Tavistock phobic section (total scores)	55	66
5. Sexual maladjustment	66	45

The study just reviewed demonstrates the amount of overlap between different inventories which measure facets of "anxiety" and the dangers of drawing conclusions from global scores as such inventories comprise a variety of components, which may be independent of one another. The caveat of Hilgard[247] still applies: personality inventories "remain fallible instruments and their improvement is one of the pressing tasks facing psychology".

Scores on the questionnaires often correlate significantly with clinical ratings of anxiety. In this study, the correlations were 0·44 for the Cornell, and 0·39 for the Tavistock phobic checklist, but only 0·21 for the N scale of the EPI. In another study of 16 phobic patients[332] the correlations with clinical ratings of anxiety were 0·63 for the Cornell, 0·52 for the Tavistock phobic checklist and 0·50 for the Neuroticism scale of the EPI (all n = 16). Thus, although these inventories consistently reflect clinical anxiety, the relationship is an imperfect one.

CONCLUSIONS

One of the drawbacks of many of the scales discussed in this chapter is that they attempt to rate "anxiety" or even "neuroticism" as if it was a unitary clinical syndrome. Anxiety is simply one group of symptoms and signs which can occur in many neurotic syndromes which differ from one another with respect to their levels of clinical anxiety, onset age, sex incidence, course and prognosis with different kinds of treatment.[79,268,330,333] There is little clinical value to be gained by grouping together neurotic syndromes which only overlap to a small extent in their distinguishing characteristics. Furthermore, anxiety has to be carefully subdivided at least into free-floating, non-situational anxiety and into phobic anxiety which is specifically aroused only by particular situations. Even then, whereas general anxiety "factors" would distinguish patients with anxiety states from normals and phobic anxiety "factors" would separate out phobic patients, sufferers from, say, writer's cramp might not be distinguishable from normals at all on these scales.

In the choice of a scale, the potential user must be clear as to his requirements. Does he want an assessment of "trait" anxiety, of "state" anxiety, of anxiety symptoms in psychiatric illnesses, or of the severity of a clinical anxiety state? Is the rating to be carried out by the psychiatrist or by self-assessment? Is the rating to be carried out once as a diagnostic tool or are repeated ratings to be taken as indices of change? For clinical anxiety to be assessed by the psychiatrist, scales like the Hamilton Scale are appropriate; for self-assessments ad hoc linear scales can be adapted.

Chapter Seven

THE PSYCHOLOGY OF ANXIETY

INTRODUCTION

This topic is large and much of it concerns anxiety proneness as a personality trait rather than anxiety as a clinical state. The effects of anxiety, defined in one way or another, have been assessed on a wide range of psychological functions and some of these studies will be summarised[122,289,467]

Two basic concepts dominate this aspect of psychology. Firstly, anxiety as an emotion can be regarded as an intervening variable which exercises a modulating influence on behaviour. In other words, if a stimulus evokes fear then subsequent behaviour may differ from that which would ensue if the stimulus did not evoke fear. The second concept is of anxiety as a drive to initiate behaviour which will reduce that drive. Anxiety as a drive state is discussed a little later in this chapter.

ANIMAL STUDIES

In animals, "fear" has been the most studied emotional state because it is easy to induce and simple to isolate behaviourally. In these experiments we do not know which emotion the animal is experiencing and have to infer this indirectly from the animal's overt motor and autonomic responses. Indeed, we can only guess that animals experience emotions. Though animal experiments on fear responses are relevant to the problem of anxiety in man, we must be guarded in translating these experimental results into human terms. It is more rigorous scientifically to describe and elucidate the animal's behaviour patterns than to attempt to assign to them properties of subjective experience. In descriptions of such experiments the terms learning and conditioning are often used interchangeably. In general, however, conditioning refers to simpler stimulus-response connections while learning refers to the acquisition of rather more complex new behaviour.

In classical Pavlovian conditioning a neutral signal (CS—the stimulus which is to be conditioned) is repeatedly presented immediately prior to an unconditional stimulus (UCS) which uniformly evokes an unconditioned response (UCR). Eventually the CS alone evokes the response which is now termed a "conditioned" response (CR). In the original example, the display of food to a hungry dog produced copious

salivation. A buzzer was sounded immediately before the food presentation, and eventually the buzzer alone resulted in a flow of saliva. A different stimulus, say a bell, produced no response.

Pavlov[375] also conditioned a dog to salivate on presentation of one visual stimulus, a circle, and to stop salivating when shown another visual stimulus, an ellipse. On subsequent occasions the dog was presented with ellipses which were increasingly more circular. The dog's discriminatory ability was eventually disrupted and its behaviour became abnormal with some features resembling behavioural phenomena in human neuroses. Autonomic signs such as mydriasis and tachycardia became apparent with posturing and tic-like movements, changes in respiratory pattern, breakdown in learned behaviour patterns, phobias, social abnormalities and sexual deviations. These aberrations persisted outside the experimental situation and were termed "experimental neuroses" (see also[142]). Among other methods used to induce such disorganised behaviour is that of training cats to lift a flap to obtain food; when the behaviour pattern is well established, a blast of air or an electric shock is given as the cat lifts the flap.[341] However, such animal models may not be analogous to human anxiety states but to the neuroses commonly seen after major disasters such as an earthquake.[418]

In avoidance conditioning, the animal learns to make a specific response to an innocuous stimulus in order to avoid a noxious stimulus.[296] Thus the animal—dog, sheep or goat—is required to flex its foreleg in response to a harmless stimulus to avoid a shock to that limb. At first the animal struggles haphazardly in its restraining harness but quite rapidly learns to make a purposive leg-flexion. Furthermore, it may delay doing so until immediately before the shock is due. In rat experiments, the animal is trained to climb a rope or pole or to run from one compartment to the other of a double cage ("shuttle-cage"). Before this stage is reached, however, the rat merely runs to the other compartment on receipt of the shock (escape behaviour). More complex avoidance responses such as pressing a lever or turning a wheel can be learnt. Natural responses may be inhibited. Cats, shocked when they pounce on a mouse, learn swiftly to leave the mouse alone ("approach-avoidance conditioning").

Since escape and avoidance conditioning depend upon the rat doing something (operating on its environment), both these situations are forms of instrumental (operant) conditioning, alternative terms for which are trial-and-error learning and law-of-effect learning. They are accompanied by all the signs of fear and correspond to the tendency of human phobic patients to escape from and to avoid those situations which frighten them.

In instrumental conditioning situations the animal's responses

determine whether he will be reinforced (i.e. rewarded or punished). This is in contrast to classical conditioning situations where the animal's responses make no difference to the reinforcing events, e.g. whether the animal is shocked or given food does not depend upon lever pressing or any other action of the animal. Free operant conditioning differs from the above procedures in that there is no conditioned stimulus and the animal "responds" at its own rate; the animal learns to carry out an item of behaviour which is then rewarded, e.g. lever-pressing for a pellet of food. There are various schedules of reinforcement such as a reward every 10 lever pressings or one every minute irrespective of rate of response.

In most of the above procedures no specific attempt is made to induce emotional responses such as fear. If however a neutral signal (CS) is repeatedly paired with an aversive unconditioned stimulus (UCS) from which there is no escape, the CS alone becomes capable of inducing a conditioned response which is termed the "conditioned emotional response" (CER).[206] The pattern of behaviour induced is characteristic of the particular species, e.g. rats crouch or "freeze", or jump and scamper round their cages, squeaking. Urination and defaecation are common. The CER itself acts as a stimulus state with the animal responding by attempting to escape. Often the CER is superimposed on free operant conditioning. For example, lever pressing for food reward is established and then a neutral signal is paired with a shock. Soon the neutral signal is followed by a reduction in or absence of lever pressings.[119] The decrease in rate of lever pressings has been employed as an index of the intensity of the conditioned emotional response but the relationships here may be complex.[207]

Another experimental situation is temporal pacing, also known as the Sidman avoidance schedule.[450] Again there is no conditioned stimulus (CS) but the rat learns to delay onset of a shock (the UCS) by pressing a lever. The schedule is arranged so that a shock is given, say, every 20 seconds, unless the rat presses a lever before those 20 seconds have passed. Pressing the lever resets the timing mechanism to start a new 20-second period. The rat soon learns to avoid shocks by pressing the lever repeatedly for long periods.

Finally there is punishment training, in which the animal is punished repeatedly for a particular response and then appears afraid of making that response.

These experimental situations are not all mutually exclusive. They produce various stimulus-response relationships in the acquisition of fear responses. With these experimental situations one can systematically study which variables are important in the learning of fear and anxiety, e.g. the species, age and sex of the animal, its physiological and psychological state, the quality of the noxious and neutral stimulus, intensity and duration of such stimuli, the time interval between the

neutral and noxious stimuli, and the manoeuvres which the animal learns in order to avoid or to escape from the fear situation. A succinct review of this area was made by Bolles.[40]

THE DRIVE FEATURES OF ANXIETY

When an organism is motivated to perform an appropriate response it is said to be in a state of drive. Primary drives are those which depend on the basic functions of an organism. Examples of primary drives are hunger, thirst and sex. A hungry or thirsty animal will learn to press levers, run down mazes and perform other tasks to obtain food or water. Strong fear equally motivates an organism to respond in some way which will reduce the fear. Pain and fears which have not been learned are primary drives. Other fears are learned by experience and become important secondary drives which motivate an animal to perform new behaviour which diminishes the fear.

Fear is that state of uneasiness which is caused by the sense of impending danger from a particular source. Anxiety is an emotion indistinguishable from fear, except that the source of danger is not clear. It results from the perception of threat—that a situation, although not currently pain producing, is potentially so. This perception is a complex process. Most fear and anxiety is the result of learning that particular stimuli *are* or *may become* noxious respectively. Anxiety can therefore be regarded as a secondary drive which will motivate an organism to lessen or avoid the threatening stimuli and the anxiety they engender. Any behaviour which happens to be associated with a lowering of anxiety will tend to be repeated on subsequent occasions, i.e. it will be reinforced by the decrease in anxiety levels. That behaviour will eventually become a regular response to anxiety even though initially the behaviour may have been random. Once the new response is regularly associated with a lessening of anxiety it becomes a secondary reinforcer which facilitates the learning of other anxiety reducing behaviour. *Anxiety* itself is thus a secondary *drive* which can change the behavioural repertoire of an organism. The *decrease in anxiety* is a secondary *reinforcer* which can also alter the behavioural repertoire. Eventually, the behavioural responses to anxiety become refined to those which are most effective in decreasing anxiety.

There are limits to the effectiveness of anxiety reducing responses especially at high anxiety levels. As anxiety increases an animal will intensify its responses to reduce that anxiety, e.g. it presses a lever or escapes from an electrified cage. However, the point is eventually reached beyond which further increases in anxiety are associated with diminutions in the anxiety reducing responses. This is the classic inverted U-shaped curve which relates drive to performance.[535] The relationship was first observed in experiments on the discriminatory ability of mice. The relationship implies that for each task there is

an optimum drive level, both above and below which performance falls off (see fig. 7.1). The optimum drive level varies with different tasks. For easy tasks this optimum drive level is high, whereas for difficult tasks it is low. A patient with an anxiety state may be so anxious that he can only perform tasks which are very easy. The drive level of an individual varies widely with many factors, some of which will be discussed later.

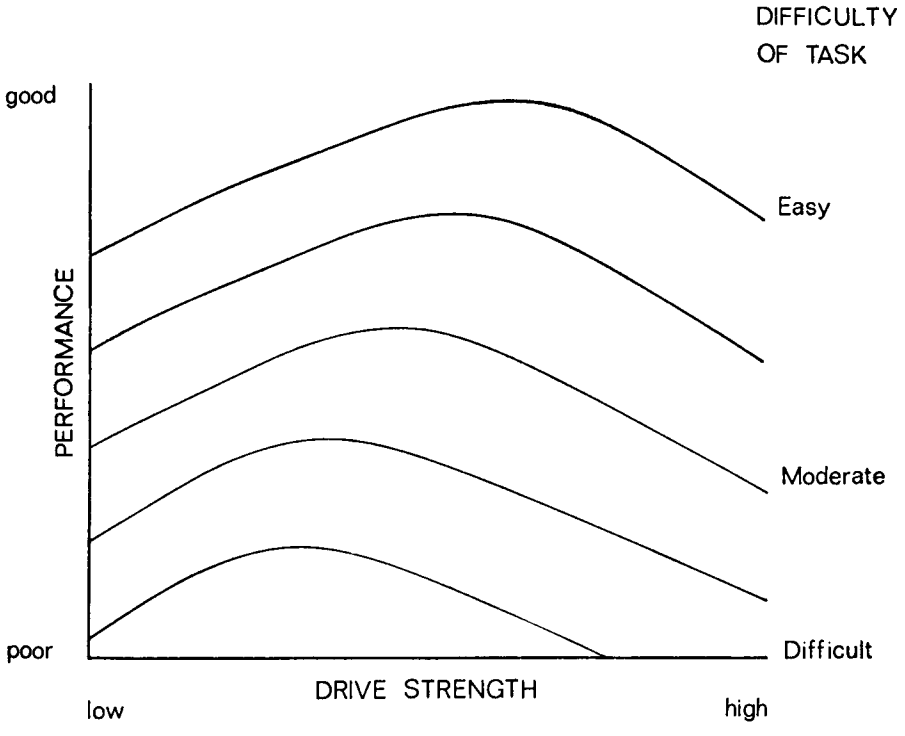


Fig. 7.1: Relationships between drive strength, difficulty of task and performance of that task. See text for explanation.

The relationship between drive and performance is also modified by the strength of an organism's habitual tendency to perform a particular response. Many theoretical attempts have been made to specify these relationships. In an attempt to predict animal behaviour in experimental situations, different algebraic equations have been devised to relate response tendency, drive and habit strength. Unfortunately none of the formulations available can cope with the complexities of anxious behaviour which are observed even in animals. Kanfer[227] noted:

"I doubt if much of our rat psychology is applicable even to the field mouse, much less to the adult human . . . the detailed findings simply do not fit the complexity of the uncontrolled every-day environment." Although the following section has little relevance to the problems of clinical anxiety, it is included as a guide to those interested in the early, rather primitive, formulations. The best known of these has been that of Hull.

Hull[205] suggested that the strength of a response could be expressed in the equation $R = f(E) = f(D \times H)$ where R was the magnitude of a response in a given situation, E was the "excitatory potential" of an organism, D was the "total effective drive state" and H was the "habit strength" of the response in question. D, the total effective drive state, was the sum of all the drives existing in an organism at the time (hunger, thirst, sex). H, habit strength, was the tendency for a particular response to occur in the situation in question. This was determined by a subject's previous experiences and their relevance to that situation. Response tendencies may be numerous, they may vary greatly in size and they may even be incompatible. For example, a new equation $2 + 2 = 5$ would be hard to perform, because $2 + 2 = 4$ has been learned so thoroughly before.

Hull's formula would predict that increased drive (D) would strengthen response strength (R) in the case of a single habit such as an unconditioned reflex. Such simple situations are rare and in the human context it is often impossible to know whether a given piece of behaviour is best regarded as a simple habit, or as part of a more complex event. In single habits, subjects in a state of high drive should respond more intensely than low drive subjects. However, beyond the "ceiling" of maximum performance, further increase in drive may even lead to a falling away in performance, as Yerkes and Dodson noted long ago, and at extremes of activity even a simple reflex may disintegrate completely. This latter phenomenon Pavlov termed "transmarginal inhibition". He first noted it after his experimental dogs nearly drowned during floods in Leningrad. His laboratory was flooded and his animals were found swimming about in terror. After rescue it was noted that some dogs had lost their conditioned reflexes which they had performed regularly and strongly before the floods.

Single response situations are uncommon in human experience. More often, many competing responses may be elicitable, only one of which is correct. Differences in drive level (anxiety in the present discussion) will have varying effects depending on the strength of various response tendencies, i.e. on their position in the habit strength hierarchy. Before a task has been learned well, the correct response will be low down in the response habit strength hierarchy. High drive or anxiety will increase the response potentials of the other responses

to a greater degree so that the correct response is less likely to be elicited. Thus, high-drive subjects will perform *worse* than low drive subjects. Once the correct response has been learned and ingrained, the habit strength of the correct response will have risen to the summit of the hierarchy. Now, high-drive subjects will perform better than their low-drive peers (see also p. 118).

Hull's original formulations dealt with drives as temporary states. Spence and Taylor later suggested that individuals vary more lastingly according to their habitual background level of anxiety, some people usually being calm, while others are usually anxious. Stressful stimuli produce an extra emotional response (labelled r_e) which is superimposed on background drive D. The Taylor MAS (see p. 85) was constructed to measure this extra emotional response (r_e) which is assumed to be related to D.[183] The r_e of habitually anxious people may differ from that of people who are usually calm because: (a) their habitual background anxiety might itself lead them to overract to any stress although the threshold of such reactions might be the same as in calmer subjects; or (b) their threshold for arousal to threat might be lower; or (c) both may apply.[458] Spence and Spence favoured the second possibility, that the MAS samples anxiety proneness in subjects. High MAS scores were supposed to reflect proneness to react with anxiety and hence raised drive levels to any situation including laboratory tasks.

Spence suggested further that very anxious subjects also produced more responses which were irrelevant to a task in hand than did people who were calmer. The more complex the task became, the greater the number of irrelevant responses which were made. Child,[72] in a review, came to the same conclusion. In simple tasks (e.g. learning easy paired-associates such as "fast—quick"), few irrelevant responses are made and increasing anxiety improves performance. In very anxious subjects doing more complex tasks, however (such as learning initially unrelated paired-associates, e.g. "gifted—river"), the increased number of irrelevant responses interfere with task performance more than the increased anxiety improves it. Performance consequently falls.

Mandler and Sarason[326] emphasised that an individual's characteristic style of response to anxiety might be more important than the complexity of a given task. An individual's perception and interpretation of a task and his interaction with an experimenter were important influences. Some recent research has in consequence concentrated on studying anxiety produced by standardised test procedures, so called "test anxiety".

ANXIETY AND HUMAN CONDITIONING

Spence and Hull's ideas would predict that anxious subjects will learn and perform a simple task better than will calm subjects. Habituation has been described as the simplest learning of all—learning not to

respond.[488] However, there is abundant evidence that habituation of the GSR is slowed in anxious subjects, i.e. the UCR persists (see p. 137). Although this contradicts the prediction, it could be argued that the prediction refers to an initial response in a series and not to its habituation.

In human work in the context of anxiety the eye-blink reflex has been most often used, i.e. the unconditioned response of an eye-blink to a puff of air on the conjunctiva.[338] The conditioned stimulus is a light or tone. Another system which has been used is conditioning of the GSR, but very vigorous controls are needed to prevent "pseudo-conditioning" and dishabituation effects.

Many of the experiments to be reviewed in the following section employed as a measure of anxiety an inventory like the Taylor Manifest Anxiety Scale or the Test Anxiety Questionnaire. "Anxiety" measured in this way is very imperfectly related to the pathological anxiety found in many psychiatric patients (see p. 88). It is therefore difficult to know how to relate experiments which employ such different measures of anxiety. The reader should bear this in mind about the work to be discussed in the rest of this chapter.

In early studies Welch and Kubis[511,512] found that GSR conditioning to nonsense syllables was more rapid and more stable when established in patients with anxiety states than in controls. It was concluded that pathological anxiety speeds conditioning and slows extinction of the conditioned response.[510] Similar findings occurred in a study of 40 male students who were allocated to high or low anxiety subgroups on the basis of an interview and Rorschach responses: conditioning of the GSR to tones was more rapid and extinction was slower in the high anxiety group.[36]

Spence and his co-workers have consistently found that anxious subjects (as assessed on the MAS) show more rapid eye blink conditioning than calm subjects.[460,463,485] In a further study anxious subjects conditioned more rapidly than calm subjects but performed worse on a stylus maze task.[125] The authors concluded that drive level but not learning ability is increased by anxiety. Spence[459] reviewed the published studies in this field and found that most investigations demonstrating a positive relationship between anxiety and conditioning had originated from his laboratory whereas no such effect was found by other workers. He emphasised that inter-subject variability was high and that his positive results were attributable at least in part to the use of large numbers of subjects. However this would suggest that the MAS score is not an important predictor of eye-lid conditioning rate. Similarly, only a small difference was found between anxious patients and normal subjects.[464] Factors which do seem important are strength of the air-puff to the eye,[463] interspersing shocks to the subject,[461] and increasing the subject's expectancy.[462] Physiological measures assumed to reflect

drive levels (skin conductance, heart rate and sternomastoid EMG) were related in the predicted direction to eyelid-conditioning.[416,417]

The difficulty of relating experiments in normals to those of psychiatric patients is emphasised by the results of Martin, Marks and Gelder.[339] They studied eyelid CR's in 62 phobic patients who were divided into 3 groups—animal phobics, social phobics and agoraphobics. Anxiety was measured on clinical scales, free floating or non-situational (state) anxiety being distinguished from phobic or situational anxiety. Trait anxiety was also measured by inventories—the Neuroticism measure of the EPI, a section of the Cornell Medical Index, and the phobic and social anxiety parts of the Tavistock Self-Assessment Inventory. Of the 3 groups, the animal phobics most closely resembled normal volunteers, in having the lowest levels of state and trait anxiety. Contrary to expectation from Spence's ideas, CR's were acquired faster and extinguished more slowly in the non-anxious animal phobic group than in the other phobics. Although within the animal phobic group CR acquisition correlated significantly positively with state anxiety (but not with trait anxiety), for all patients together CR acquisition correlated significantly *negatively* both with state and with trait anxiety. To check on the possibility of a non-linear relationship, scattergrams were plotted relating anxiety to conditioning in each type of phobia, but there was no evidence of a curvilinear trend. There was also no relationship between acquisition of CR's and skin resistance measures, although the latter are often used as indices of arousal and emotionality.

Evidence from patients thus fails to support Spence's ideas that indicate that anxiety has drive properties. Other workers (e.g. [194]) have pointed out that the eyelid reflex is protective and may differ from non-defensive reflexes. Non-defensive reflexes such as heart rate responses are more difficult to quantify than defensive ones so the crucial experiment in this area remains to be carried out. It is clear, though, that generalisations on the basis of a single reflex-system may be premature.

In fact there is no evidence to support the notion of a general factor of conditionability across reflex systems.[133] Franks and Franks subjected 50 normal men to a partial reinforcement conditioning procedure involving the following reflex systems: eyelid conditioning to sound, GSR conditioning to light, salivary conditioning to sound, and finger withdrawal to a complex light pattern. Although different measures of conditioning for any one reflex system tended to correlate significantly with each other, no significant correlations were obtained *between* the various systems. The results of this study indicate that we cannot assume a simple relationship between the speed of acquisition of a particular conditioned reflex and other variables.

The complexity of these factors was shown by a study of Berry and Martin[33] where men and women underwent GSR conditioning to tones

under three sets of instructions—reassuring, neutral, and apprehension-arousing. Men showed less and women showed more conditioning when reassured; no relationship was found between conditioning and test anxiety questionnaire scores. Beam[26] using real-life stress situations, e.g. imminent examinations, noted that GSR conditioning to visual stimuli was more rapid under stress but conditioning rate was not related to MAS scores.

EFFECT OF ANXIETY ON COMPLEX TASKS

Perpetual tasks

Measures of flicker fusion entail the presentation of a flickering light to the subject and increasing the rate of flicker until the subject reports that the light is continuous. A similar task can be done using clicks. In an early study,[256] fifty patients with anxiety states were found to have a lower frequency of flicker fusion than normal control subjects. Similar results were found by Goldstone[156] who divided both a group of psychiatric outpatients and a group of normals into high anxiety and low anxiety sub-groups on the basis of a questionnaire; in each sub-group a lower flicker threshold was found for anxious subjects. Jones[223] confirmed this finding for fusion of both flicker and clicks. It appears, therefore, that clinical anxiety consistently decreases the threshold for fusion.

Anxiety impairs the perception of three-word sentences flashed on a screen for a brief time (tachistoscopic perception).[389] Highly anxious patients performed worse on a tachistoscopic task involving the recognition of letters than did less anxious patients.[11]

Complex learning

Although theories of anxiety would generally predict that anxious subjects would perform complex tasks more poorly than calm subjects, experiments involving subjects in finding routes through plans of mazes have yielded contradictory results. In one study,[344] subjects in the middle range of MAS scores performed best; in another,[16] no differences were found.

The digit symbol substitution task requires the subject to substitute figures for patterns according to a code. The code is generally learned by practice as the task proceeds. Using the MAS, Matarazzo and Phillips[343] found that anxious subjects performed worse than calm subjects. In another study,[326] calm subjects (differentiated by the Test Anxiety Questionnaire) performed better than anxious subjects in early stages of the experiment, but as the learning process continued anxious subjects improved greatly. The subjects were also told that they had either performed very badly or very well. This report, especially

if of failure, improved the performance of calm subjects but impaired that of anxious subjects. These results may be interpreted in terms of low levels of anxiety aiding performance but high levels impeding it. However, no difference was found between anxious and calm subjects until all were told that they were doing very badly: performance then improved in the calm but deteriorated in the anxious.[231] Westrope[518] had also found that "stress", in the form of electric shocks, diminished performance.

Rote learning

A clear-cut difference was found by Montague[357] between 60 subjects who were in the upper twenty per cent range of the MAS and 60 subjects in the lower twenty per cent range with respect to a task in which subjects were required to learn nonsense syllables. There were three grades of difficulty of the task. On the easiest task the anxious subjects did better than the others; on the two harder tasks, however, the anxious subjects did worse than those who were calm. This is one of the most clear-cut studies to relate differences in task performance to scores on the MAS but it may be noted that the difference between the groups was only about 15 to 20 per cent. In a serial learning task anxious subjects made more errors than calm subjects, the more difficult the item, the greater the difference between the groups.[487] A more complicated study was carried out by I. G. Sarason[423] on subjects who scored high, medium or low on the MAS. In each group there were three sub-groups who were given one of the three sets of instructions designed to involve self-esteem, or to be neutral, or to lead the subject to believe that good results would help the experimenter with his thesis. Under neutral instructions the high anxiety subjects learnt nonsense syllables more quickly than the other two groups; in the self-esteem group the low anxiety subjects did best; in the "experimenter-oriented" sub-groups no differences were found. The complicated interactions between task, subject and experimenter would repay further studies. From experiments carried out on anxious patients and controls, Malmo and Amsel[319] attributed the forgetfulness of anxious patients to interference between the relevant response and those irrelevant responses which are generated by the patient's anxiety state. The digit span—the number of digits which the subject can remember at a time—was found to be diminished in a group of college students tested under anxiety evoking conditions as compared with a group tested under reassuring conditions.[356] As intelligence tests obtained at the same time were less affected, the authors concluded that the learning of new tasks was more impaired by anxiety than the performance of tasks which had already been learned. Subjects with high test anxiety scores had poorer memory spans than low scoring subjects.[235] The digit span

has also been found to be impaired in anxious normals and patients.[100] Again in these learning tasks complicated interactions were found among anxiety of subjects and of experimenters, sex, and task parameters.[306,425,427,526] In one experiment, eighteen subjects with high MAS scores, eighteen with low scores and seventeen anxious patients were compared on two tasks. In the first task, which consisted of easy word associations, the anxious subjects did worse than calm subjects; in a much more difficult task involving false multiplications (e.g. $2\times2=5$), the anxious subjects performed much worse.[253]

Reaction time tends to be faster in anxious subjects, according to Wenar,[514] but the opposite was found by Kamin and Clark.[225] In a task in which subjects were instructed to respond to only one out of eleven lamp flashes, the anxious subjects responded more incorrectly than calm subjects.[351] As in the experiments on conditioning, physiological measures also reflect task variables. In a complex perceptual motor task the more anxious subjects showed an increase in skin conductance during the task whereas calmer subjects showed a decrease.[395]

Intelligence tests

Low but significant negative correlations have been described between Taylor MAS scores and intelligence; for example, in Air Force trainees,[245] the higher the intelligence, the lower was the MAS score. However, in a large student sample, Spielberger,[465] was unable to discern any such relationship. On detailed analysis, Spielberger[468] concluded that the negative correlation would only occur in a large sample covering the whole range of intelligence. In a student sample, confined to the upper half or less of the intelligence range, the relationship would not be significant.

There are two possible mechanisms usually advanced to explain this relation. Firstly, anxiety may have a detrimental effect on performance in the tests. Secondly, less intelligent subjects may be made more anxious by the tests because they find them difficult. A third explanation is also possible. Subjects of lower intelligence may formulate their awareness of emotional states such as anxiety primarily in somatic terms, e.g., sweaty palms and palpitations, rather than psychological, e.g., feeling of apprehension. Consequently, their MAS scores will tend to be higher as the scale contains many somatic symptoms.

In addition Siegman[452] found that subjects with high MAS scores performed better than low MAS scorers in untimed subtests of the Wechsler Adult Intelligence Scale; conversely, they had lower scores in the timed tests. Overall, the effects cancel out which explains, in part, the lack of correlation between MAS and I.Q. Where an entire intelligence test is timed, significant negative correlations are more likely to occur.

In general, significant negative relationships have been found between Test Anxiety Questionnaire scores and Intelligence test scores. In this instance, the most reasonable explanation is that anxiety interferes with intelligence test performance. Sarason and Palola[427] conclude that a subject's performance is more frequently related to test anxiety scores than to general (trait) anxiety scores. Difficult tasks and highly motivating instructions will combine to affect adversely the performance of anxious subjects.

S. B. Sarason has investigated the complex relationships between Test Anxiety Scores in children, their tendency to bias their reports (Lie Scale), and their intelligence.[428] Several intensive longitudinal studies have been carried out.[195,429,431] Calm children tended to have higher intelligence scores than their anxious peers. Within each group, the children with high bias scores were more intelligent than those with low scores. That is, children "who tend not to admit to universal worries (e.g., nobody has ever been able to scare me) outperform those who tend to admit such worries".

Negative correlations have also been found in samples of psychiatric patients. In one study, a correlation of −0·41 was found between the Taylor MAS and Raven's Progressive Matrices in 35 male patients.[452] Digit span and attention are impaired in patients with pathological anxiety so that results of tests of intellectual functioning in such patients need cautious interpretation.[100]

Academic achievement[468]

It is a common complaint of students that they do poorly in examinations because, although they possess the necessary information, their production and marshalling of it is disrupted by anxiety induced by the examination.[55] While some anxiety is probably conducive to optimum performance, an excess is undoubtedly deleterious. Furthermore, most examinations are timed, which is an additional complication (see above).

An interesting study involved 100 girl psychology students who were administered the Test Anxiety Questionnaire and a test of scholastic ability.[374] They sat the routine course examination in the usual way but later the same day they were re-examined in small groups in a situation intended to minimise anxiety. Significant negative correlations were found between the TAQ scores and scholastic ability and also regular examination results, anxious students being less able and obtaining worse results than less anxious girls. For the sample as a whole there was no relationship between TAQ scores and the difference in performance between the two examinations. However, if students in only the middle ability range were included, a significant relationship emerged: girls above the median TAQ did as well or better in the "relaxed" exam as in the regular one; girls below the median TAQ did worse.

A detailed study has been carried out in this area by Spielberger and Katzenmeyer.[470] 140 male students scoring in the top 20 per cent of MAS scores were compared with 144 in the lowest 20 per cent. Each group was subdivided into five levels of intelligence and their academic achievement was assessed over one term. At both the lowest and the highest ability levels there was no difference between the anxiety groups with respect to achievement. At the three intermediate ability levels, anxious students did worse during the term than calmer students. It seems that highly intelligent students will do well whatever their anxiety level; students of low aptitude do poorly. Only students of intermediate intelligence are impaired in their academic achievement by high anxiety levels. (However, Katahn[230] found both low and medium aptitude highly anxious students to show impaired academic performance.)

The graduation status of each of the students was determined in a follow-up study carried out three years after the original collection of data.[466] More than 20 per cent of the anxious students were academic failures as compared with 6 per cent of their low anxiety peers. Only at the highest levels of ability was there no difference in proportion of failures. It appeared that some prediction could be made of students at especial risk of academic failure who, due to emotional problems, did not function at levels commensurate with their ability. In an attempt to deal with this problem, freshmen considered to be at risk were offered group-counselling sessions.[472]

In an investigation carried out on 305 students at Yale University, I. G. Sarason[424] found that test anxiety scores correlated negatively with academic achievement; that is, the higher the score the worse the students' performance. However, this effect tended to diminish the longer the student remained at Yale suggesting that some adaptation to test anxiety or increased learning to cope with examination had taken place. Conversely, general anxiety correlated positively with academic performance, high scores tending to go with good performance.

In a large study, Hill and S. B. Sarason[195] followed up groups of children throughout primary school. There were changes in test anxiety scores on repeated testing but children showing marked increase or decrease in anxiety scores over five years showed significant changes in the opposite direction with respect to intelligence tests and achievement. With the factor of intelligence held constant, low anxiety children did better than high anxiety children.

In summary, it is students in the middle range of ability in whom anxiety exerts a deleterious effect. This effect is better predicted by specific anxiety scales than by general ones.[9]

Finally, it should be noted that not only can anxiety affect achievement but achievement can modify anxiety. Attainment of a coveted situation may be followed by a reduction of anxiety especially if the

position is a secure one. Similarly, repeated successes will lessen examination anxiety as Sarason[424] found.

Speech

Speech can be disrupted by anxiety and in one study a significant relationship was found between number of disruptions and palmar sweating, the latter increasing with the number of disruptions.[229]

Speech disturbances can be divided into two categories. Firstly, "Ah" occurs as an interjection and this category does not correlate with anxiety nor with the other speech disturbance. Secondly, the "non-ah" disturbances such as repetition, stutter, and omissions are related to anxiety. The "Non-ah Ratio"—the number of "non-ah" disturbances as a proportion of all words in a sample—has been proposed as an anxiety index.[316,317]

Geer[145] divided 80 women students into those who became anxious during public speaking and those remaining calm, on the basis of replies to a Fear Survey Schedule. The subjects spoke before a one-way screen believing they were being observed. Analysis of the speech samples showed that the anxious girls had a high "non-ah" ratio, more episodes of silence and spoke more slowly than the calm girls.

CONCLUSIONS

The bulk of human studies on the relationship between anxiety and behaviour has concentrated on anxiety as a trait in normal subjects. Defined in this way, anxiety impairs performance under many conditions and much of the experimental evidence is consistent with the time-honoured inverted U-shaped curve and its attendant hypotheses.

In the case of morbid, clinical anxiety, the evidence is less copious but generally shows that performance is impaired, often to a marked extent. This is certainly in accord with clinical experience.

Chapter Eight

THE PHYSIOLOGY OF ANXIETY

INTRODUCTION

As outlined in Chapter Two, subjective feelings of anxiety are usually accompanied by overt bodily changes. Facial expression is the most obvious indicator of anxiety and the clinician attempts to elicit physical signs such as tachycardia, sweating palms, and cold extremities. The detailed study of these physiological changes, their delineation and measurement, and the elucidation of the relationships between these observable phenomena and concomitant psychological events is the task of psychophysiology. Darrow[89] defined this discipline as "the science which concerns those physiological activities which underly or relate to psychic functions". The definition permits great latitude and psychophysiologists have tended to concentrate on the physiological changes accompanying emotional states. A description of psychophysiology has been given by Sternbach:[477] "It typically employs human subjects, whose physiological responses are usually recorded on a polygraph while stimuli are presented which are designed to influence mental, emotional or motor behavior. . . ."

Anxiety has been of especial interest to psychophysiologists because of the marked bodily changes which accompany the emotion. This chapter will outline the techniques used in such studies and summarise the findings obtained with them.

TECHNIQUES

Psychophysiology has its roots in physiology as far as its techniques are concerned. Since there is no meaningful distinction between the disciplines with respect to the techniques themselves, the difference in emphasis is merely in their application and interpretation. Nevertheless, in practice, psychophysiologists have used relatively few measures, the majority of which are autonomic.[53,499]

Palmar skin conductance

Unlike sweat glands in most parts of the body, those in the palms of the hands and the soles of the feet do not appear to act as part of the thermoregulatory mechanisms of the body except under climatic extremes. Rather, the palmar sweat glands are sensitive to psychological

factors and may serve to optimise tactile sensitivity and to facilitate grip. The number of active sweat glands can be counted, or the amount of sweat secreted can be estimated by passing dry gas over the sweating areas and measuring its subsequent moisture content. These techniques are cumbersome and complicated and simpler electrical methods are available. The electrical conductivity of the skin is a measure of sweat gland activity.[265,271] For technical reasons the electrical resistance is usually measured and varies widely from subject to subject, between about 25 and 250 kilohms/cm^2. Alterations in resistance level in response to stimuli always take the form of a decrease and are termed galvanic skin response (GSR's) or psychogalvanic reflexes (PGR's). A related measure is the skin potential in which responses are often biphasic.

Cardiovascular measures

The most widely used cardiovascular measure is the heart rate which is most conveniently measured by recording the electrocardiogram. Other methods include photoelectric and mechanical pulse detectors. The blood pressure is not easy to measure by any automated technique and consequently has not achieved the same research popularity as the heart rate. Estimates of regional blood flow can be made and the two most commonly used techniques are finger pulse volume which provides an estimate of skin blood flow, and forearm blood flow usually assessed by the intermittent venous occlusion plethysmograph[19,240] which predominantly reflects blood flow through the muscles.

Other autonomic measures

Salivary secretion can be estimated in a variety of ways, for example, by placing a suction cup over the parotid duct orifice, or, more simply, by weighing dental rolls before and after a standard time in the floor of the mouth.[376] Pupillography is another technique which ranges from the simple such as disc comparison to the complex such as infra-red photography. Other autonomic measures include the measurement of pressures and movements in hollow organs such as the stomach and bladder but have been relatively little used.

Somatic measures

A widely used measure is surface electromyography (EMG) which utilises disc electrodes attached a standard distance apart to the skin overlying the muscles under study.[301] The action potentials from the muscles are picked up by the electrodes, amplified and then usually integrated in order to provide a more easily quantifiable recording. Related techniques involve the measurement of tremor by attaching various transducers to the appropriate extremity such as a finger[63] and the counting of eye-blink rate. Finally, respiration may be assessed in a

semiquantitative way by strapping a transducer round the chest or by fixing a temperature sensitive device in the nostril.

Electroencephalogram

Although the electroencephalogram (EEG) is mainly used in the context of clinical neurophysiology it has provided useful psychophysiological information. The usual way of recording the EEG onto paper records is very limited; the variable usually estimated is the per cent alpha time, i.e., the proportion of the recording in which alpha waves fulfilling certain criteria can be distinguished. Recently the advent of laboratory computers has enabled more sophisticated mathematical analyses of the wave forms to be carried out. Of these techniques analysis of the EEG into its constituent sine waves and measurement of the energy in each of these frequencies has been widely used (Fourier frequency analysis). Another technique is to split the EEG into three or four broad wavebands using electronic filters and to measure the mean voltage of each waveband by computer analysis. The variability of the electroencephalogram is also easily estimated in this way.

ANALYSIS OF RECORDINGS

Examples of recordings are shown in Figs. 8.1, 8.2, and 8.3. As a general rule three aspects of each measure are available for analysis.

1. The resting, background or baseline level of activity is estimated; for example, the forearm blood flow level immediately before a stressful task. Usually several readings are taken and averaged.

2. In many variables brief fluctuations in the background activity level are counted. The most obvious fluctuation of this sort is sinus arrhythmia occurring in the heart rate records of young subjects and obscuring other types of fluctuation in heart rate. The most widely analysed fluctuation measure is in skin conductance tracings. As the fluctuations do not usually correlate with any identifiable ambient events they are termed "spontaneous".

3. A response may be shortlasting as in the case of an electric shock stimulus or more tonic as in the case of a stressful mental arithmetic task or a long term vigilance task. The stimulus can be repeated in order to provide an habituation procedure during which the responses of the subject usually diminish exponentially. Finally, more complex stimulus procedures can be utilised in conditioning experiments.

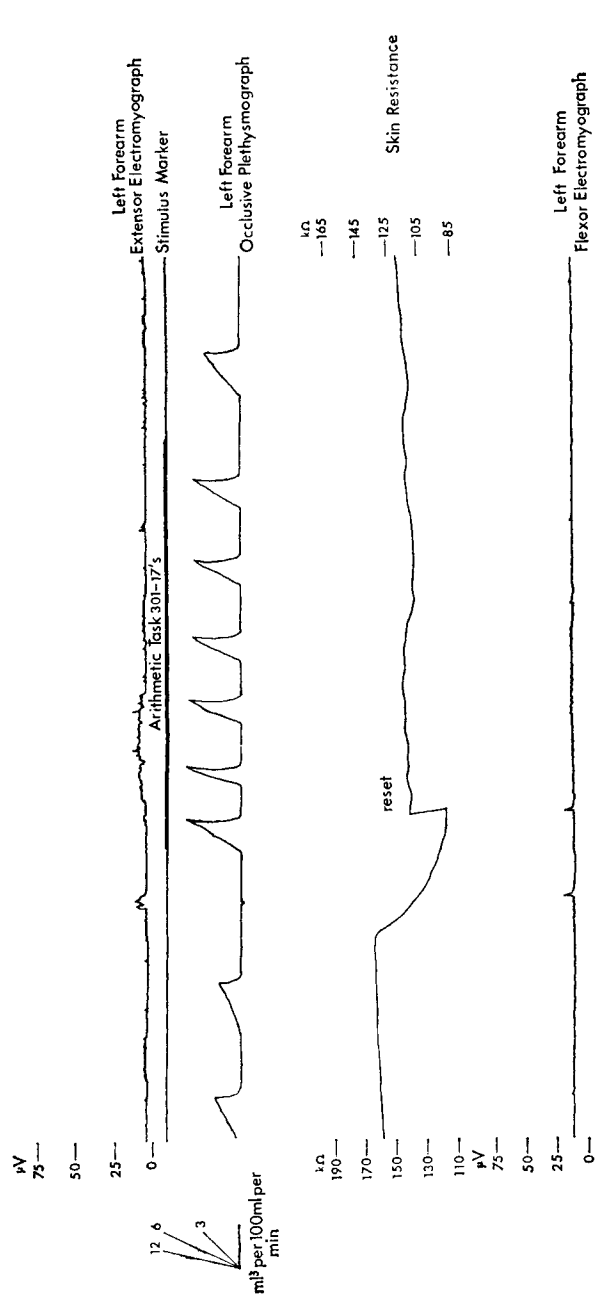


Fig. 8.1: Polygraph record from a normal subject before, during and after the performance of a difficult task. Note the marked increase in forearm blood flow and drop in skin resistance (increase in sweating).

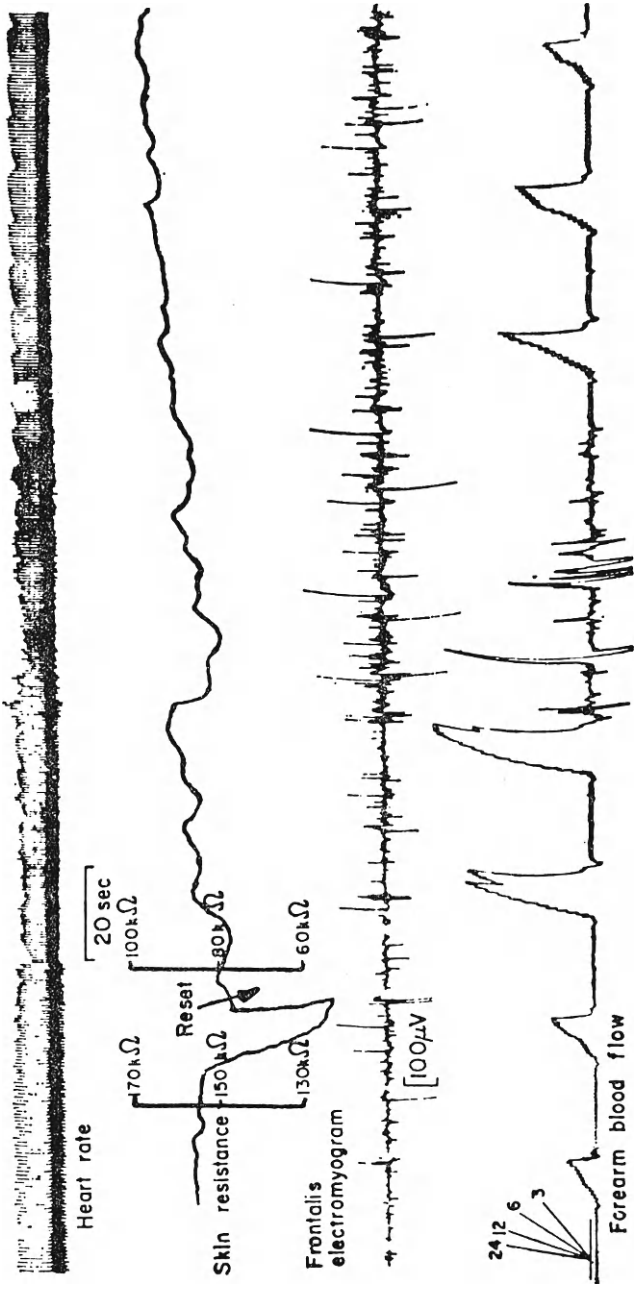


Fig. 8.2: Polygraph record from an anxious patient during a panic attack. (Reproduced from [269a] by kind permission of the editor of the Journal of Psychosomatic Research.)

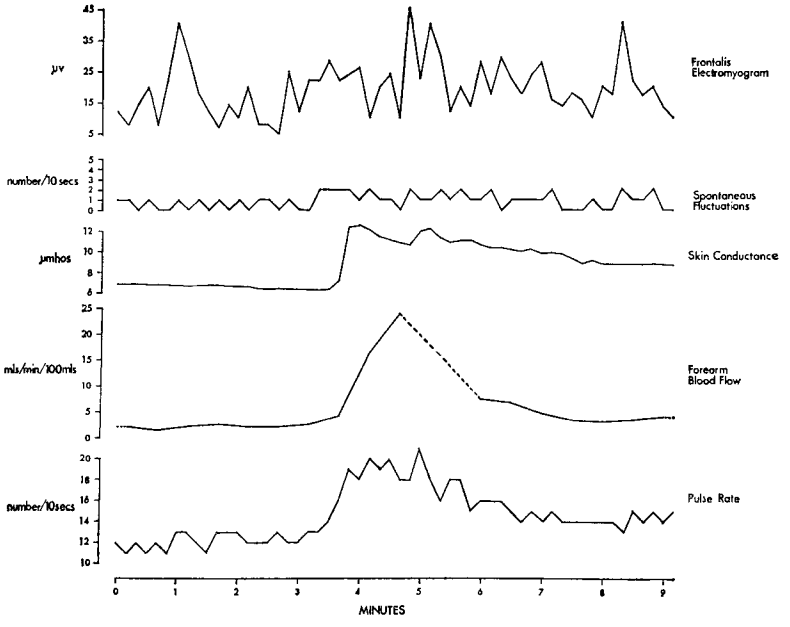


Fig. 8.3: Physiological changes in an anxious patient during the panic attack shown in Fig. 8.2. (Reproduced from [269a] by kind permission of the editor of the Journal of Psychosomatic Research.)

RESEARCH STRATEGIES

The type of study which an investigator will carry out is governed by the nature of the information which he requires. His choice of measure will depend on whether he wants continuous monitoring of the subject's condition or whether readings at intervals will suffice as well as practical considerations such as availability of equipment. If a new technique is being developed or adapted for psychophysiological use, exploratory studies under varied conditions in normals are essential before use in patients.

Of the many variations on research strategies which can be employed two main approaches stand out. Firstly, groups of anxious patients can be compared with a group of normal subjects with respect to the physiological measures under study. The main difficulty here is deciding which other variables in the two groups to match. Age, sex, and social class are generally important but there is a vast range of demographic and psychological factors which might be of relevance in this context and of which very little is known. The other approach is to induce anxiety in both normal and anxious patients. This is a reasonable strategy in studying normal subjects but may be less appropriate to

anxious patients where the emotion which the procedure is designed to produce is already present. Furthermore, anxiety induced by such stressful procedures *may* differ fundamentally from the morbid affect present in patients with anxiety states.

In this connection the use of so-called stressful procedures appears to be a widespread practice. Unfortunately, the whole concept of stress is an ambiguous one and ranges from the widespread and complex endocrinological and morphological changes described by Selye to the psychological concept of a powerful stimulus;[282,284] thus, the concept of stress is an ambiguous one since it can refer both to the pattern of response and to a presumed property of the stimulus situation.[251] Nevertheless, in psychophysiology a stressful procedure is usually taken to mean one which produces an unpleasant affect together with unequivocal changes in the physiological measures under investigation.[323]

STUDIES IN NORMAL SUBJECTS

Many studies have been carried out using normal subjects and exposing them to anxiety-provoking procedures. Only a few can be outlined here.

Strong aversive stimuli such as loud sounds and electric shocks usually produce marked acceleration in the heart rate,[161] accompanied by a GSR, vasoconstriction in skin blood vessels, a burst of increased muscle tone, transient pupillary dilatation and other autonomic and somatic changes. These, if pronounced, constitute a "startle" reaction.[275] Anxiety, if it occurs, follows the stimulus, often with an appreciable delay.

An experimental situation more relevant to the study of clinical anxiety is the assessment of the physiological changes accompanying the anticipation of a painful stimulus such as an electric shock. Heart rate acceleleration occurs in the 30 sec. period preceding an expected shock except for the last few seconds when deceleration occurs. Subjects who have not experienced the shock before show more tachycardia than subjects who have been shocked previously.[96,97] This finding has been confirmed in another study in which greater accelerations were found in the no-experience group whether the shock was to be mild (0·2 mA) or strong (4·0 mA).[111] In a third study, the anticipatory tachycardias were similar in size in subjects scoring high or low on the Taylor MAS.[199] Similarly, skin conductance rises (more sweating) and the number of fluctuations in the tracing increases during anticipation of shock.[232,233,353]

Other stimulation procedures which have been used include difficult tasks such as mirror-drawing and mental arithmetic and the showing of films with "stressful" content. Real-life situations have included imminent examinations and parachute jumping. Cardiovascular concomitants of anxiety include rise in blood-pressure, mainly systolic and not usually sustained at a high level for very long, increase in heart-rate, vasoconstriction in skin and splanchnic regions but dilatation

in muscle.[3,193] There is a net drop in total peripheral resistance so that the stroke volume and especially the cardiac output rise. Palmar sweating increases (rise in skin conductance), the pupil dilates, and salivation diminishes. In general, there is thus a generalised increase in sympathetic activity.

Very interesting physiological studies of anxiety in sport parachutists were made by Fenz and Epstein.[115,127] A novice parachutist shows a gradient of GSR activity which increases steadily towards the moment of the jump, and in a word association test, to words which are increasingly associated with parachuting. As he gains successful experience the gradient becomes inverted V-shaped, the peak appearing progressively earlier, and with cues more remote from the stressful situation. Fig. 8.4 shows this phenomenon in a single subject tested longitudinally.[127] The gradient is monotonic before the 2nd jump, inverted V-shaped before the 5th jump, and the same but with an earlier peak before the 19th jump. The same pattern was found in all 7 subjects tested. The inverted V is only exhibited shortly before a jump, and does not appear after repeated testing in the absence of experience. A relationship to the mastery of anxiety is suggested because the pattern has reversed itself after a mishap, and better jumpers, who have greater emotional control when jumping, show an accelerated pattern.

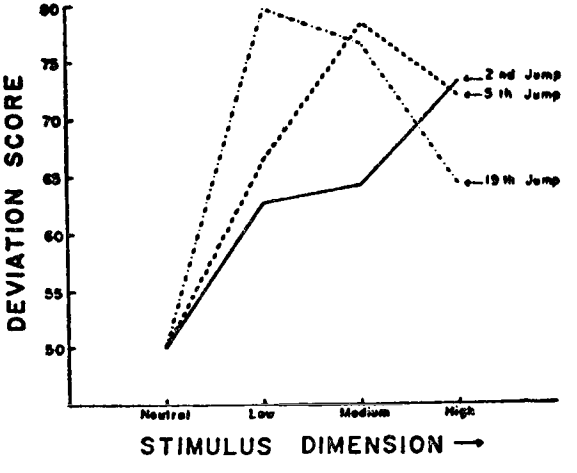


Fig. 8.4: GSR curves produced to a stimulus dimension in a word association test by a single parachutist tested after 2, 5 and 19 jumps. Deviation score refers to a correction for differences on GSR lability and mean reaction to neutral stimuli on the three occasions. (Reproduced from [115] by kind permission of the author and of the University of Nebraska Press.)

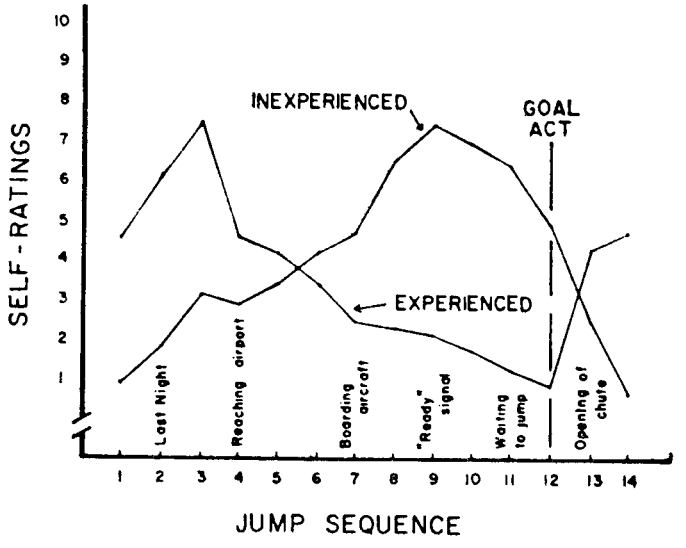


Fig. 8.5: Self-ratings of fear for novice and experienced parachutist along a dimension of events leading up to and following a parachute jump. N = 33 Ss per group. (Reproduced from [127] by kind permission of the authors and the editor of Psychosomatic Medicine.)

Subjective fear ratings show the same pattern as GSR records.[115] Fig. 8.5 shows this for novice and experienced parachutists at 14 points in time from a week before a jump to some time after landing. A rating of 1 is least fear and of 10 most fear. Peak fear appears earlier in experienced than in novice jumpers. Reported fear is greatest not at the time of the jump, which is the point of maximum danger, but at decision points, which advance with experience. The critical decision for novices is at the ready signal, when they can delay or cancel the jump. For experienced jumpers the decision is on waking in the morning, as it depends largely upon the weather. Once they have decided to jump they have no doubt in their minds that they will in fact do so. Other peaks for their anxiety are the time of opening of the parachute and the time of landing.

In a final study 10 novices were compared with 10 experienced parachutists. A transistorised polygraph enabled recordings to be made of skin conductance, heart rate and respiration rate continuously during ascent in the aircraft, and at selected periods before and after the jump. Fig. 8.6 shows results for skin conductance.[115] On all measures the curves of novices and veterans were similar to begin with, but then diverged. Thus, the novices' heart rate rose sharply to a mean 145

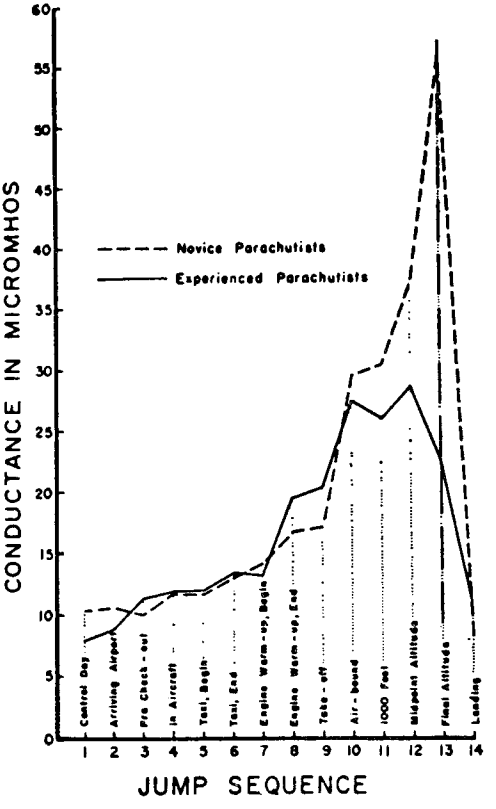


Fig. 8.6: Basal skin conductance of experienced and novice parachutists as a function of the sequence of events leading up to and following a jump. N = 10 Ss per group. (Reproduced from [127] by kind permission of the authors and the editor of Psychosomatic Medicine.)

beats/min. just before the jump, while the experienced parachutists showed a drop at that point. Their peak for the inverted V was earliest for skin conductance, next for heart rate and latest for respiration rate, so breath control could not produce this phenomenon. The peaks for subjective fear occurred much earlier than those of the three physiological measures.

A similar phenomenon is observed during combat flying. Bond[41] noted: "Every dangerous event, as it comes up, is broken off and isolated to become the subject of rumination and repetitive conversation.

Every possibility is explored, every potential outcome considered, and all defensive action carefully rehearsed. Once mastered, the event drops into the preconscious, and attention is then turned to a new one. . . ." For Epstein[117] the last sentence might correspond to the advancing inverted V in the parachuting studies. Further observations by Bond illustrate how the same event can have different stressful significance depending upon its timing. Something which would profoundly influence a cadet in his first flight would mean less in the basic phase and be hardly noticed by a seasoned flyer.

Epstein cited additional support for his ideas from Pavlov's findings in testing his dogs after they were nearly drowned in their cages during the Leningrad flood. Weekly testing showed a change in their conditioned response hierarchies. First there was a total loss of response ("trans-marginal inhibition"), then the normal hierarchy of responses to stimulus dimensions was reversed ("ultraparadoxical phase"). Later the greatest responses were produced by intermediate points along the stimulus dimension ("paradoxical responses"). Finally, the peaks of these curves shifted in the direction of the original gradient.

A simple explanation could account for the development of inverted V-shaped curves, the peaks of which became increasingly displaced with experience.[116] If repeated successful exposure to threat raises the entire anxiety gradient while an inhibitory gradient develops which is steeper than the anxiety gradient, the net anxiety resulting from the interaction could produce an inverted V-shaped curve with the peak advancing earlier as inhibition increases. This process could be adaptive. The advancing peak of anxiety directs attention to more and more potential cues of danger. The inhibitory gradient permits this expansion of awareness to occur at optimum rate without overwhelming the organism. The process is thought to account for findings in a wide variety of situations.

That active inhibition of anxiety occurs is supported by the after discharge of anxiety found in experienced parachutists after the jump is completed. These have greatest inhibitory control. Fig. 8.5 shows the after-discharge for self-rating of fear, and it also occurred for heart rate and respiration rate after the jump. The same effect in parachutists was noted by Basowitz et al.[23] Sometimes inhibitory control breaks down, e.g., when experienced parachutists show surprising anxiety following unexpected changes in the normal jumping routine that did not objectively justify the anxiety.

It is not yet clear how far Epstein's findings in parachutists can be generalised to most anxiety-provoking situations. In other experiments relating anxiety to expectancy he did not find an inverted V-shaped curve before noxious stimulation, with peaks displacing earlier with experience, or he found this for heart rate but not for skin conductance. The factors eliciting the phenomenon have still to be defined more rigorously.

STUDIES IN PATIENTS

Resting baseline activity

Numerous psychophysiological measures have been examined with regard to possible differences between anxious patients and normal control subjects.[10] Pulse rate and electromyogram activity were found to be higher in patients than in normal controls.[525] Similarly, skin conductance (sudomotor activity) is generally higher in patients with anxiety states.[273] The electromyogram recorded from the frontalis muscle was reported to be reliably higher in anxious patients than in controls but recordings from forearm muscles showed less consistent intergroup differences.[322,325] Simultaneous recording of the electromyogram from seven recording sites was carried out by Iris Goldstein[152] in 21 anxious female patients and 21 female controls. At rest, activity levels were higher in the patients only at the masseter and forearm extensor sites. However, in other work, no differences between patients and normals have been found.[273] The heart rate is elevated in patients with anxiety states in confirmation of clinical experience[482,525] and forearm blood flow is consistently increased in anxious patients.[239] The amount of alpha activity in the electroencephalogram diminishes with increasing anxiety,[478,496] and it has been reported that the dominant alpha frequency in normal subjects is 10 Hz (cycles per sec) whereas in anxiety states it is 11·2 Hz.[46] However, in general, electroencephalographic studies have not shown any specific abnormality in patients with anxiety.[110] Respiration is more rapid in anxious patients[152] and respiratory efficiency is impaired.[80,222] Similarly, in normal students nearing examination time, increase in heart rate and blood pressure and a drop in peripheral resistance were found; blood pressure is also elevated in anxious patients.[211] Salivation has been reported as being about equal in anxiety states and normal subjects,[376] despite dry mouth being a sign of anxiety.

These studies mentioned above have tended to show that various measures are elevated in anxious patients as compared with normals. A complimentary approach has been to attain a resting baseline by inducing sleep in both groups. Anxious patients show greater changes as sleep supervenes than normals; this has been reported for both finger pulse volume and heart rate.[4] A similar approach has been the sedation threshold test as originally described by Shagass together with its more recent variations.[446] Amylobarbitone sodium is injected intravenously at a constant rate until an end point is reached. This end point may be electroencephalographic such as the onset of fast low voltage activity or behavioural such as slurring of speech or of inability to do simple mental arithmetic. Significantly more drug is needed to reach the criterion in anxious patients than in normal subjects and this

has been interpreted as meaning that at the start of the injection the anxious patients were more active physiologically.

Spontaneous activity

Relatively few studies have examined this aspect of physiological functioning. Spontaneous skin conductance fluctuations are consistently higher in anxious patients than in control subjects.[262]

Responses

Physiological responses in anxious patients have been widely studied, usually with the notion that anxious patients, being neurotic, must therefore be more reactive physiologically.

Reactivity refers to the *tendency* of a subject to respond to a stimulus in terms of magnitude of response, duration of response or both. However, examination of the results of several studies suggests that no easy generalisation is possible.[153] For example, Kelly[239] showed that anxious patients were less reactive than normals with respect to their forearm blood flow when stressed by being asked to do mental arithmetic under harassment. Similarly, galvanic skin responses tend to be smaller in patients than in normals.[273] Wing[525] showed that electromyographic activity changed less in anxious patients than in controls during a difficult colour-naming task. Conversely, other studies have suggested that patients were more reactive than controls and in general these studies have used the electromyogram.[92,152,322,337] The reasons for this discrepancy are complex but may be partly due to the higher "resting" activity of the patients precluding a marked response when a stimulus is applied. In the case of the electromyogram, however, both resting and response levels of anxious patients are still low in comparison to those which could be reached during extreme conditions such as severe exercise, so increased reactivity could still manifest itself.

When several physiological measures are examined simultaneously complex results are obtained. It was originally suggested by Lacey and his colleagues that each subject tends to exhibit a reproducible pattern of response to a repeated stimulus (intrastressor stereotypy).[257,261] Later the concept was widened to include responses when different types of stimuli were applied when each individual still appeared to give the same pattern of response (interstressor stereotypy).[259,260] These concepts fit into the general idea of response specificity which implies, for example, that one individual will show most reactivity in the heart rate measure while another will show most sudomotor reactivity. In opposition to these views, Davis[93] regarded "situational stereotypy" as being more important, the response pattern depending upon the type of stimulus situation. More recently, Lacey[258] has modified his position and now proposes that different somatic processes

have different roles to play in the execution of different types of behaviour and thus the response pattern is also dependent on the properties of the stimulus. The concept of response specificity has found clinical application in the experiments of Malmo and Shagass[320] who divided a group of anxious patients into those with complaints involving the cardiovascular system and those with head and neck pains. The former group had a higher mean heart rate and heart rate variability than the latter group whereas for electromyographic levels the position was reversed. The principle of "symptom specificity" was propounded: "In psychiatric patients presenting a somatic complaint, the particular physiological mechanism of that complaint is specifically susceptible to activation by stressful experience." Within the electromyographic system, Sainsbury and Gibson[421] showed that anxious patients with headaches had high frontalis EMG levels whereas patients with aches in the limbs and "rheumaticky pains" had high forearm EMG's.

Adaptation refers to changes in the background level after a stimulus returning to prestimulus levels, while habituation refers to the decrement in response as discrete stimuli are repeated. Anxious patients consistently adjust more slowly after stimulation than do normal subjects. For example, Rubin[414] reported that pupillary dilation in response to a painful stimulus quickly disappeared when the stimulus was discontinued in normal subjects whereas patients' pupils remained dilated for several minutes. Martin[337] demonstrated that EMG levels remained high in patients during a sequence of stimulation procedures whereas it steadily diminished in controls. Similar findings have been reported for the blood pressure,[211,321,324] forearm blood flow[239] and electromyograph.[91,525]

The second way in which it can be shown that anxious patients have impaired homeostatic processes is to apply repeated identical stimuli to the subjects. Slower extinction of galvanic skin responses in anxious patients than control subjects has been reported[204,273] and Davis, Malmo and Shagass[92] demonstrated a greater decrement in the EMG responses in normal subjects to repeated bursts of white noise than in anxious patients. The exciting film "Wages of Fear" was shown twice with a one-week interval to groups of anxious and non-anxious patients. Non-anxious patients showed decreased physiological activity on the second occasion, i.e. they adapted; anxious subjects showed increased activity.[75]

ENDOCRINOLOGICAL STUDIES

Studies of the neuro-endocrine system have mainly concerned adrenal function, both of the cortex and of the medulla.[149] 17-hydroxycorticosteroid levels in the blood and excretion products in the urine have been most intensively examined. In general, raised levels have been found during stressful, anxiety-provoking life-situations such as examinations;

however, the levels were still within physiological levels.[39] More specifically, plasma levels in patients undergoing major surgery appeared to be more closely related to the degree of the patient's emotional involvement in the situation than to his anxiety level *per se*.[391]

Stressful situations have included soldiers in combat or in training and their corticosteroid responses have been assessed, e.g. the work on paratroop trainees by Grinker and his co-workers.[23] Similarly, Berkun, Bialek, Kern and Yagi[31] exposed soldiers to five simulated situations: (1) aircraft emergency during flight; (2) disruption of military exercise by misdirected shells; (3) forest fire; (4) radioactive fallout; and (5) the soldier believed himself responsible for a situation in which a colleague appeared to be seriously injured. Affect ratings and urinary corticosteroids were measured. Situations (1) and (2) produced rises in the physiological indices with (3) and (4) having less effect. Situation (5) had the greatest effect.

Hypnotic induction of anxiety has been used in attempts to raise plasma hydrocortisone (cortisol) levels but the changes induced were small.[383] Similarly, infusions of hydrocortisone did not increase the amount of anxiety experienced by hypnotised subjects instructed to feel anxious.[290] Hydrocortisone infusions hardly affected anxiety levels in non-hypnotised subjects.[509]

In studies with anxious patients, raised cortisol levels have been described but the increases were only moderate.[384,386] Increases could be induced in the patients by means of stressful interviews, the further increase tending to be related to the amount of anxiety engendered. Further studies showed that the cortisol changes paralleled total emotional changes (anxiety, anger and depression) more closely than any one emotion.[385] More recently, techniques have been developed to assess the cortisol turnover rate in the plasma which was about 50 per cent higher in a small group of anxious patients than in a group of normals.[380]

Other indices of adrenal cortical functions include the eosinophil count which drops appreciably in conditions of emotional stress;[74, 104,379] however, this measure is no longer accepted as a specific indicator of adrenocortical function.

One may conclude that the pituitary-adrenal cortical system is sensitive to psychological influences and that ACTH release and subsequent rise in cortisol occurs, "not in association with a specific emotional state, but rather with a wide variety of emotional disturbances which may have the relatively undifferentiated element of distress or arousal".[340]

Although cortisol has been the most studied corticosteroid in the context of stress and anxiety, aldosterone has also been found to be raised in anxiety states.[112]

Adrenal medulla

The adrenal medulla secretes adrenaline (epinephrine) and small amounts of noradrenaline (norepinephrine), the ratio between the two varying from species to species. Noradrenaline is produced at sympathetic nerve endings.

Several experiments have examined the effects of adrenaline and noradrenaline given by intramuscular injection or by intravenous infusion.[47] The first study[505] involved the injection of 5 mg of adrenaline intramuscularly in army recruits suffering from the "irritable heart" syndrome—dizziness, fatigue, palpitations. Symptoms characteristic of their acute anxiety reactions were induced in the patients together with observable physiological changes. The normal controls reported no symptoms following the injection and their physiological reactions were smaller.

More recent investigations have followed the pattern of this pioneer work. In general, the symptoms induced by adrenaline and noradrenaline and the physiological changes observed resemble closely those which occur in response to stress in normal subjects and those occurring spontaneously in anxious patients. For example, Basowitz and his coworkers[22] interviewed 12 normal subjects (young interns) to ascertain their specific reactions to previous stress, e.g. palpitations, tremor, etc. Adrenaline (5 μg/kg body weight/hour) was infused intravenously and its effects compared with saline using double-blind procedures. Adrenaline produced symptoms consistent with those elicited in the history taken at the initial interview. Cardiovascular changes included a mean rise in pulse rate of 13 beats/min. and in pulse pressure of 20 mm of mercury. Excessive symptoms but few cardiovascular changes were noted in emotionally labile subjects; conversely, no symptoms but marked physiological changes occurred in subjects with rigid personalities. In another study, no systematic relationship was found between the intensity of the physiological and subjective reactions.[130] Subjective estimates of anxiety declined as each infusion proceeded.

In general, normal subjects tend to report not anxiety but "feeling as if I were anxious" (e.g.[130]). In patients, however, the symptoms closely resemble those of spontaneous morbid anxiety. Breggin[47] regards two factors as crucial in the interpretation of such data; firstly, the strength of the subject's previously learned association between psychological feelings of acute anxiety and sympathomimetic symptoms such as palpitations; secondly, the degree of current anxiety engendered by the experimental setting. He suggested that the sympathomimetic symptoms produced by the adrenaline further reinforced the subject's anxiety induced by the experimental situation.

Another approach has been to measure urinary catecholamine excretion during stressful procedures. The amounts of adrenaline and

noradrenaline relate to the secretion of this substance into the blood. Urinary measures have the disadvantage of reflecting changes over a time scale of not less than an hour. Plasma measures reflect changes over shorter periods and are now becoming available.

In behavioural tasks the amount of noradrenaline excreted is positively correlated with improvement in performance during stress.[131]

An extensive series of experiments in this field were carried out by Levi and colleagues at the Laboratory for Stress Research in Stockholm.[286,287] Urinary excretion of both adrenaline and noradrenaline increased when subjects carried out a difficult task, sorting out small steel balls of four very similar sizes over a two-hour period. Some subjects showed great rises in catecholamine excretion from values of 15–30 ng/min. to values over 300 ng/min. Office work—proof-reading with typewriter noise as a distraction—was also effective in increasing catecholamine excretion rates.

Levi also used film-viewing as a stimulation procedure. Bland natural-scenery films lowered catecholamine excretion, which reflected feelings of calmness. A tragic, moving film increased catecholamine excretion, but so did a comedy film. Thus, the intensity, not the quality, of affective arousal appeared to determine the rate of catecholamine excretion. In general, moderately anxious individuals did not excrete more catecholamines than did normal subjects. However, considerable inter-individual variability did occur although within-individual consistency was quite good.

Other measures

Thyroid function has been much less extensively studied and the results are less conclusive.[150] Some thyroid functions increase during stress and acute anxiety.[8,192]

Plasma free fatty acids have been used as an index of response to stressful procedures. For example, speech samples from 10 male non-psychotic inpatients and 14 students were scored for their anxiety content. A significant positive correlation was found between these scores and plasma free fatty acid concentrations. Similar correlations were also found with plasma triglyceride concentration.[160]

The amount of hippuric acid excreted after the injection of a substance like sodium benzoate is an index of liver detoxifying functions. It has also been found to relate to the level of anxiety in subjects and as anxious patients were treated and their anxiety levels decreased, hippuric acid excretion went down.[381,382] Johannsen and his co-workers [220] injected 1·77 G of sodium benzoate intravenously and assessed hippuric acid excretion in a group of mixed psychiatric patients; it correlated to some extent with the Taylor MAS scores and the MMPI A scale and Pt scale.

Lactate

Much interest was aroused recently by the work of Pitts and McClure[388] on the role of lactate ions in anxiety attacks. Their work stems from the finding that exercise produces more lactate in patients with anxiety states than in controls. Pitts and McClure "developed the idea that perhaps the lactate ion itself could produce anxiety attacks in susceptible persons". To test this idea they performed a double-blind controlled experiment in which the following were infused in random order intravenously into a group of 14 patients with anxiety neurosis and into a group of 10 normal controls: 500 millimols sodium (DL) lactate, 500 millimols sodium (DL) lactate with 20 millimols calcium chloride and 555 millimols glucose in 167 millimols sodium chloride. These solutions have similar osmolarities and were given as 20 ml/kg body weight during a 20-minute period to each subject. Symptoms were rated.

The infusion of sodium lactate produced symptoms which "were markedly similar or identical" to those experienced in their "worst attacks" by the anxious patients. Such reports were fewer from normal subjects. The anxiety symptoms caused by lactate infusion were greatly reduced in frequency when the lactate plus calcium chloride was infused and the glucose in saline infusion produced almost no symptoms in either patients or controls.

The authors suggested that anxiety symptoms were related to hypocalcaemia produced by lactate infusion and that "anxiety symptoms could occur in the normal person under stress as a consequence of marked increase in lactate production in response to increased epinephrine release; the patient with anxiety neurosis would be someone especially subject to this mechanism because of chronic overproduction of epinephrine, overactivity of the central nervous system, a defect in aerobic or anaerobic metabolism resulting in excess lactate production, a defect in calcium metabolism or some combination of these".

These suggestions were strongly criticised by Grosz and Farmer[169] who pointed out how tenuous the link was between anxiety symptoms and hypocalcaemia. Anxiety can occur without high blood lactate levels and high blood lactate levels without anxiety. The infusion of sodium lactate produces a metabolic *alkalosis* whereas endogenously produced lactate ion shifts the acid-base balance of the body towards metabolic *acidosis*. Sodium bicarbonate levels rise with sodium lactate infusion and the compensatory respiratory acidosis (adaptive hypoventilation) could be accompanied by feelings of discomfort. Grosz and Farmer further pointed out that the rise in lactate produced by the infusion would cause but a trivial change in ionised calcium level in the blood. They concluded that the hypothesis "as a generalised explanation for anxiety neurosis seems to be incompatible or irreconcilable with many

and diverse clinical physiological and biochemical findings and considerations".

Although the infusion of sodium lactate may not produce its effect by affecting calcium levels, there is definite evidence that it can cause anxiety, especially in anxious patients. Furthermore, such subjective reports of anxiety are accompanied by appropriate physiological changes such as increases in forearm blood flow and tachycardia.[242] As shown earlier, adrenaline infusions produce autonomic symptoms which are described as anxiety-like by anxious patients but not by controls. The expectation of the subject is also important. It is known from animal studies that lactic acid causes a marked release of adrenaline and noradrenaline from the adrenal medulla.[60,533] Thus the simplest explanation is that lactate infusions are an indirect way of raising plasma catecholamine levels with the expected results in anxious patients. The catecholamines in turn could produce more lactate in the manner suggested by Pitts and McClure: a vicious circle could then result. Whatever the explanation, further studies are necessary to establish the probable mechanism. In this connexion it is unlikely that lactate exerts its effects via beta adrenergic receptors as propranolol, a beta adrenergic blocking agent, does not attenuate lactate-induced psychological and physiological effects.[13] The possibility still remains that lactate can act at least in part through catecholamine release from the adrenal medulla, as alpha effects are not blocked by propranolol.

Physiological patterns accompanying anxiety and other emotions

The psychophysiological, neuroendocrinological and biochemical measures reviewed in this chapter are less indices of anxiety than of general emotional arousal. Much discussion has concerned the problem of differentiating anxiety from other emotions by means of characteristic physiological patterns. Nonetheless, experimental work on this important topic has been sparse.[335]

Some studies have tried to differentiate anger from anxiety. Ax[15] exposed 43 normal subjects to two experimental situations, one designed to induce anxiety (actually fear of electrocution), the other to induce anger (towards the experimenter's stooge who behaved overbearingly). Rise in diastolic blood-pressure, drop in heart-rate, sudomotor variability and muscle tension level were all greater in anger; sweat-gland activity, number of muscle tension peaks and respiratory rate increases were greater with fear. Correlations between the measures were low but greater in anxiety than in anger, a finding interpreted as showing "greater physiological integration" in the former condition. A second suggestion was that the physiological changes with fear resembled those of adrenaline infusion whereas those with anger resembled the effects of adrenaline and noradrenaline combined. Similar findings for anxiety were claimed by Funkenstein et al.[141] and by Schachter:[434]

diastolic blood pressure increased more in anger; heart rate, cardiac output, palmar conductance and respiration rate rose more with fear. All the investigators concluded that anxiety gave an adrenaline-like response but the anger pattern was variously interpreted as noradrenaline-like (Funkenstein), mixed (Ax) and adrenaline-like at high intensities but noradrenaline-like at lower levels (Schachter). However, attempts to describe physiological patterns in terms of adrenaline and noradrenaline infusions should merely be regarded as a convenient shorthand as there is no evidence that widely differing patterns of catecholamine secretion can occur naturally.

There are other objections to these types of study: the emotions aroused should be equated for severity and length of time sustained, a counterbalanced order should be used and detailed enquiry made into the emotions actually engendered. Specific physiological correlates with specific emotions are so far neither impressive nor encouraging. What Johnson[220a] noted about different states of consciousness applies with equal force to different feeling states. The same EEG and autonomic changes occur in different states of consciousness, and cannot be used to define those states. The state of consciousness of the subject must first be known before the physiological significance and possible behavioural meaning of the EEG and autonomic responses can be inferred. At the present time, psychophysiological measures have limited meaning for the clinician unless they are combined with data about the patient's feeling state while those measures are taken.

CONCLUSIONS

It should not be thought that physiological and biochemical measures provide an easy answer to the problem of measuring emotions in general and anxiety in particular. The techniques are often complex and require physiological or biochemical expertise and an awareness of the difficulties of adapting such techniques to the study of patients. Analysis of recordings is time-consuming and subject to error, and experience is required to detect artefacts.

The measures are best regarded as aids to clinical observation which can be refined to a fair degree of accuracy. They are most successful when used to monitor emotional changes within patients during single recording sessions, e.g., during relaxation training. Physiological recordings are also useful in comparing patients between sessions, for example, with different treatments. They are least satisfactory in comparing patients with each other or with normal subjects.

Of the measures, heart rate is the easiest to record but, without automatic processing, the analysis of records is tedious. Forearm blood flow is a cumbersome method, even when a strain-gauge is substituted for the plethysmograph. It gives intermittent readings only but, in experienced hands, accurate recordings can be made. Skin conductance

is relatively easy to record, free from artefact, and provides a continuous detailed recording. It is most useful for measuring responses to discrete stimuli.

It is most important for someone considering the use of a physiological measure to be clear as to the type of information he wants, e.g., changes with stimulation or relaxation, between-groups comparison and the frequency with which measures need to be taken. He should not underestimate the complexities of the techniques but should seek expert advice.

Chapter Nine

CONCLUSION

In this chapter we will attempt to draw together some of the threads which run through the topic of anxiety. However, it is impossible to reconcile all the differing views on anxiety[128] as the term is used to cover a series of widely disparate concepts. The importance of certain studies will be re-emphasised in the following sections but we will be particularly concerned with the introduction of some key concepts such as arousal and emotional response. One problem is to suggest a consistent plan or model of the mechanisms underlying the production of anxiety, both normal and clinical. Anxiety can be regarded as an intrapsychic phenomenon (or even as a noumenon*), as a behavioural response, as an intervening variable modifying behavioural styles, as a central concomitant to a specific physiological pattern, etc., depending on one's viewpoint. We shall explore the advantages of an eclectic examination of anxiety from several aspects simultaneously by regarding it as a syndrome of emotional response.

Anxiety as an emotional response syndrome

Anxiety is an emotion and like other emotions can be regarded as a response syndrome. This useful concept has been elaborated by Lazarus and co-workers[14,283] and others.[471] A disease syndrome is not defined by any single symptom, or set of symptoms, nor is an emotion defined by a feeling in isolation, nor has it one centre or locus. Both diseases and emotions can be classified according to their aetiology, phenomenology and course. The character and identity of an emotion is inferred from the pattern and development of reactions in relation to the eliciting conditions and to the state of the individual. Each emotion has a variety of response patterns, so that it is only a conceptual convenience to call an emotion such as anxiety a unitary phenomenon. Each emotion can have many component reactions which occur concurrently and sequentially and which are often poorly correlated with one another. Anxiety as an emotional response is an organised syndrome across three main dimensions: *cognitive-subjective* which involves the appraisal of threat or danger with its accompanying sensation of fear; *motor-behavioural* with certain action tendencies;

* Object of intellectual intuition devoid of all phenomenal attributes—O.E.D.

and *physiological* changes which are part of the mobilisation to action, whether or not these tendencies are actually expressed or inhibited. These three dimensions are integral parts of an emotional response, and the particular patterns which they display provide the distinguishing characteristic of each emotion.

Emotions such as anxiety can thus be conceived as response systems. "They are systems because they entail the operation of interrelated units. They are response systems because emotions are largely distinguished from other psychological phenomena, and one from another, on the basis of their response characteristics."[14]

Anxiety, like other emotions, can be analysed into component parts, some of which may be primarily biologically determined and others culturally influenced. Lazarus et al.[283] point out that phylogenesis predisposes the organism to respond adaptively to certain types of stimuli in a manner contributing to species survival. Similarly, through the process of socialisation, a culture imposes on its members certain ideas which shape their appraisal of emotional stimuli and their modes of response to those stimuli. People have dispositions to search out, respond to and selectively attend to stimuli of certain types, and these dispositions result from an interplay of phylogenetic, cultural and ontogenetic influences. In some emotions, e.g. sudden fright, biological expressors are very important, while in others, such as guilt, conventions and cognitive reactions are dominant. "Emotional reactions can be likened to a rope, with one end anchored in the biological and the other in the cultural. No single strand (type of reaction) runs through the entire rope, yet they are interwoven to form a single concept—emotional response."[14]

Cognitive aspects

With respect to the cognitive aspect of anxiety it was stressed that first a person must evaluate that he is in fact threatened—a process of appraisal.[14] Then that person must evaluate what can be done to cope with that threat—secondary appraisal. If threat is not appraised a person may cope with dangerous situations without developing any anxiety, e.g. avoiding a hot stove in the kitchen or an oncoming car while crossing a road. The appraisal of threat involves a continual searching for, sifting through and evaluation of cues. The rises and falls of anxiety levels and shifts in their quality reflect a continual process of appraisal and reappraisal.

After sudden transient danger has been dealt with promptly and coolly, subjective alarm may be experienced shortly after the moment of peril has passed, e.g. an experienced driver might brake hard automatically and thus avoid a serious accident, yet shake with anxiety for the next few minutes when he is no longer in danger. This could

be due to retrospective appraisal of the situation. It might also reflect the time it takes for some physiological responses to develop.

A given situation may be evaluated as threatening for a variety of reasons. In soldiers undergoing paratroop training Basowitz et al.[23] found two types of anxiety. One they called shame-anxiety, the fear of failure, while the other was termed harm-anxiety—the fear of physical injury or death. Greater anxiety was evoked by the anticipation of failure than by the fear of physical injury. No clearcut relationship has yet been found with either of these anxieties and the habitual level of anxiety in an individual, i.e., trait-anxiety.[471]

Relations between cognitive and physiological aspects

As Schachter[435] and Lazarus et al.[283] emphasise, anxiety often begins with the appraisal of danger, and physiological changes quickly follow. These physiological changes do not actually endure long after the subjective feeling of danger has disappeared and it is an open question whether even chronic anxiety can by itself produce lasting disease. Gorlin[159] noted that "anxiety can transiently provoke cardiovascular responses, but it is unproved that it can lead to persistent abnormality . . . most patients with anxiety-provoked cardiovascular responsiveness do not develop cardiovascular disease". In keeping with this idea, Wheeler et al.[520] followed up 173 patients with anxiety neurosis for 20 years, yet found no evidence that they developed any lasting physiological changes or special diseases as a consequence.

Though anxiety usually starts with a cognition, it can also begin with physiological changes which are then followed by the subjective sensation of anxiety, e.g. anxiety can *result* from tachycardia as well as cause it.

The mechanism might be along the lines "my heart is beating fast; when I am frightened it usually speeds up, so I must be frightened now," i.e., tachycardia first becomes a learned cue for the perception of anxiety and later triggers it by itself. Frohlich et al.[139] described 2 patients in whom severe tachycardia, palpitations and anxiety were produced in response to increased beta-adrenergic activity, this activity being especially provoked by standing. Selective blocking of beta-adrenergic receptors by drugs such as propranolol abolished both the tachycardia and the anxiety. Similarly Maranon (described by [435]) reported that the injection of adrenaline into normal subjects secondarily produced sensations resembling anxiety. Schachter[435] has shown that inexplicable mild autonomic sensations can also get labelled with whatever emotional tag is regarded as appropriate to the situation prevailing at the time. Finally, Breggin[47] suggested that initial adrenal medullary secretion during the anxiety may evoke sympathetic symptoms or cues which further reinforce anxiety responses whilc a more prolonged secretion may evoke parasympathetic and fatigue or sedative-like effects. Breggin thought that since adrenaline is more prominently secreted in anxiety

than in other responses such as anger, it might account for many of the clinical phenomena associated with anxiety.

Another mechanism is also important in the maintenance of anxiety. This is physiological feedback. When anxiety occurs there are changes in effector systems like the cardiovascular and respiratory systems. In time, these changes are signalled back to the central nervous system. Such feedback is, of course, routine in physiological reflex systems but often in anxiety it reaches conscious levels so that the subject becomes aware of, say, palpitations. This may reinforce the feeling of anxiety. The physiological changes are not a prerequisite of anxiety as the James-Lange hypothesis required nor does the emotion arise solely from awareness of an abnormal physiological change. Instead a positive feed-back mechanism is involved with heightened emotion producing physiological changes, awareness of which begets further anxiety and so on.

Dissonance between different components of anxiety response

We have noted that the different components of an emotional response like anxiety may be poorly correlated with one another, e.g., a person may claim that he feels anxious yet look calm and show no physiological changes, or he may appear agitated and show gross physiological concomitants of anxiety while maintaining that he is not anxious or he may say he is anxious and look it, yet show no autonomic changes. Theoretically there are seven possibilities which can be seen from Table 9.1. The frequency of each of these patterns and the conditions which generate them remain to be determined experimentally. At the moment we can only guess their relative occurrence.

Table 9.1

Main possible patterns of the anxiety response

Component	1	2	3	4	5	6	7
Subjective-cognitive	+	+	+	−	−	−	+
Motor-behavioural	+	+	−	+	−	+	−
Physiological	+	−	−	+	+	−	+

\+ indicates the component shows the response appropriate for anxiety.
− indicates the component does not show the response appropriate for anxiety.

Pattern 1 is undoubtedly the commonest to be found with marked anxiety. Here there is congruence between subjective, behavioural and physiological features of the emotion. In pattern 2 the absence of physiological indices of anxiety is often surprising and inexplicable. This pattern occurs rarely in patients experiencing anxiety under "resting" laboratory conditions. One possible explanation when it does appear is that the subject is in fact responding physiologically, but with

responses which are not being measured at the time, e.g., salivation and tachypnoea, rather than tachycardia and sweating. Another possibility is that the subject may have a high threshold for autonomic responses which are triggered by emotion. A related explanation would account for pattern 3, which is common in mild anxiety. Here the subject feels slight qualms of anxiety but gives no evidence for this in his behaviour or physiology. Patterns 4, 5 and 6 might perhaps be found in certain states which are variously labelled as stoicism or belle indifference. Finally patterns 3, 5 and 7 could result from self-control learned for cultural or personal reasons. One possible sequence here is that a subject starts life with pattern 1, is then taught to suppress outward signs of anxiety, showing pattern 7 at that stage. He might go on to learn to suppress physiological effects as in pattern 3, and subjective sensations as in pattern 5.

As Lazarus et al.[283] have commented, "The precise pattern of agreement and disagreement between different components of anxiety contains within it information about the kind of transaction which a person is having within himself and with various aspects of his environment. A particular pattern might be the characteristic way for that person to respond physiologically or result from his attempt to disguise his anxiety, to simulate it, or to make his response conform to what is acceptable for him and his culture." Assessment of a patient's state should take the context and his background into account.

ANXIETY AS A FORM OF AROUSAL

Both the physiological and motor-behavioural components can be examined further within the context of arousal theory. Unfortunately, there is no general agreement regarding the concept of arousal and greatly disparate views have been expressed by psychologists and physiologists. Epstein[116,117a] has presented a balanced review of the topic and also described empirical data to support his formulation of the subject. In the literature arousal is sometimes spoken of as vigilance, and anxiety is said to develop from this.[295] Normally the vigilance or orienting response enables the individual to attend more closely to environmental changes. This response is usually brief. However, if vigilance is maintained for long then anxiety appears, and in animals, experimental neurosis occurs. "When the capacity for maintaining intense and unremitting vigilance is exceeded (e.g. during long difficult regimes of conditioning) the pent-up nervous tension thereby released will disrupt the operation of the complex and delicate conditioning machinery and lead to chronic states of diffuse or concealed vigilance —experimental neurosis. . . . It is . . . as if the animal were compelled to keep senselessly repeating, 'what is it, what is it, what is it?'" (p. 190–1). This state was produced in sheep by presenting them with repeated trials of shock preceded by a tone of 10 sec. duration.[295] As

presentation of shocks alone on the same schedule did not cause an experimental neurosis, it was inferred that it was the vigilance produced by the tone signal which was operating.

Goldstein[154] observed that brain injured soldiers became afraid and defensive when in unfamiliar situations. He concluded that anxiety resulted from an inability to cope with vague threats to the organism from the environment.

Working with client-centred psychotherapy, Rogers[409] noted that people become anxious when they perceive a threat to their self-concept. This occurs when there are discrepancies between the subject's image of himself and other perceptions of himself which cannot be ignored. ". . . if the individual becomes to any degree aware of this tension or discrepancy he feels anxious, feels that he is not united or integrated, that he is unsure of his direction" (p. 511).

An existential analysis of anxiety by May[349] is similar to that of Rogers and of Goldstein. He regarded anxiety as a feeling of diffuse apprehension which is vague and objectless, and is associated with feelings of uncertainty and helplessness. It is "the apprehension cued off by a threat to some value which the individual holds essential to his existence as a personality" (p. 191). May posited three stages in response to threat—first startle, followed by anxiety, and finally, when the source of threat has been assessed, by fear. Lazarus[282] too, has defined anxiety as a reaction to threat when the source of threat remains ambiguous. Epstein[117a] pointed out the advantage of identifying anxiety as an emotional state only, without reference to the conditions that give rise to it.

Anxiety has also been thought of as a failure in assimilating percepts.[313] Berlyne[32] has noted how people continually seek new experiences. McReynolds suggests that there is an optimum rate for obtaining and assimilating new percepts. When this is too low it gives rise to boredom, and when too high, anxiety. Anxiety is also generated by the surplus of unassimilated percepts which accumulates with extreme novelty or by incongruencies in the content of percepts and the systems into which they are to be assimilated.

There is some experimental evidence to support the notion that each individual has an optimal level of arousal. Taylor[484a] recorded the skin conductance (palmar sweat-gland activity) of subjects driving in traffic. He found that fluctuations in activity tended to occur fairly constantly within each individual and to vary little with traffic conditions. There was great inter-individual variability. He analysed his data with great care and concluded that it supported the "idea that drivers adopt a level of anxiety that they wish to experience when driving, and then drive so as to maintain it. . . ."

Indecision and the necessity to make a choice produce anxiety, according to Kierkegaard[246] (see also p. 20). For him, anxiety was a

state of incompletion or lack of closure. Decision-making arouses diffuse or conflicting action tendencies which lead to anxiety unless they are expressed in directed action or a commitment to action.

A related concept is that of Mandler and Watson,[327] who described the anxiety which results from interruption of organised behavioural sequences or plans. Interruption is said to increase arousal and finally to lead to anxiety. When an alternative response cannot be made anxiety will increase and the subject will feel helpless. The idea of anxiety as a function of unsatisfied needs is also put forward by Cattell.[67] He regards anxiety as associated with uncertainty and anticipation with regard to unfulfilled needs or values. It is fostered by the existence of incompatible needs and by inability to focus upon external fears.

Epstein[117a] thought these different formulations of anxiety had the common denominator of high arousal, which could result from primary overstimulation, cognitive incongruity and/or response unavailability. Primary overstimulation can result from pain or from stimuli whose significance has been learned. It is associated with feelings of being overwhelmed.

Cognitive incongruity results from violation of expectancies for emotionally-significant stimuli. It involves an inability to form an adequate cognitive model of events. Pavlov's dogs became disturbed by difficult perceptual discriminations and long delays which impaired discriminative performance. Failure to integrate data into the self-concept or predictive model of the environment is implicit in the ideas of Goldstein, Rogers, May and McReynolds. Mandler's formulation involved incongruity between planned sequences of behaviour and the possibility of their execution. All these ideas centre round a "mismatch between a cognitive model, or expectancy, and reality. . . . individuals have a need to organise the data of the world into a consistent and integrative predictive system, and . . . anxiety results when the system or its elements, corresponding to hypotheses, are disconfirmed, or seen as inconsistent with each other." The subjective feelings which accompany cognitive incongruity are said to include disorganisation and disintegrations.

Cognitive incongruity also contributes to response unavailability, since it is hard to make a correct response without knowing which stimulus to respond to. Response unavailability can also occur for other reasons, e.g., because delay is necessary before the response can be made, or there are conflicting response tendencies, or the individual's repertoire does not include the appropriate response. The idea of response unavailability is implicit in Mandler's interrupted responses, Freud's early ideas about blocked sexual impulses, Kierkegaard's state of incompletion, and May and Lazarus's unknown threat which cannot be responded to. The subjective feeling associated with response unavailability is said to be helplessness.

Epstein thought that the major significance for psychopathology of primary overstimulation, cognitive incongruity and response unavailability was that they all produce high arousal. He defined anxiety as an unresolved fear, or alternatively, as a state of undirected arousal following the perception of threat. Fear is defined in terms of avoidance behaviour. "When there is perception of threat in a contest which evokes flight tendencies, an incipient fear motive involving a diffuse state of arousal and avoidance tendencies is produced, and evokes a unique experience that can be identified as anxiety. The anxiety remains until the diffuse arousal is channeled into some directed motive state, such as fear that supports directed action, such as flight."

Arousal is defined by Epstein[117,117a] as the varying level of excitation of an individual along a dimension from relaxed sleep to emotional excitement. It is the total result of inner and outer stimulation of that individual, and is a component of all states of motivation. Being energy systems, organisms must cope with the total level of stimulation to which they are subjected, and control of this within homeostatic limits must occur within the nervous system, possibly through several levels. Epstein sees arousal as more fundamental than fear or anxiety, since it also underlies other emotions such as sexual excitement, anger or intense joy. When a subject is aroused by fear he tends to escape from or to avoid the situation producing it, e.g., a man will run out of the path of an oncoming car. In contrast, anxiety-arousal is a more diffuse and helpless response to an unknown threat. It can be seen as unresolved fear, unresolved in the sense of not knowing what to do to reduce the perceived threat. Some evidence suggests that anxiety can be more unpleasant than fear. Bond[41] observed that a few combat flyers could not stand the anxiety between missions and committed suicide by crashdiving their planes, in this way replacing an uncertain by a certain fate.

The factors determining arousal level were listed by Epstein[117a] as intensity of stimulation, rate of stimulation, expectancy, opportunity for motor discharge and the preceding excitatory state of the organism. Any increase in stimulation, whether internal or external, will heighten arousal. Excessive arousal may be distressing if the accompanying emotion is unpleasant such as anxiety or fear in which case the organism tries to reduce the high arousal. If the emotion is pleasant as in joy, avoidance will not occur. However, excessive arousal even in pleasant emotional states may be tinged with unpleasant feelings as in ecstasy. Experimental neurosis occurs in conditions which are arousing rather than frightening, e.g. difficult discriminations and unexpected events. Emotional states like intense joy or rage can also disrupt behaviour by producing extreme arousal. Different physiological systems have varying relationships to given levels of arousal.[264]

Unlike Epstein[117a] we prefer to restrict the concept of arousal to levels

of vigilance during the waking state and would exclude sleep from this dimension. Johnson and Lubin[220b] have shown that physiological habituation during sleep does not follow the course to be expected from regarding sleep as decreased arousal.

Anxiety is but one form of overarousal.[335,336] Other kinds of overarousal include horror, rage and ecstasy. The concept of arousal permits better understanding of the relationship between physiological changes and emotion. Physiological changes reflect arousal and not any particular emotion. It is therefore misleading to regard physiological measures such as sweat-gland activity as "measures" of anxiety. Taken in isolation such measures simply indicate the level of arousal. Which particular emotion is occurring has to be inferred from the context of that arousal, from overt behaviour and from introspective accounts, all taken together. Physiological changes are but one part of an overall pattern which is construed to be anxiety.

The concept of arousal is imprecise and has been criticised because its practical application is complex and can be confusing. Even measurement of the *level* of arousal involves many problems. If arousal is a unitary phenomenon then several physiological measures reflecting its level should correlate appreciably with one another. In general this has not been found, so attempts have been made to fragment the concept into many components such as "autonomic" arousal, "cortical" arousal, etc. However, there are good reasons why such measures may not interrelate highly, e.g. the overriding physiological needs of the body. These create "floor" and "ceiling" effects which reduce correlations between measures of various systems with differing physiological limits. An illustration of the "floor" effect can be found in a relaxed individual, whose forearm blood flow is low. If he becomes even more relaxed, a further drop in blood flow may not occur as a minimum flow is required to maintain function in even relaxed muscles. The "ceiling effect" occurs in a person whose heart rate is already markedly raised. With further anxiety his heart rate cannot rise much more before it reaches the limits of capability of the cardiovascular system.

HABITUATION

Unexpected events heighten and familiar ones lower arousal. As a stimulus is repeated several times the response to it usually diminishes, a phenomenon which is termed habituation.[267] Habituation is an inhibitory process which is different from fatigue, since the insertion of an extraneous stimulus between habituation trials reinstates the response, while a fatigue effect would reduce it yet further. This inhibition is highly selective and discriminating. It is related to the development of expectancies in which incoming stimuli are matched to a cognitive model of the stimulus situation.[456] The more a stimulus is expected, the less the reaction to it.

Rather paradoxically habituation can lead to a broadening of awareness. As an organism becomes less reactive to one stimulus it attends more to other sources. In addition, stimulus dimensions are outlined and integrative schemata built up through successive processes of habituation to different stimuli. A stimulus thus acquires cue value through the mechanism of habituation, which "transmute(s) stimulus energy into meaning".[117] Eventually the stimulus becomes mastered in the sense that awareness is increased while stimulus-induced arousal is reduced.

For habituation to occur the stimulus must not be too strong, when it will evoke either continued strong responses or diffuse inhibition; the latter reduces receptivity to stimulation in general rather than the fine-tuned selective inhibitory control associated with habituation. Nor should the stimulus be so weak as to fail to elicit an alerting reaction, in which case it does not rate as a stimulus for the organism.

The overall arousal of an organism influences habituation. If it is too low then a moderately intense stimulus is experienced as excessive, e.g., the exaggerated startle response of someone who is drowsy. If the total arousal level is too high, protection against excessive stimulation can be expected to come into play. Moderately strong stimuli might not then be habituated to.

Psychosomatic implications

This ill-defined area of medicine is concerned *inter alia* with the influence of emotional states on bodily conditions. Anxiety has been regarded as an important factor in the genesis of some psychosomatic illnesses and the recent demonstration that autonomic responses can be operantly conditioned has indicated new possible mechanisms for the induction of such illnesses.[354] Possible psychophysiological bases for psychosomatic illness have been reviewed elsewhere:[266] physiological changes ensue following various stimuli such as life-stresses and individual patterns of response may differ widely. The emotion produced in any individual by one particular stimulus varies a great deal and the accompanying physiological patterns will also vary. Of course, stress can produce emotions other than anxiety. For example, a hectoring spouse may induce anxiety in one man, resentment in another, and blissful indifference in a third. In fact there is no consistent evidence that chronic anxiety is associated with any *specific* disease pattern. It is more probable that anxiety increases susceptibility to many illnesses and impedes healing when an illness is established.

A MODEL OF ANXIETY

Before ending this book it is worth an attempt to draw a model of "normal" anxiety. Various authorities on anxiety emphasise totally

different aspects and are on occasion contradictory. Despite this, a model relevant to clinical problems can be synthesised (Fig. 9.1), based on that of Spielberger.[468] Anxiety is divided into three components due to heredity, past experience and current status. These components interact with one another to produce the enduring proneness to anxiety which we call "trait anxiety". The three components also interact with other points in the chain of events which produces and results from anxiety. Incoming external stimuli are screened for their dangerous qualities. This cognitive appraisal of threat is influenced by the trait anxiety of the person concerned. If the external stimuli are judged to be threatening then three aspects of anxiety are activated: (1) the central nervous system is aroused; (2) anxiety is felt; and (3) ways of coping with anxiety and with its precipitants are brought into play. CNS arousal is accompanied by peripheral physiological changes, from which in turn feedback increases arousal. Awareness of physiological changes alters cognitive appraisal, the subject now being aware that he is anxious. He may cope with anxiety by changing the threatening situation or reacting appropriately to it, re-appraising the threat, and sometimes modifying his physiological status directly by methods such as autogenic or muscular relaxation. Successful use of coping responses will modify the way "past experience" will be utilised to meet future threats.

Our cybernetic model, although complex, undoubtedly oversimplifies many factors. It can be translated into physiological terms—the cognitive appraisal occurring in the cerebral cortex, arousal being a property of the reticular formation, emotions being linked in some way to that vague entity, the limbic system—but such exercises are too speculative at present in the human.

Our model has so far dealt with normal anxiety, which is initiated by external stimuli. In clinical anxiety, however, the anxiety is out of proportion to external precipitants, so that cognitive appraisal is unrealistic. Often no external cause at all is apparent. In contrast to normal anxiety, clinical anxiety in patients may begin not with external stimuli but instead with a subjective feeling, with CNS arousal, or with physiological changes. These can act as triggers to a self-perpetuating chain of anxiety. Excessive arousal might then interfere with coping mechanisms, of which the simplest is habituation, so that effective action becomes impossible.[269] Sedative drugs might break this vicious circle by lowering CNS arousal directly, and beta-blockers indirectly by reducing autonomic changes. Why internal triggers start the clinical anxiety in the first place is usually a mystery. The postulation of unconscious mechanisms usually explains one unknown in terms of another; rarely, improvement after uncovering forgotten memories does hint at this possibility. It is sometimes suggested that the triggers to clinical anxiety are in fact not internal

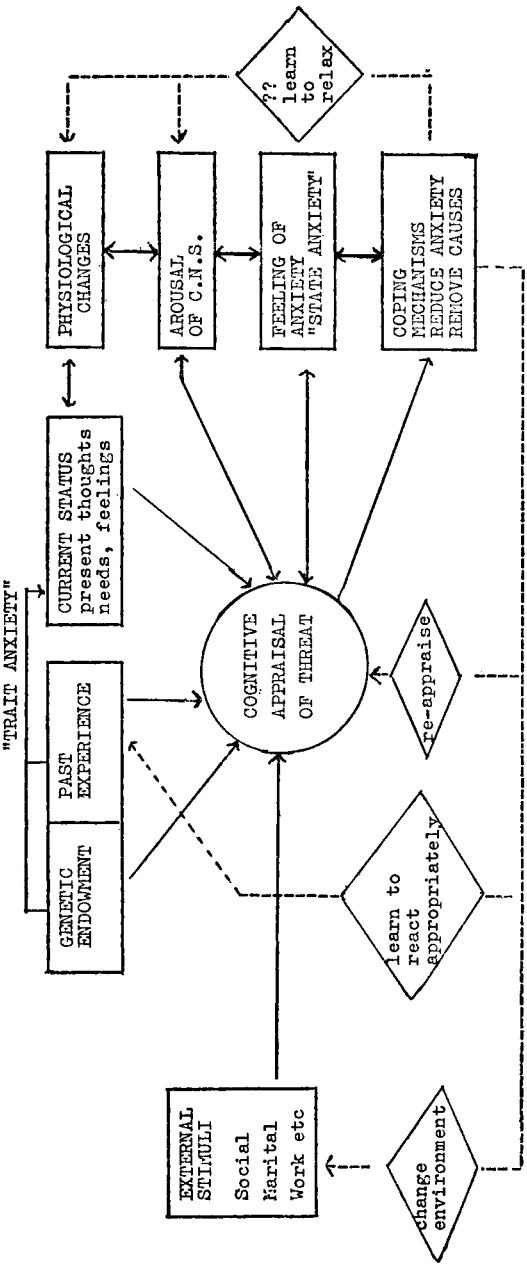


Fig. 9.1: A model of normal anxiety. Pathways which may increase anxiety are shown with solid lines; those reducing anxiety are shown with broken lines.

but external, in the form of ubiquitous stimuli like light to which anxiety has been conditioned. The search for consistent stimuli of this kind does not usually result in evidence which fits clinical facts convincingly.

CONCLUSION

Anxiety is an emotion with protean manifestations about which there is no agreed corpus of theory. When present in an abnormal form as clinical anxiety in our patients, the problems of studying this phenomenon are multiplied. There are few scientific growing points. Increased precision of measurement of anxiety is essential to progress in this field and relevant rating scales and standardised interviews will make it possible to assess symptoms more accurately. Physiological methods will enable the patient's signs to be quantified.

More precise techniques may also aid objective assessment of anxiety by delineating specific patterns of response peculiar to anxiety. Tentative beginnings in this area have not been followed up with more modern techniques. Meticulous recording procedures and sophisticated statistical analyses might reveal patterns of bodily responses which occur only during the experience of anxiety and not during anger, revulsion or any other emotion. By this means the detection of anxiety in our patients might be made more sensitive.

Finally, what are the hopes for more effective treatment? The recent introduction of new sedatives has increased the options open to the treating physician and pharmacotherapy may remain the mainstay of treatment. New compounds which reduce anxiety with less tendency to induce drownsiness are certainly feasible. The increased teaching of psychotherapeutic techniques and wider use of simpler psychological techniques might be at least as beneficial. It will enable anxious patients to receive compassion, understanding, and possibly lead to other ways of reducing anxiety effectively.

References

1 ABRUZZI, W. A. A long release dose form of pentobarbital compared with meprobamate in the management of anxiety states. *Clinical Medicine*, **71**, 1231–1234, 1964.

2 ACKER, M. and McREYNOLDS, P. On the assessment of anxiety: III. By self-ratings. *Psychological Reports*, **19**, 251–254, 1966.

3 ACKNER, B. Emotions and the peripheral vasomotor system. A review of previous work. *Journal of Psychosomatic Research*, **1**, 3–20, 1956.

4 ACKNER, B. The relationship between anxiety and the level of peripheral vasomotor activity. *Journal of Psychosomatic Research*, **1**, 21–48, 1956.

5 ADCOCK, C. J. A comparison of the concepts of Cattell and Eysenck. *British Journal of Educational Psychology*, **35**, 90–97, 1965.

6 AITKEN, R. C. B. Measurement of feelings using visual analogue scales. *Proceedings of the Royal Society of Medicine*, **62**, 989–993, 1969.

7 AIVAZIAN, G. H. Clinical evaluation of diazepam. *Diseases of the Nervous System*, **25**, 491–496, 1964.

8 ALEXANDER, F., FLAGG, G. W., FOSTER, S., CLEMENS, T. and BLADH, W. Experimental studies of emotional stress: I. Hyperthyroidism. *Psychosomatic Medicine*, **23**, 104–114, 1961.

9 ALPERT, R. and HABER, R. N. Anxiety in academic achievement situations. *Journal of Abnormal and Social Psychology*, **61**, 207–215, 1960.

10 ALTSCHULE, M. D. *Bodily Physiology in Mental and Emotional Disorders.* Grune and Stratton, New York, 1953.

11 ANGYAL, A. F. The diagnosis of neurotic traits by means of a new perceptual test. *Journal of Psychology*, **25**, 105–135, 1948.

12 ANTHONY, S. *The Child's Discovery of Death.* Kegan Paul, Trench and Trubner, London, 1940.

13 ARBAB, A. G., BONN, J. A. and HICKS, D. C. Effect of propranolol on lactate induced phenomena in normal subjects. *British Journal of Pharmacology*, **41**, 430P, 1971.

14 AVERILL, J. R., OPTON, E. M. and LAZARUS, R. S. Cross-cultural studies of psychophysiological responses during stress and emotion. *International Journal of Psychology*, **4**, 83–102, 1969.

15 AX, A. F. The physiological differentiation between fear and anger in humans. *Psychosomatic Medicine*, **15**, 433–442, 1953.

16 AXELROD, H. S., COWEN, E. L. and HEILIZER, F. The correlates of manifest anxiety in stylus maze learning. *Journal of Experimental Psychology*, **51**, 131–138, 1956.

17 AZIMA, H., ARTHURS, D. and SILVER, A. The effects of chlordiazepoxide (Librium) in anxiety states. A multi-blind study. *Canadian Psychiatric Association Journal*, **7**, 44–50, 1962.

18 BARBER, T. X. *Hypnosis: A Scientific Approach.* Van Rostrand, London, 1970.

19 BARCROFT, H. and SWAN, H. J. C. *Sympathetic Control of Human Blood Vessels.* Edward Arnold, London, 1953.

20 BARRETT, C. L. Systematic desensitisation versus implosive therapy. *Journal of Abnormal Psychology*, **74**, 587–592, 1969.

21 BARRETT, J. E. and DiMASCIO, A. Comparative effects on anxiety of the "minor tranquillizers" in "High" and "Low" anxious student volunteers. *Diseases of the Nervous System*, **27**, 483–486, 1966.

22 BASOWITZ, H., KORCHIN, S. J., OKEN, D., GOLDSTEIN, M. S. and GUSSACK, H. Anxiety and performance changes with a minimal dose of epinephrine. *Archives of Neurology and Psychiatry (Chicago)*, **76**, 98–108, 1956.

23 BASOWITZ, H., PERSKY, H., KORCHIN, S. J. and GRINKER, R. R. *Anxiety and Stress. An Interdisciplinary Study of a Life Situation.* McGraw-Hill, New York, 1955.

24 BATTERMAN, R. C., MOURATOFF, G. J. and KAUFMAN, J. E. Comparative treatment of the psychoneurotic reactive-type anxiety state with fluphenazine and chlordiazepoxide. *Journal of New Drugs*, **3**, 297–301, 1963.

25 BAUM, M. Extinction of avoidance responding through response prevention (flooding). *Psychological Bulletin*, **74**, 276–284, 1970.

26 BEAM, J. C. Serial learning and conditioning under real-life stress. *Journal of Abnormal and Social Psychology*, **51**, 543–551, 1955.

27 BEARD, G. M. Neurasthenia or nervous exhaustion. *Boston Medical and Surgical Journal*, **3**, 217, 1869.

28 BENDIG, A. W. The development of a short form of the manifest anxiety scale. *Journal of Consulting Psychology*, **20**, 384, 1956.

29 BENJAMIN, S. *The Role of Active Muscular Relaxation in Desensitisation.* M.Phil. Dissertation, University of London, 1970.

30 BERGER, F. M. The similarities and differences between meprobamate and barbiturates. *Clinical Pharmacology and Therapeutics*, **4**, 209–231, 1962.

31 BERKUN, M. M., BIALEK, H. M., KERN, R. P. and YAGI, K. Experimental studies of psychological stress in man. *Psychological Monographs*, **76**, No. 15, Whole No. 534, 1962.

32 BERLYNE, D. E. *Conflict, Arousal and Curiosity.* McGraw-Hill, London, 1960.

33 BERRY, J. L. and MARTIN, B. GSR reactivity as a function of anxiety, instructions, and sex. *Journal of Abnormal and Social Psychology*. **54**, 9–12, 1957.

34 BESSER, G. M. and DUNCAN, C. The time course of action of single doses of diazepam, chlorpromazine and some barbiturates as measured by auditory flutter fusion and visual flicker fusion thresholds in man. *British Journal of Pharmacology*, **30**, 341–348, 1967.

35 BESTERMAN, E. M. M. and FRIEDLANDER, D. H. Clinical experiences with propranolol. *Postgraduate Medical Journal*, **41**, 526–535, 1965.

36 BITTERMAN, M. E. and HOLTZMANN, W. H. Conditioning and extinction of the galvanic skin response as a function of anxiety. *Journal of Abnormal and Social Psychology*, **47**, 615–623, 1952.

37 BLACK, A. A. Factors predisposing to a placebo response in new out-patients with anxiety states. *British Journal of Psychiatry*, **112**, 557–567, 1966.

38 BLAIR, R., GILROY, J. M. and PILKINGTON, F. Some observations on outpatient psychotherapy with a follow up of 235 cases. *British Medical Journal*, **1**, 318–321, 1957.

39 BLISS, E. L., MIGEON, C. J., BRANCH, C. H. H. and SAMUELS, L. T. Reaction of the adrenal cortex to emotional stress. *Psychosomatic Medicine*, **18**, 56–76, 1956.

40 BOLLES, R. C. Species-specific defense reactions and avoidance learning. *Psychological Reviews*, **77**, 32–48, 1970.

41 BOND, D. D. *The Love and Fear of Flying.* International Universities Press, New York, 1952.

42 BOULOUGOURIS, J. and MARKS, I. M. Implosion (flooding): a new treatment for phobias. *British Medical Journal*, **2**, 721–723, 1969.

43 BOWLBY, J. Psychopathology of anxiety: the role of affectional bonds. p. 80–86 in LADER, M. H. (Ed.) *Studies of Anxiety.* Royal Medico-Psychological Association, London, 1969.

44 BRACKBILL, G. and LITTLE, K. B. MMPI correlates of the Taylor scale of manifest anxiety. *Journal of Consulting Psychology*, **18,** 433–436, 1954.
45 BRATFOS, O., LINGJAERDE, O. and SALVESEN, C. Symptomatic relief of neurotic symptoms with tybamate: a double-blind, placebo-controlled study. *Acta Psychiatrica Scandinavica*, **43,** 282–285, 1967.
46 BRAZIER, M. A. B., FINESINGER, J. E. and COBB, S. A contrast between the electroencephalograms of 100 psychoneurotic patients and those of 500 normal adults. *American Journal of Psychiatry*, **101,** 443–448, 1945.
47 BREGGIN, P. R. The psychophysiology of anxiety with a review of the literature concerning adrenaline. *Journal of Nervous and Mental Diseases*, **139,** 558–568, 1964.
48 BRILL, N. Q., KOEGLER, R. R., EPSTEIN, L. J. and FORGY, E. W. Controlled study of psychiatric outpatient treatment. *Archives of General Psychiatry*, **10,** 581–595, 1964.
49 BROADHURST, P. L. and BIGNAMI, G. Correlative effects of psychogenetic selection: A study of the Roman High and Low Avoidance strains of rats. *Behaviour Research and Therapy*, **2,** 273–280, 1965.
50 BRODMAN, K., ERDMANN, A. J., LORGE, I., WOLFF, H. G. and BROADBENT, T. H. The Cornell Medical Index—an adjunct to medical interview. *Journal of American Medical Association*, **140,** 530–534, 1949.
51 BROWN, A. C. and FRY, J. The Cornell Medical Index Health Questionnaire in the identification of neurotic patients in general practice. *Journal of Psychosomatic Research*, **6,** 185–190, 1962.
52 BROWN, B. B. Recognition of aspects of consciousness through association with EEG alpha activity represented by a light signal. *Psychophysiology*, **6,** 442–450, 1970.
53 BROWN, C. C. (Ed.) *Methods in Psychophysiology*. Williams and Wilkins, Baltimore, 1967.
54 BROWN, F. W. Heredity in the psychoneuroses. *Proceedings of the Royal Society of Medicine*, **35,** 785–790, 1942.
55 BUCKLE, R. C. Examination anxiety. *Australian and New Zealand Journal of Psychiatry*, **4,** 126–130, 1970.
56 BUDZYNSKI, T. H., STOYVA, J. S. and ADLER, C. Feedback induced muscle relaxation and application to tension headache. *Behaviour Therapy and Experimental Psychiatry*, **1,** 205–210, 1970.
57 BUSS, A. H. A follow-up item analysis of the Taylor anxiety scale. *Journal of Clinical Psychology*, **11,** 409–410, 1955.
58 BUSS, A. H., WIENER, M., DURKEE, A. and BAER, M. The measurement of anxiety in clinical situations. *Journal of Consulting Psychology*, **19,** 125–129, 1955.
59 CALLIS, S. B. A new drug available for treatment of neurosis: double-blind study of tybamate. *International Journal of Neuropsychiatry*, **2,** 645–650, 1966.
60 CANNON, W. B., LINTON, J. R. and LINTON, R. R. Conditions of activity in endocrine glands. XIV. The effects of muscle metabolites on adrenal secretion. *American Journal of Physiology*, **71,** 153–162, 1924.
61 CAPSTICK, N. S., CORBETT, M. F., PARE, C. M. B., PRYCE, I. G. and LINFORD REES, W. A comparative trial of diazepam (Valium) and amylobarbitone. *British Journal of Psychiatry*, **111,** 517–519, 1965.
62 CARMICHAEL, H. T. and MASSERMAN, J. H. Results of treatment in a psychiatric outpatient department: a follow up study of 166 cases. *Journal of the American Medical Association*, **113,** 2292–2298, 1939.
63 CARRIE, J. R. G. Visual effects on finger tremor in normal subjects and anxious patients. *British Journal of Psychiatry*, **111,** 1181–1184, 1965.
64 CASTANEDA, A., McCANDLESS, B. R. and PALERMO, D. S. The children's form of the manifest anxiety scale. *Child Development*, **27,** 317–326, 1956.

65 CATTELL, R. B. *Handbook for the I.P.A.T. Anxiety Scale*. Institute for Personality and Ability Testing, Champaign, Illinois, 1957.
66 CATTELL, R. B. Advances in the measurement of neuroticism and anxiety in a conceptual framework of unitary-trait theory. *Annals of the New York Academy of Sciences*, **93**, 815–839, 1962.
67 CATTELL, R. B. Anxiety and motivation: theory and crucial experiments. p. 23–62 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.
68 CATTELL, R. B., SAUNDERS, D. R. and STICE, G. *Handbook for the Sixteen Personality Factor Questionnaire*. Institute for Personality and Ability Testing, Champaign, Illinois, 1957.
69 CATTELL, R. B. and SCHEIER, I. H. *The Meaning and Measurement of Neuroticism and Anxiety*. Ronald Press, New York, 1961.
70 CAWTE, J. E. Psychological adjustment to cultural change: the case of the Australian aborigines. *Australian and New Zealand Journal of Psychiatry*, **3**, 343–347, 1969.
71 CHAMPLIN, F. B. et al. A comparison of chlormezanone, meprobamate and placebo. *Clinical Pharmacology and Therapeutics*, **9**, 11–15, 1968.
72 CHILD, I. L. Personality. *Annual Review of Psychology*, **5**, 149–170, 1954.
73 CHODOFF, P. and LYONS, H. Hysteria: the hysterical personality and hysterical conversion. *American Journal of Psychiatry*, **114**, 734–740, 1958.
74 CLEGHORN, R. A. and GRAHAM, B. F. Studies of adrenal cortical activity in psychoneurotic subjects. *American Journal of Psychiatry*, **106**, 668–672, 1950.
75 CLEMENS, T. L. and SELESNICK, S. T. Psychological method for evaluating medication by repeated exposure to a stressor film. *Diseases of the Nervous System*, **28**, 98–104, 1967.
76 COBB, S. *Borderlands of Psychiatry*. Harvard University Press, Cambridge, 1943.
77 COHEN, M. E., BADAL, D. W., KILPATRICK, A., REED, E. W. and WHITE, P. D. The high familial prevalence of neuro-circulatory asthenia (anxiety neurosis, effort syndrome). *American Journal of Human Genetics*, **3**, 126–158, 1951.
78 COLEMAN, E. L., NELSON, S. E., OLSON, F. P., RATHS, O. N. and WIENER, D. N. A controlled study of the use of meprobamate in a mental hygiene clinic. *Journal of Clinical and Experimental Psychopathology*, **19**, 323–329, 1958.
79 COOPER, J. E., GELDER, M. G. and MARKS, I. M. Results of behaviour therapy in 77 psychiatric patients. *British Medical Journal*, **1**, 1222–1225, 1965.
80 COPPEN, A. J. and MEZEY, A. G. The influence of sodium amytal on the respiratory abnormalities of anxious psychiatric patients. *Journal of Psychosomatic Research*, **5**, 52–55, 1960.
81 CROWDER, J. E. and THORNTON, D. W. Effects of systematic desensitization, programmed fantasy and bibliotherapy on a specific fear. *Behaviour Research and Therapy*, **8**, 35–41, 1970.
82 CROWN, S. and CRISP, A. H. A short clinical diagnostic self-rating scale for psychoneurotic patients. *British Journal of Psychiatry*, **112**, 917–923, 1966.
83 CROWN, S. and CRISP, A. H. *Manual of The Middlesex Hospital Questionnaire*. Psychological Test Publications, Barnstaple, Devon, 1970.
84 CROWN, S., DUNCAN, K. P. and HOWELL, R. W. Further evaluation of the Middlesex Hospital Questionnaire. *British Journal of Psychiatry*, **116**, 33–37, 1970.
85 CSILLAG, E. R. A sequential trial of Adumbram (oxazepam). *Australian and New Zealand Journal of Psychiatry*, **1**, 211–213, 1967.

86 Da COSTA, J. M. On irritable heart: a clinical study of a functional cardiac disorder and its consequences. *American Journal of Medical Science*, **61,** 17–52, 1871.
87 DAHLSTROM, W. G. and WELSH, G. S. *An MMPI Handbook. A Guide to Use in Clinical Practice and Research.* University of Minnesota Press, Minneapolis, 1960.
88 DANEMAN, E. A. Double blind study with diazepam, chlordiazepoxide and placebo in the treatment of psychoneurotic anxiety. *Journal of the Medical Association, Georgia*, **53,** 55–58, 1964.
89 DARROW, C. W. Psychophysiology, yesterday, today, and tomorrow. *Psychophysiology*, **1,** 4–7, 1964.
90 DAVIDIAN, H. Aspects of anxiety in Iran. *Australian and New Zealand Journal of Psychiatry*, **3,** 254–258, 1969.
91 DAVIDOWITZ, J., BROWNE-MAYERS, A. N., KOHL, R., WELCH, L. and HAYES, R. An electromyographic study of muscular tension. *Journal of Psychology*, **40,** 85–94, 1955.
92 DAVIS, J. F., MALMO, R. B. and SHAGASS, C. Electromyographic reaction to strong auditory stimulation in psychiatric patients. *Canadian Journal of Psychology*, **8,** 177–186, 1954.
93 DAVIS, R. C. Response patterns. *Transactions of the New York Academy of Sciences*, **19,** 731–739, 1957.
94 DAVISON, K. Evaluation of a new tranquillizer—Benzquinamide (P2647)—by a sequential method. *British Journal of Psychiatry*, **109,** 539–543, 1963.
95 DAVITZ, J. R. *The Language of Emotion.* New York, Academic Press, 1970.
96 DEANE, G. E. Human heart rate responses during experimentally induced anxiety. *Journal of Experimental Psychology*, **61,** 489–493, 1961.
97 DEANE, G. E. Human heart rate responses during experimentally induced anxiety: a follow up with controlled respiration. *Journal of Experimental Psychology*, **67,** 193–195, 1964.
98 De RISIO, C. and MURMANN, W. Anxiety and the pulse. *British Medical Journal*, **2,** 373, 1967.
99 DICKEL, H. A., DIXON, H. H., SHANKLIN, J. G. and DIXON, H. H. A clinical, double-blind comparison of Librium, meprobamate and phenobarbital. *Psychosomatics*, **3,** 129–133, 1962.
100 DIETHELM, O. and JONES, M. R. Influence of anxiety on attention, learning, retention and thinking. *Archives of Neurology and Psychiatry (Chicago)*, **58,** 325–336, 1947.
101 DIGGORY, J. C. and ROTHMAN, D. Z. Values destroyed by death. *Journal of Abnormal and Social Psychology*, **63,** 205–210, 1961.
102 DIXON, J. J., De MONCHAUX, C. and SANDLER, J. Patterns of anxiety: the phobias. *British Journal of Medical Psychology*, **30,** 34–40, 1957.
103 DIXON, J. J., De MONCHAUX, C. and SANDLER, J. Patterns of anxiety: an analysis of social anxieties. *British Journal of Medical Psychology*, **30,** 107–112, 1957.
104 DREYFUSS, F. and FELDMAN, S. Eosinopenia induced by emotional stress. *Acta Medica Scandinavica*, **144,** 107–113, 1952.
105 DUNLOP, E. and WEISBERG, J. Double-blind study of prazepam in the treatment of anxiety. *Psychosomatics*, **9,** 235–238, 1968.
106 DYKMAN, R. A., MURPHREE, O. D. and ACKERMAN, P. T. Litter patterns in the offspring of nervous and stable dogs. II: Autonomic and motor conditioning. *Journal of Nervous and Mental Diseases*, **141,** 419–431, 1965.
107 EITINGER, L. Studies in neuroses. *Acta Psychiatrica et Neurologica Scandinavica*, Supplement 101, 1955.
108 EITINGER, L. Anxiety in concentration camp survivors. *Australian and New Zealand Journal of Psychiatry*, **3,** 348–351, 1969.

109 ELIZUR, A. Content analysis of the Rorschach with regard to anxiety and hostility. *Rorschach Research Exchange*, **13,** 247–284, 1949.
110 ELLINGSON, R. J. The incidence of EEG abnormality among patients with mental disorders of apparently nonorganic origin: a critical review. *American Journal of Psychiatry*, **11,** 263–275, 1954.
111 ELLIOT, R. Effects of uncertainty about the nature and advent of a noxious stimulus (shock) upon heart rate. *Journal of Personality and Social Psychology*, **3,** 353–356, 1966.
112 ELMADJIAN, F. Aldosterone excretion in behavioral disorders. *Research Publications of the Association for Research into Nervous and Mental Diseases*, **40,** 414–419, 1962.
113 EMERY, J. R. and KRUMBOLTZ, J. D. Standard vs. individualised hierarchies in desensitisation to reduce test anxiety. *Journal of Counselling Psychology*, **14,** 204–207, 1967.
114 ENDLER, N. S., HUNT, J. McV. and ROSENSTEIN, A. J. An S-R inventory of anxiousness. *Psychological Monograph*, **76,** No. 17, Whole No. 536, 1962.
115 EPSTEIN, S. The measurement of drive and conflict in humans: theory and experiment. p. 127–206 in JONES, M.R. (Ed.) *Nebraska Symposium on Motivation*. University of Nebraska Press, Lincoln, 1962.
116 EPSTEIN, S. Toward a unified theory of anxiety, p. 1–89 in MAHER, B. A. (Ed.) *Progress in Experimental Personality Research*, Vol. 4, Academic Press, New York, 1967.
117 EPSTEIN, S. Anxiety, reality and schizophrenia. *Schizophrenia*, **2,** 11–35, 1970.
117a EPSTEIN, S. The nature of anxiety with emphasis upon its relationship to expectancy. In CATTELL, R. B. (Ed.) *Handbook of Modern Personality Theory*. Aldine, Chicago, 1971.
118 ERNST, K. *Die Prognose der Neurosen*. Monographien aus dem Gesamt gebiete der Neurologie und Psychiatrie. Springer, Berlin, 1959.
119 ESTES, W. K. and SKINNER, B. F. Some quantitative properties of anxiety. *Journal of Experimental Psychology*, **29,** 390–400, 1951.
120 EYSENCK, H. J. *The Manual of the Maudsley Personality Inventory*. University of London Press, London, 1959.
121 EYSENCK, H. J. *The Biological Basis of Personality*. Charles C. Thomas, Springfield, Illinois, 1967.
122 EYSENCK, H. J. Psychological aspects of anxiety, p. 7–20 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.
123 EYSENCK, H. J. and EYSENCK, S. B. G. *The Manual of the Eysenck Personality Inventory*. University of London Press, London, 1964.
124 EYSENCK, H. J. and EYSENCK, S. B. G. *Personality Structure and Measurement*. Routledge, London, 1969.
125 FARBER, I. E. and SPENCE, K. W. Complex learning and conditioning as a function of anxiety. *Journal of Experimental Psychology*, **45,** 120–125, 1953.
126 FENICHEL, O. *The Psychoanalytic Theory of Neurosis*. Norton, New York, 1945.
127 FENZ, W. D. and EPSTEIN, S. Gradients of physiological arousal of experienced and novice parachutists as a function of an approaching jump. *Psychosomatic Medicine*, **29,** 33–51, 1967.
128 FISCHER, W. F. *Theories of Anxiety*. Harper and Row, New York, 1970.
129 FLEISHMAN, E. A. Psychomotor tests in drug research. p. 273–296 in UHR, L. and MILLER, J. G. *Drugs and Behavior*. Wiley, New York, 1960.
130 FRANKENHAEUSER, M. and JÄRPE, G. Psychophysiological changes during infusions of adrenaline in various doses. *Psychopharmacologia*, **4,** 424–432, 1963.

131 FRANKENHAEUSER, M. and PÁTKAI, P. Inter-individual differences in catecholamine excretion during stress. Report no. 178 of the Psychological Laboratory, University of Stockholm 1964.

132 FRANKL, V. E. Paradoxical intention: a logotherapeutic technique. *American Journal of Psychotherapy*, **14,** 520–535, 1960.

133 FRANKS, C. M. and FRANKS, V. "Conditionability" as a general factor of man's performance in different conditioning situations. Abstracts Vol. 1, p. 331 of XVIII International Congress of Psychology, Moscow, 1966.

134 FREEMAN, M. J. The development of a test for the measurement of anxiety: a study of its reliability and validity. *Psychology Monograph*, **67,** no. 3, whole no. 353, 1953.

135 FREUD, S. The justification for detaching from neurasthenia a particular syndrome: the anxiety neurosis. (1894.) Collected Works, Vol. 1, p. 76–106. Hogarth Press and Institute of Psychoanalysis, London. Paper reprinted in 1946.

136 FREUD, S. A reply to criticisms on the anxiety neurosis. (1895.) Collected Works, Vol. I, p. 107–127. Hogarth Press and Institute of Psychoanalysis, Paper reprinted in 1946.

137 FRIEDLANDER, A. and FREYHOF, W. L. Intensive study of 50 cases of neurocirculatory asthenia. *Archives of Internal Medicine*, **22,** 693–718, 1918.

138 FRITZ, C. E. and MARKS, E. S. The National Opinion Research Centre. *Journal of Sociological Issues*, **10,** 26–41, 1954.

139 FROHLICH, E. D., DUSTAN, H. P. and PAGE, I. H. Hyperdynamic beta adrenergic circulatory state. *Archives of Internal Medicine*, **117,** 614–619, 1966.

140 FROHLICH, E. D., TARAZI, R. C. and DUSTAN, H. P. Hyperdynamic beta-adrenergic circulatory state. *Archives of Internal Medicine*, **123,** 1–7, 1969.

141 FUNKENSTEIN, D. H., KING, S. H. and DROLETTE, M. E. *Mastery of Stress*. Harvard University Press, Cambridge, 1957.

142 GANTT, W. H. *Experimental Basis for Neurotic Behavior. Origin and Development of Artificially Produced Disturbances of Behavior in Dogs*. Hoeber, New York, 1944.

143 GARMANY, G. Anxiety states. *British Medical Journal*, **1,** 943–946, 1956.

144 GEER, J. The development of a scale to measure fear. *Behaviour Research and Therapy*, **3,** 45–53, 1965.

145 GEER, J. H. Effect of fear arousal upon task performance and verbal behavior. *Journal of Abnormal Psychology*, **71,** 119–123, 1966.

146 GELDER, M. G. and MARKS, I. M. Severe agoraphobia: a controlled prospective therapeutic trial. *British Journal of Psychiatry*, **112,** 309–319, 1966.

147 GELDER, M. G., MARKS, I. M. and WOLFF, H. H. Desensitisation and psychotherapy in phobic states: a controlled enquiry. *British Journal of Psychiatry*, **113,** 53–73, 1967.

148 GENERAL PRACTITIONER CLINICAL TRIALS. Phenobarbitone compared with an inactive placebo in anxiety states. *Practitioner* (*London*), **192,** 147–151, 1964.

149 GIBBONS, J. L. The adrenal cortex and psychological distress, p. 220–236 in MICHAEL, R. P. (Ed.) *Endocrinology and Human Behaviour*. Oxford University Press, London, 1968.

150 GIBSON, J. G. Emotions and the thyroid gland: a critical appraisal. *Journal of Psychosomatic Research*, **6,** 93–116, 1962.

151 GJERRIS, F. Poisoning with chlordiazepoxide (Librium). *Danish Medical Bulletin*, **13,** 170–180, 1966.

152 GOLDSTEIN, I. B. Physiological responses in anxious women patients. A study of autonomic activity and muscle tension. *Archives of General Psychiatry*, **10**, 382–388, 1964.
153 GOLDSTEIN, I. B. The relationship of muscle tension and autonomic activity to psychiatric disorders. *Psychosomatic Medicine*, **27**, 39–52, 1965.
154 GOLDSTEIN, K. *The Organism, a Holistic Approach to Biology*. American Book Company, New York, 1939.
155 GOLDSTEIN, L. and BECK, R. A. Amplitude analysis of the electroencephalogram. *International Review of Neurobiology*, **8**, 265–312, 1967.
156 GOLDSTONE, S. Flicker fusion measurements and anxiety level. *Journal of Experimental Psychology*, **49**, 200–202, 1955.
157 GOMEZ-MARTINEZ, I. Preliminary double-blind clinical trial with a new antidepressive doxepin. *Current Therapeutic Research*, **10**, 116–118, 1968.
158 GORE, C. P. and McCOMISKY, J. G. A study of the comparative effectiveness of librium, amylobarbitone, and a placebo in the treatment of tension and anxiety states. *Proceedings of the Third World Congress of Psychiatry*, **2**, 979–982, 1961.
159 GORLIN, R. Hyperkinetic heart syndrome. *Journal of the American Medical Association*, **182**, 823–829, 1962.
160 GOTTSCHALK, L. A., CLEGHORN, J. M., GLESER, G. C. and IACONO, J. M. Studies of relationships of emotions to plasma lipids. *Psychosomatic Medicine*, **27**, 102–111, 1965.
161 GRAHAM, F. K. and CLIFTON, R. K. Heart-rate change as a component of the orienting response. *Psychological Bulletin*, **65**, 305–320, 1966.
162 GRANT, R. T. Observations on the after-histories of men suffering from the effort syndrome. *Heart*, **12**, 121–142, 1925.
163 GRANVILLE-GROSSMAN, K. L. and TURNER, P. The effect of propranolol on anxiety. *Lancet*, **1**, 788–790, 1966.
164 GRAY, A. *Peking Diary*. Michael Joseph, London, 1970.
165 GREER, S. The prognosis of anxiety states. p. 151–157 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.
166 GREER, S. and CAWLEY, R. H. *Some Observations on the Natural History of Neurotic Illness*, Archdall Medical Monograph, No. 3. Australasia Medical Publishing Company, Sydney, 1966.
167 GROSS, W. M. Mental health survey in a rural area. *Eugenics Review*, **40**, 140, 1948.
168 GROSSBERG, J. M. and WILSON, H. K. A correlational comparison of the Wolpe-Lang F. S. S. and Taylor M. A. S. *Behaviour Research and Therapy*, **3**, 125–128, 1965.
169 GROSZ, H. J. and FARMER, B. B. Blood lactate in the development of anxiety symptoms. A critical examination of Pitts and McClure's hypothesis and experimental study. *Archives of General Psychiatry*, **21**, 611–619, 1969.
170 GURNEY, C., ROTH, M., KERR, T. A. and SCHAPIRA, K. The bearing of treatment on the classification of the affective disorders. *British Journal of Psychiatry*, **117**, 251–255, 1970.
171 HAGNELL, O. *A Prospective Study of the Incidence of Mental Disorder*. Scandinavian University Books, Lund, 1966.
172 HALL, G. S. A study of fears. *American Journal of Psychology*, **8**, 147–249, 1897.
173 HAMBURG, D. A. et al. Classification and rating of emotional experiences. Special reference to reliability of observation. *Archives of Neurology and Psychiatry (Chicago)*, **79**, 415–426, 1958.

174 HAMILTON, D. M., VARNEY, H. J. and WALL, J. H. Hospital treatment of patients with psychoneurotic disorders. *American Journal of Psychiatry*, **99**, 243–247, 1942.

175 HAMILTON, D. M. and WALL, J. H. Hospital treatment of patients with psychoneurotic disorders. *American Journal of Psychiatry*, **98**, 551–557, 1942.

176 HAMILTON, M. The assessment of anxiety states by rating. *British Journal of Medical Psychology*, **32**, 50–55, 1959.

177 HAMILTON, M. Diagnosis and rating of anxiety. p. 76–79 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.

178 HANNAH, F., STORM, T. and CAIRD, W. K. Sex differences and relationships among neuroticism, extraversion and expressed fears. *Perceptual and Motor Skills*, **20**, 1214–1216, 1965.

179 HARE, E. H. Triennial Statistical Report. Bethlem Royal and the Maudsley Hospitals, London, 1968.

180 HARE, E. H. and SHAW, G. K. *Mental Health on a New Housing Estate*. Maudsley Monograph No. 12, Oxford University Press, London, 1965.

181 HARE, H. P. Comparison of diazepam, chlorpromazine and a placebo in psychiatric practice. *Journal of New Drugs*, **3**, 233–240, 1963.

182 HARGREAVES, G. R., HAMILTON, M. and ROBERTS, J. M. Treatment of anxiety states. II—Clinical trial of benactyzine in anxiety states. *Journal of Mental Science*, **104**, 1056–1061, 1958.

183 HARLESTON, B. W. Test anxiety and performance in problem-solving situations. *Journal of Personality*, **30**, 557–573, 1962.

184 HARTENBERG. P. *La Névrose d'Angoisse, Etude Historique et Critique*. Ancienne Librairie Germer Bailliere et Cie, Paris, 1902.

185 HARTSHORNE, H. Heart disease in the army. *American Journal of Medical Science*, **48**, 89–92, 1864.

186 HATHAWAY, S. R. and MEEHL, P. E. *An Atlas for the Clinical Use of the MMPI*. University of Minnesota Press, Minneapolis, 1951.

187 HAVARD, J. D. J. Drugs and driving. *British Journal of Hospital Medicine*. **4**, 455–458, 1970.

188 HECKEL, F. *La Névrose d'Angoisse et les Etats d' Emotivité Anxieuse*. Masson, Paris, 1917.

189 HECKER, E. Der Behandlung der neurasthenischen Angstzustände. *Berliner Klinische Wochenschrift*, **47**, 1–7, 1892.

190 HECKER, E. Ueber larvirte und abortive Angstzustände bei Neurasthenie. *Zentralblatt fur Nervenheilkranken*, **16**, 565–572, 1893.

191 HENDERSON, D. and BATCHELOR, I. R. C. *Henderson and Gillespie's Textbook of Psychiatry*, 9th ed., p. 161. Oxford University Press, London, 1962.

192 HETZEL, B. S., SCHOTTSTAEDT, W. W., GRACE, W. J. and WOLFF, H. G. Changes in urinary nitrogen and electrolyte excretion during stressful life experiences, and their relation to thyroid function. *Journal of Psychosomatic Research*, **1**, 177–185, 1956.

193 HICKAM, J. B., CARGILL, W. H. and GOLDEN, A. Cardiovascular reactions to emotional stimuli. Effect on the cardiac output, arteriovenous oxygen difference, arterial pressure, and peripheral resistance. *Journal of Clinical Investigation*, **27**, 290–298, 1948.

194 HILGARD, E. R., JONES, L. V. and KAPLAN, S. J. Conditioned discrimination as related to anxiety. *Journal of Experimental Psychology*, **42**, 94–99, 1951.

195 HILL, K. T. and SARASON, S. B. The relation of test anxiety and defensiveness to test and school performance over the elementary-school years: a further longitudinal study. *Child Development Monograph*, Serial No. 104, **31,** No. 2, 1–76, 1966.

196 HILTNER, S. and MENNINGER, K. *Constructive Aspects of Anxiety.* Abingdon Press, New York, 1963.

197 HINTON, J. M. A controlled trial of meprobamate in anxious out-patients. *Journal of Neurology, Neurosurgery and Psychiatry*, **21,** 301–304, 1958.

198 HINTON, J. *Dying.* Pelican Books No. A866, London, 1967.

199 HODGES, W. F. and SPIELBERGER, C. D. The effects of threat of shock on heart rate for subjects who differ in manifest anxiety and fear of shock. *Psychophysiology*, **2,** 287–294, 1966.

200 HOGAN, R. A. and KIRCHNER, J. H. Preliminary report of the extinction of learned fears via short term implosive therapy. *Journal of Abnormal Psychology*, **72,** 106–109, 1967.

201 HOGAN, R. A. and KIRCHNER, J. H. Implosive, eclectic, verbal and bibliotherapy in the treatment of fears of snakes. *Behaviour Research and Therapy* **6,** 167–171, 1968.

202 HOLLISTER, L. E. Methodological considerations in evaluating anti-anxiety drugs. *Journal of Clinical Pharmacology*, **10,** 12–18, 1970.

203 HOLLISTER, L. E., STANNARD, A. N. and DRAKE, C. F. Treatment of anxious patients with drugs. *Diseases of the Nervous System*, **17,** 289–293, 1956.

204 HOWE, E. S. GSR conditioning in anxiety states, normals, and chronic functional schizophrenic subjects. *Journal of Abnormal and Social Psychology*, **56,** 183–189, 1958.

205 HULL, C. L. *Principles of Behavior.* Appleton, New York, 1943.

206 HUNT, H. F. Effects of drugs on emotional responses and abnormal behavior in animals. p. 268–279 in COLE, J. O. and GERRARD, R. W. (Eds.) *Psychopharmacology. Problems in Evaluation.* National Academy of Science, National Research Council, Washington, 1959.

207 HUNT, H. F. Methods for studying the behavioral effects of drugs. *Annual Review of Pharmacology*, **1,** 125–144, 1961.

208 HUNTER, J. *Treatise on Venereal Disease.* (2nd Ed.) p. 203–4. Hunter, No. 13, Castle-Street, Leicester-Square, London, 1788.

209 INGHAM, J. G. and ROBINSON, J. O. Personality in the diagnosis of hysteria. *British Journal of Psychology*, **55,** 276–284, 1964.

210 INGRAM, P. W., EVANS, G. and OPPENHEIM, A. N. Right iliac fossa pain in young women, with appendix on the Cornell Medical Index Questionnaire. *British Medical Journal*, **2,** 149–151, 1965.

211 INNES, G., MILLAR, W. M. and VALENTINE, M. Emotion and blood-pressure. *Journal of Mental Science*, **105,** 840–851, 1959.

212 JACOBSEN, E. *Progressive Relaxation.* University of Chicago Press, Chicago, 1938.

213 JANECEK, J., VESTRE, N. D., SCHIELE, B. C. and ZIMMERMAN, R. Oxazepam in the treatment of anxiety states: a controlled study. *Journal of Psychiatric Research*, **4,** 199–206, 1966.

214 JANIS, I. L. Problems of theory in the analysis of stress behaviour. *Journal of Sociological Issues*, **10,** 12–25, 1954.

215 JANIS, I. L. *Psychological Stress.* Wiley, New York, 1958.

216 JEFFERS, F. C., NICHOLS, C. R. and EISDORFER, C. Attitudes of older persons towards death: a preliminary study. *Journal of Gerontology*, **16,** 53–56, 1961.

217 JENNER, F. A., KERRY, R. J. and PARKIN, D. A controlled trial of methaminodiazepoxide (chlordiazepoxide, "Librium") in the treatment of anxiety in neurotic patients. *Journal of Mental Science*, **107,** 575–582, 1961.

218 JENNER, F. A., KERRY, R. J. and PARKIN, D. A controlled comparison of methaminodiaxepoxide (chlordiazepoxide, "Librium") and amylobarbitone in the treatment of anxiety in neurotic patients. *Journal of Mental Science*, **107,** 583–589, 1961.

219 JENNINGS, L. S. Minnesota Multiphasic Personality Inventory. Differentiation of psychologically good and poor combat risks among flying personnel. *Journal of Aviation Medicine*, **19,** 222–226, 237, 1948,

220 JOHANNSEN, W. J., FRIEDMAN, S. H., FELDMAN, E. I. and NEGRETE, A. A re-examination of the hippuric acid-anxiety relationship. *Psychosomatic Medicine*, **24,** 569–578, 1962.

220a JOHNSON, L. C. A psychophysiology for all states. *Psychophysiology*, **6,** 501–516, 1970.

220b JOHNSON, L. C. and LUBIN, A. The orienting reflex during waking and sleeping. *Electroencephography and Clinical Neurophysiology*, **22,** 11–21, 1967.

221 JOHNSTONE, E. E. and CLAGHORN, J. L. Doxepin vs. chlordiazepoxide. A controlled comparison in neurotic outpatients. *Current Therapeutic Research*, **10,** 514–519, 1968.

222 JONES, M. and MELLERSH, V. A comparison of the exercise response in anxiety states and normal controls. *Psychosomatic Medicine*, **8,** 180–187, 1946.

223 JONES, O. Relationship between visual and auditory discrimination and anxiety level. *Journal of General Psychology*, **59,** 111–118, 1958.

224 JULIER, D. *Agoraphobia in Men.* D.P.M. Dissertation, University of London, 1967.

225 KAMIN, L. J. and CLARK, J. W. The Taylor scale and reaction time. *Journal of Abnormal and Social Psychology*, **54,** 262–263, 1957.

226 KAMIYA, J. Operant control of the EEG alpha rhythm and some of its reported effects on consciousness. p. 507–518 in TART, C. T. (Ed.) *Altered States of Consciousness*, Wiley, London, 1969.

227 KANFER, F. H. Vicarious human reinforcement: a glimpse into the black box. p. 244–267 in KRASNER, L. and ULLMAN, L. P. (Eds.) *Research in Behaviour Modification.* Holt, Rinehart and Wilson, London, 1965.

228 KANNEL, W. B., DAWBER, T. R. and COHEN, M. E. The electrocardiogram in neurocirculatory asthenia (anxiety neurosis or neurasthenia): a study of 203 neurocirculatory asthenia patients and 757 healthy controls in the Framingham study. *Annals of Internal Medicine*, **49,** 1351–1360, 1958.

229 KASL, S. V. and MAHL, G. F. The relationship of disturbances and hesitations in spontaneous speech to anxiety. *Journal of Personality and Social Psychology*, **1,** 425–433, 1965.

230 KATAHN, M. Interaction of anxiety and ability in complex learning situations. *Journal of Personality and Social Psychology*, **3,** 475–479, 1966.

231 KATCHMAR, L. T., ROSS, S. and ANDREWS, T. G. Effects of stress and anxiety on performance of a complex verbal-coding task. *Journal of Experimental Psychology*, **55,** 559–564, 1958.

232 KATKIN, E. S. Relationship between manifest anxiety and two indices of autonomic stress. *Journal of Personality and Social Psychology*, **2,** 324–333, 1965.

233 KATKIN, E. S. The relationship between a measure of transitory anxiety and spontaneous autonomic activity. *Journal of Abnormal Psychology*, **71,** 142–146, 1966.

234 KAUSLER, D. H. and TRAPP, E. P. Methodological considerations in the construct validation of drive-oriented scales. *Psychological Bulletin*, **56,** 152–157, 1959.

235 KAYE, D., KIRSCHNER, P. and MANDLER, G. The effect of test anxiety on memory span in a group test situation. *Journal of Consulting Psychology*, **17**, 265–266, 1953.

236 KEARNEY, T. and BONIME, H. C. Problems of drug evaluation in out-patients. *Diseases of the Nervous System*, **27**, 604–606, 1966.

237 KEDWARD, H. B. and COOPER, B. Neurotic disorders in urban practice: a 3 year follow up. *Journal of College of General Practitioners*, **12**, 148–163, 1966.

238 KEGELES, S. S. Some motives for seeking preventive dental care. *Journal of American Dental Association*, **7**, 90–98, 1963.

239 KELLY, D. H. W. Measurement of anxiety by forearm blood flow. *British Journal of Psychiatry*, **112**, 789–798, 1966.

240 KELLY, D. H. W. The technique of forearm plethysmography for assessing anxiety. *Journal of Psychosomatic Research*, **10**, 373–382, 1967.

241 KELLY, D., BROWN, C. C. and SHAFFER, J. W. A controlled physiological, clinical and psychological evaluation of chlordiazepoxide. *British Journal of Psychiatry*, **115**, 1387–1392, 1969.

242 KELLY, D., MITCHELL-HEGGS, N. and SHERMAN, J. Anxiety and sodium lactate assessed clinically and physiologically. *British Journal of Psychiatry*, **119**, 129–142, 1971.

243 KENDALL, E. The validity of Taylor's manifest anxiety scale. *Journal of Consulting Psychology*, **18**, 429–432, 1954.

244 KERLE, R. H. and BIALEK, H. M. The construction, validation and application of a subjective stress scale. Staff Memorandum, U.S. Army Leadership Human Research Unit, Monterey, California, 1958.

245 KERRICK, J. S. Some correlates of the Taylor manifest anxiety scale. *Journal of Abnormal and Social Psychology*, **50**, 75–77, 1955.

246 KIERKEGAARD, S. *The Concept of Dread.* English translation of *Begrebet Angst* (1844). University Press, Princeton, 1946.

247 KIMBLE, G. A. *Hilgard and Marquis' Conditioning and Learning.* Methuen, London, 1961.

248 KLAUSNER, S. Z. The transformation of fear: a study of parachuting. Abstracts, Volume 11, p. 29 of XVIII International Congress of Psychology, Moscow, 1966.

249 KNIGHT, G. The orbital cortex as an objective in the surgical treatment of mental illness. The results of 450 cases of open operation and the development of the stereotactic approach. *British Journal of Surgery*, **51**, 114–124, 1964.

250 KNIGHT, G. Stereotactic tractotomy in the surgical treatment of mental illness. *Journal of Neurology, Neurosurgery and Psychiatry*, **28**, 304–310, 1965.

251 KOLLAR, E. J. Psychological stress: a re-evaluation. *Journal of Nervous and Mental Diseases*, **132**, 382–396, 1961.

252 KORA, T. A method of instruction in psychotherapy. *Jikeikai Medical Journal*, **15**, 316–325, 1968.

253 KORCHIN, S. J. and LEVINE, S. Anxiety and verbal learning. *Journal of Abnormal and Social Psychology*, **54**, 234–240, 1957.

254 KORNETSKY, C., HUMPHRIES, O. and EVARTS, E. V. Comparison of psychological effects of certain centrally acting drugs in man. *Archives of Neurology and Psychiatry (Chicago)*, **77**, 318–324, 1957.

255 KREITMAN, N. The patient's spouse. *British Journal of Psychiatry*, **110**, 159–173, 1964.

256 KRUGMAN, H. E. Flicker fusion frequency as a function of anxiety reaction; an exploratory study. *Psychosomatic Medicine*, **9**, 269–272, 1947.

257 LACEY, J. I. Individual differences in somatic response patterns. *Journal of Comparative and Physiological Psychology*, **43**, 338–350, 1950.

258 LACEY, J. I. Somatic response patterning and stress: some revisions of activation theory. p. 14–37 in APPLEY, M. H. and TRUMBULL, R. (Eds.) *Psychological Stress*. Appleton-Century-Crofts, New York, 1967.

259 LACEY, J. I., BATEMAN, D. E. and VAN LEHN, R. Autonomic response specificity and Rorschach color responses. *Psychosomatic Medicine*, **14**, 256–260, 1952.

260 LACEY, J. I. and LACEY, B. C. Verification and extension of the principle of autonomic response-stereotypy. *American Journal of Psychology*, **71**, 50–73, 1958.

261 LACEY, J. I. and VANLEHN, R. Differential emphasis in somatic response to stress. An experimental study. *Psychosomatic Medicine*, **14**, 71–81, 1952.

262 LADER, M. H. Palmar skin conductance measures in anxiety and phobic states. *Journal of Psychosomatic Research*, **11**, 271–281, 1967.

263 LADER, M. H. The effect of anxiety on response to treatment. *Australian and New Zealand Journal of Psychiatry*, **3**, 288–292, 1969.

264 LADER, M. H. Psychophysiological aspects of anxiety. p. 53–61 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.

265 LADER, M. H. The unit of quantification of the G.S.R. *Journal of Psychosomatic Research*, **14**, 109–110, 1970.

266 LADER, M. H. Psychosomatic and psychophysiological aspects of anxiety. p. 35–52 in HILL, O. W. (Ed.) *Modern Trends in Psychosomatic Medicine*. Vol. 2. Butterworths, London, 1970.

267 LADER, M. H. The responses of normal subjects and psychiatric patients to repetitive stimulation, in press in LEVI, L. (Ed.) *Stress, Society and Disease*. Oxford University Press, London, 1971.

268 LADER, M. H., GELDER, M. G. and MARKS, I. M. Palmar skin conductance measures as predictors of response to desensitization. *Journal of Psychosomatic Research*, **11**, 283–290, 1967.

269 LADER, M. H. and MATHEWS, A. M. A physiological model of phobic anxiety and desensitization. *Behaviour Research and Therapy*, **6**, 411–418, 1967.

269a LADER, M. H. and MATHEWS, A. M. Physiological changes during spontaneous panic attacks. *Journal of Psychosomatic Research*, **14**, 377–382, 1970.

270 LADER, M. H. and MATHEWS, A. M. A comparison of methods of relaxation using physiological measures. *Behaviour Research and Therapy*, **8**, 331–337, 1970.

270a LADER, M. H. and MATHEWS, A. M. Electromyographic studies of tension. *Journal of Psychosomatic Research*, 1971, in press.

271 LADER, M. H. and MONTAGU, J. D. The psycho-galvanic reflex: a pharmacological study of the peripheral mechanism. *Journal of Neurology, Neurosurgery and Psychiatry*, **25**, 126–133, 1962.

272 LADER, M. and SARTORIUS, N. Anxiety in patients with hysterical conversion symptoms. *Journal of Neurology, Neurosurgery and Psychiatry*, **31**, 490–495, 1968.

273 LADER, M. H. and WING, L. *Physiological Measures, Sedative Drugs, and Morbid Anxiety*. University of Oxford Press, London, 1966.

274 LADER, M. H. and WING, L. Physiological measures in agitated and retarded depressed patients. *Journal of Psychiatric Research*, **7**, 89–100, 1969.

275 LANDIS, C. and HUNT, W. A. *The Startle Pattern*. Farrar and Rinehart, New York, 1939.

276 LANG, P. J. The mechanics of desensitisation and the laboratory study of human fear. p. 160–191 in FRANKS, C. M. (Ed.) *Behavior Therapy Appraisal and Status*. McGraw-Hill, New York, 1969.

277 LANG, P. J. and LAZOVIK, A. D. Experimental desensitisation of a phobia. *Journal of Abnormal and Social Psychology*, **66,** 519–525, 1963.

278 LANG, P. J., LAZOVIK, A. D. and REYNOLDS, D. J. Desensitisation, suggestibility and pseudotherapy. *Journal of Abnormal Psychology*, **70,** 395–402, 1965.

279 LANGEN, D. Relaxation therapy. p. 143–146 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.

279a LANYON, R. I. and MANOSEVITZ, M. Validity of self-reported fear. *Behaviour Research and Therapy*, **4,** 17–24, 1966.

280 LATIES, V. G. and WEISS, B. A critical review of the efficacy of meprobamate (Miltown, Equanil) in the treatment of anxiety. *Journal of Chronic Diseases*, **7,** 500–519, 1958.

281 LAUTERBACH, C. G. The Taylor A scale and clinical measures of anxiety. *Journal of Consulting Psychology*, **22,** 314, 1958.

282 LAZARUS, R. S. *Psychological Stress and the Coping Process*. McGraw-Hill, New York, 1966.

283 LAZARUS, R. S., AVERILL, J. R. and OPTON, E. M. Towards a cognitive theory of emotion. Paper in Symposium on Feelings and Emotion at Loyola University, Chicago, October, 1968.

284 LAZARUS, R. S. and OPTON, E. M. The study of psychological stress: a summary of theoretical formulations and experimental findings. p. 225–262 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.

285 LEGGE, D., STEINBERG, H. and SUMMERFIELD, A. Simple measures of handwriting as indices of drug effects. *Perceptual and Motor Skills*, **18,** 549–58, 1964.

286 LEVI, L. (Ed.) Emotional stress. *Försvarsmedicin*, Vol. 3, suppl. 2, 1967.

287 LEVI, L. Neuro-endocrinology of anxiety, p. 40–52 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.

288 LEVINSON, F. and MEYER, V. Personality changes in relation to psychiatric status following orbital cortex undercutting. *British Journal of Psychiatry*, **111,** 207–218, 1965.

289 LEVITT, E. E. *The Psychology of Anxiety*. Staples Press, London, 1968.

290 LEVITT, E. E., PERSKY, H., BRADY, J. P. and FITZGERALD, J. A. The effect of hydrocortisone infusion on hypnotically induced anxiety. *Psychosomatic Medicine*, **25,** 158–161, 1963.

291 LEWIS, A. J. Obsessional illness. La enfermedad obsessiva. *Acta Neuropsiquiatrica Argentina*, **3,** 323–325, 1957.

292 LEWIS, A. Problems presented by the ambiguous word "anxiety" as used in psychopathology. *Israel Annals of Psychiatry and Related Disciplines*, **5,** 105–121, 1967.

293 LEWIS, T. *The Soldier's Heart and the Effort Syndrome*. Shaw, London, 1919.

294 LEWIS, W. C. and BERMAN, M. Studies of conversion hysteria. 1: Operational study of diagnosis. *Archives of General Psychiatry*, **13,** 275–282, 1965.

295 LIDDELL, H. S. The role of vigilance in the development of animal neurosis. p. 183–196 in HOCH, P. H. and ZUBIN, J. (Eds.) *Anxiety*. Grune and Stratton, New York, 1950.

296 LIDDELL, H. S. A comparative approach to the dynamics of experimental neuroses. *Annals of the New York Academy of Sciences*, **56,** 164–170, 1953.

297 LINDEMANN, E. The symptomatology and management of acute grief. *American Journal of Psychiatry*, **101,** 141–148, 1944.

298 LINDEMANN, E. The timing of psychotherapy. Part 4 of the Proceedings of the Psychotherapy Conference in London, 1964, p. 75–90. Karger, Basle.

299 LINDZEY, G. and NEWBURG, A. S. Thematic apperception test: a tentative appraisal of some "signs" of anxiety. *Journal of Consulting Psychology*, **18,** 389–395, 1954.

300 LINGJAERDE, O. Diazepam bei nervöser Angst und Spannung. Ein doppel blind Versuch mit Placebokontrolle und Anwendung von Sequenzanalyse. *Psychopharmacologia*, **6,** 159–162, 1964.

301 LIPPOLD, O. C. J. Electromyography. p. 245–297 in VENABLES, P. H. and MARTIN, I. (Eds.) *Manual of Psycho-physiological Methods.* North-Holland Amsterdam, 1967.

302 LOOMIS, T. A. and WEST, T. C. Comparative sedative effects of a barbiturate and some tranquilizer drugs on normal subjects. *Journal of Pharmacology and Experimental Therapeutics*, **22,** 525–531, 1958.

303 LORR, M. Rating scales, behaviour inventories, and drugs. p. 519–539 in UHR, L. and MILLER, J. G. (Eds.) *Drugs and Behavior.* Wiley, New York, 1960.

304 LORR, M., McNAIR, D. M. and WEINSTEIN, G. J. Early effects of chlordiazepoxide (Librium) used with psychotherapy. *Journal of Psychiatric Research*, **1,** 257–270, 1963.

305 LORR, M., McNAIR, D. M., WEINSTEIN, G. J., MICHAUX, W. W. and RASKIN, A. Meprobamate and chlorpromazine in psychotherapy. Some effects on anxiety and hostility of outpatients. *Archives of General Psychiatry*, **4,** 381–389, 1961.

306 LUCAS, J. D. The interactive effects of anxiety, failure, and intraserial duplication. *American Journal of Psychology*, **65,** 59–66, 1952.

307 LUFF, M. C. and GARROD, M. The after results of psychotherapy in 500 adult cases. *British Medical Journal*, **2,** 55–59, 1935.

308 LYKKEN, D. T. and KATZENMEYER, W. G. *Manual for the Activity Preference Questionnaire.* Department of Psychiatry, University of Minnesota, Minneapolis, 1968.

309 McEVEDY, C. P., GRIFFITH, A. and HALL, T. Two school epidemics. *British Medical Journal*, **2,** 1300–1302, 1966.

310 McINNES, R. G. Observations on heredity in neurosis. *Proceedings of the Royal Society of Medicine*, **30,** 895–904, 1937.

311 McNAIR, D. M., GOLDSTEIN, A. P., LORR, M., CIBELLI, L. A. and ROTH, I. Some effects of chlordiazepoxide and meprobamate with psychiatric outpatients. *Psychopharmacologia*, **7,** 256–265, 1965.

312 McNAIR, D. M. and LORR, M. An analysis of mood in neurotics. *Journal of Abnormal and Social Psychology*, **69,** 620–627, 1964.

313 McREYNOLDS, P. Anxiety, perception and schizophrenia. p. 248 in JACKSON, D. (Ed.) *The Etiology of Schizophrenia.* Basic, New York, 1960.

314 McREYNOLDS, P. and ACKER, M. On the assessment of anxiety: II. By a self-report inventory. *Psychological Reports*, **19,** 231–237, 1966.

315 MAGGS, R. and NEVILLE, R. Chlordiazepoxide (Librium). A clinical trial of its use in controlling symptoms of anxiety. *British Journal of Psychiatry*, **110,** 540–543, 1964.

316 MAHL, G. F. Disturbances and silences in the patient's speech in psychotherapy. *Journal of Abnormal and Social Psychology*, **53,** 1–15, 1956.

317 MAHL, G. F. Measuring the patients' anxiety during interviews from "expressive" aspects of his speech. *Transactions of the New York Academy of Sciences*, **21,** 249–257, 1959.

318 MALLESON, N. Panic and phobia: possible method of treatment. *Lancet*, **1,** 225–227, 1959.

319 MALMO, R. B. and AMSEL, A. Anxiety-produced interference in serial rote learning with observations on rote learning after partial frontal lobectomy. *Journal of Experimental Psychology*, **38,** 440–454, 1948.
320 MALMO, R. B. and SHAGASS, C. Physiologic study of symptom mechanisms in psychiatric patients under stress. *Psychosomatic Medicine*, **11,** 25–29, 1949.
321 MALMO, R. B. and SHAGASS, C. Studies of blood pressure in psychiatric patients under stress. *Psychosomatic Medicine*, **14,** 82–93, 1952.
322 MALMO, R. B., SHAGASS, C. and DAVIS, J. F. Electromyographic studies of muscular tension in psychiatric patients under stress. *Journal of Clinical and Experimental Psychopathology*, **12,** 45–66, 1951.
323 MALMO, R. B., SHAGASS, C., DAVIS, J. F., CLEGHORN, R. A., GRAHAM, B. F. and GOODMAN, A. J. Standardized pain stimulation as controlled stress in physiological studies of psychoneurosis. *Science*, **108,** 509–511, 1948.
324 MALMO, R. B., SHAGASS, C. and HESLAM, R. M. Blood pressure response to repeated brief stress in psychoneurosis: a study of adaptation. *Canadian Journal of Psychology*, **5,** 167–179, 1951.
325 MALMO, R. B. and SMITH, A. A. Forehead tension and motor irregularities in psychoneurotic patients under stress. *Journal of Personality*, **23,** 391–406, 1955.
326 MANDLER, G. and SARASON, S. B. A study of anxiety and learning. *Journal of Abnormal and Social Psychology*, **47,** 166–173, 1952.
327 MANDLER, G. and WATSON, D. L. Anxiety and the interruption of behavior. p. 263–288 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.
328 MANOSEVITZ, M. and LANYON, R. L. Fear Survey Schedule—a normative study. *Psychological Reports*, **17,** 699–703, 1965.
329 MARKS, I. M. Components and correlates of psychiatric questionnaires. *British Journal of Medical Psychology*, **40,** 261–272, 1967.
329a MARKS, I. M. Measurement of personality and attitude: applications to clinical research. *Postgraduate Medical Journal*, **44,** 279–285, 1968.
330 MARKS, I. M. *Fears and Phobias*. Heinemann Medical, London, 1969.
331 MARKS, I. M., BIRLEY, J. L. T. and GELDER, M. G. Modified leucotomy in severe agoraphobia: a controlled serial inquiry. *British Journal of Psychiatry*, **112,** 757–769, 1966.
332 MARKS, I. M., BOULOUGOURIS, J. and MARSET, P. Flooding versus desensitisation in the treatment of phobic patients: a crossover study. *British Journal of Psychiatry*, **117,** 1971, in press.
333 MARKS, I. M., CROWE, M., DREWE, E., YOUNG, J. and DEWHURST, W. G. Obsessive compulsive neurosis in identical twins. *British Journal of Psychiatry*, **115,** 991–998, 1969.
334 MARKS, I. M. and HERST, E. R. A survey of 1,200 agoraphobics in Britain. *Social Psychiatry*, **5,** 16–24, 1970.
335 MARTIN, B. The assessment of anxiety by physiological behavioral measures. *Psychological Bulletin*, **58,** 234–255, 1961.
336 MARTIN, B. Anxiety. p. 216–259 in COSTELLO, C. G. (Ed.) *Symptoms of Psychopathology. A Handbook*. Wiley, New York, 1970.
337 MARTIN, I. Levels of muscle activity in psychiatric patients. *Acta Psychologica (Amsterdam)*, **12,** 326–341, 1956.
338 MARTIN, I. and LEVEY, A. B. *The Genesis of the Classical Conditioned Response*. Pergamon, Oxford, 1969.
339 MARTIN, I., MARKS, I. M. and GELDER, M. G. Conditioned eyelid responses in phobic patients. *Behaviour Research and Therapy* **7,** 115–124, 1969.
340 MASON, J. W. Psychological influences on the pituitary-adrenal cortical system. *Recent Progress in Hormone Research*. **15,** 245–378, 1959.

341 MASSERMAN, J. H. Drug effects on experimental neuroses in animals. p. 250–254 in UHR, L. and MILLER, J. G. (Eds.) *Drugs and Behavior*. Wiley, New York, 1960.

342 MATARAZZO, J. D., GUZE, S. B. and MATARAZZO, R. G. An approach to the validity of the the Taylor anxiety scale: scores of medical and psychiatric patients. *Journal of Abnormal and Social Psychology*, **51,** 276–280, 1955.

343 MATARAZZO, J. D. and PHILLIPS, J. S. Digit symbol performance as a function of increasing levels of anxiety. *Journal of Consulting Psychology*, **19,** 131–134, 1955.

344 MATARAZZO, J. D., ULETT, G. A. and SASLOW, G. Human maze performance as a function of increasing levels of anxiety. *Journal of General Psychology*, **53,** 79–95, 1955.

345 MATHEWS, A. M. Reciprocal inhibition: habituation or extinction? Paper to Conference on Behaviour Modification, Dublin, September, 1969.

346 MATHEWS, A. M. and GELDER, M. G. Psychophysiological investigations of brief relaxation training. *Journal of Psychosomatic Research*, **13,** 1–8, 1969.

347 MAUPIN, E. W. Zen Buddhism. a psychological review. *Journal of Consulting Psychology*, **26,** 362–378, 1962.

348 MAWSON, A. *Rival Treatments in the Phobias*. M.Phil. Dissertation, University of London, 1969.

349 MAY, R. *The Meaning of Anxiety*. Ronald Press, New York, 1950.

350 MEALIEA, W. L. *The Comparative Effectiveness of Systematic Desensitisation and Implosive Therapy in the Elimination of Snake Phobia*. Unpublished doctoral dissertation, University of Missouri, 1967.

351 MEDNICK, S. A. Generalization as a function of manifest anxiety and adaptation to psychological experiments. *Journal of Consulting Psychology*, **21,** 491–494, 1957.

352 MILES, H. W. M., BARRABEE, E. L. and FINESINGER, J. E. Evaluation of psychotherapy, with a follow-up study of 62 cases of anxiety neurosis. *Psychosomatic Medicine*, **13,** 83–105, 1951.

353 MILLER, L. H. and SHMAVONIAN, B. M. Replicability of two GSR indices as a function of stress and cognitive activity. *Journal of Personality and Social Psychology*, **2,** 753–756, 1965.

354 MILLER, N. E. Learning of visceral and glandular responses. *Science, N.Y.*, **163,** 434–438, 1969.

355 MIRSKY, A. F. and KORNETSKY, C. On the dissimilar effects of drugs on the digit symbol substitution and continuous performance tests. A review and preliminary integration of behavioral and physiological evidence. *Psychopharmacologia*, **5,** 161–177, 1964.

356 MOLDAWSKY, S. and MOLDAWSKY, P. C. Digit span as an anxiety indicator. *Journal of Consulting Psychology*, **16,** 115–118, 1952.

357 MONTAGUE, E. K. The role of anxiety in serial rote learning. *Journal of Experimental Psychology*, **45,** 91–96, 1953.

358 MORGAN, G. A. and RICCIUTI, H. N. Infants' response to strangers during the first year. p. 253–272 in FOSS, B. M. (Ed.) *Determinants of Infants Behaviour*. Methuen, London, 1967.

359 MORIARTY, J. D. and MEBANE, J. C. Comparative studies of chlordiazepoxide in office practice. *Journal of Neuropsychiatry*, **3,** 241–245, 1962.

360 MOSS, P. D. and McEVEDY, C. An epidemic of overbreathing among schoolgirls. *British Medical Journal*, **2,** 1295–1300, 1966.

361 MURMANN, W., ALMIRANTE, L. and SACCANI-GUELFI, M. Central nervous system effects of four β-adrenergic receptor blocking agents. *Journal of Pharmacy and Pharmacology*, **18,** 317–318, 1966.

362 MURPHREE, O. D., DYKMAN, R. A. and PETERS, J. E. Objective measures of behaviour in two strains of the pointer dog. Paper, in Symposium on Higher Nervous Activity, IV World Psychiatry Congress, Madrid, 1966.

363 NEIL, W. H. Influence of drugs on driving. *Texas State Journal of Medicine*, **58,** 92–97, 1962.

364 NGUI, P. W. The Koro epidemic in Singapore. *Australian and New Zealand Journal of Psychiatry*, **3,** 263–266, 1969.

365 NIEBUHR, R. *The Nature and Destiny of Man; a Christian Interpretation.* Charles Scribner, New York, 1941.

366 NORDENFELDT, O. Orthostatic E.C.G. changes and the adrenergic beta receptor blocking agents. *Acta Medica Scandinavica*, **178,** 4, 393–401, 1965.

367 NORRIS, H. The time course of barbiturate action in man investigated by measurement of smooth tracking eye movement. *British Journal of Pharmacology and Chemotherapy*, **33,** 117–128, 1968.

368 NOWLIS, V. and GREEN, R. F. Factor-analytical studies of the mood adjective checklist. Technical Report, Office of Naval Research, San Diego, U.S.A., 1965.

369 O'CONNOR, J. P., LORR, M. and STAFFORD, J. W. Some patterns of manifest anxiety. *Journal of Clinical Psychology*, **12,** 160–163, 1956.

370 OPPENHEIMER, B. S., LEVINE, S. A., MORISON, R. A., ROTHSCHILD, M. A., ST. LAWRENCE, W. and WILSON, F. N. Report on neurocirculatory asthenia and its management. *Military Surgeon*, **42,** 409–426, 1918.

371 OPPENHEIMER, B. S. and ROTHSCHILD, M. A. The psychoneurotic factor in the irritable heart of soldiers. *Journal of American Medical Association*, **70,** 1919–1922, 1918.

372 PARKES, C. M. Separation anxiety: an aspect of the search for a lost object. p. 87–92 in LADER, M. H. (Ed.) *Studies of Anxiety.* Royal Medico-Psychological Association, London, 1969.

373 PAUL, G. L. *Insight versus Desensitisation in Psychotherapy: An Experiment in Anxiety Reduction.* Stanford University Press, Stanford, 1966.

374 PAUL, G. L. and ERIKSEN, C. W. Effects of test anxiety on "real-life" examinations. *Journal of Personality*, **32,** 480–494, 1964.

375 PAVLOV, I. P. *Conditioned Reflexes. An Investigation of the Physiological Activity of the Cerebral Cortex.* Oxford University Press, London, 1927.

376 PECK, R. E. Observations on salivation and palmar sweating in anxiety and other psychiatric conditions. *Psychosomatics*, **7,** 343–348, 1966.

377 PERKINS, C. W. *The Effect of Muscle Relaxation and Suggested Therapeutic Benefit on the Reduction of Anxiety.* Ph.D. Dissertation, University of Illinois, 1966.

378 PERLOFF, B. *Influence of Muscular Relaxation and Positive Imagery on Extinction of Avoidance Behaviour Through Systematic Desensitisation.* Ph.D. Dissertation, Stanford University, 1970.

379 PERSKY, H. Response to a life stress: evaluation of some biochemical indices. *Journal of Applied Physiology*, **6,** 369–374, 1953.

380 PERSKY, H. Introduction and removal of hydrocortisone from plasma: rates in normal subjects and anxious patients. *Archives of General Psychiatry (Chicago)*, **7,** 93–97, 1962.

381 PERSKY, H., GAMM, S. R. and GRINKER, R. R. Correlation between fluctuation of free anxiety and quantity of hippuric acid excretion. *Psychosomatic Medicine*, **14,** 34–40, 1952.

382 PERSKY, H., GRINKER, R. R. and MIRSKY, I. A. Excretion of hippuric acid in subjects with free anxiety. *Journal of Clinical Investigation*, **29,** 110–114, 1950.

383 PERSKY, H. GROSZ, H. J., NORTON, J. A. and McMURTRY, M. Effect of hypnotically-induced anxiety on the plasma hydrocortisone level of normal subjects. *Journal of Clinical Endocrinology and Metabolism*, **19,** 700–710, 1959.

384 PERSKY, H. et al. Adrenal cortical function in anxious human subjects. Plasma level and urinary excretion of hydrocortisone. *Archives of Neurology and Psychiatry (Chicago)*, **76,** 549–558, 1956.

385 PERSKY, H. et al. Relation of emotional responses and changes in plasma hydrocortisone level after stressful interview. *Archives of Neurology and Psychiatry (Chicago)*, **79,** 434–447, 1958.

386 PERSKY, H. et al. Effect of two psychological stresses on adrenocortical function studies on anxious and normal subjects. *Archives of Neurology and Psychiatry (Chicago)*, **81,** 219–232, 1959.

387 PFEIFFER, C. C. and GOLDSTEIN, L. Assay of anti-anxiety drugs by quantitative electronencephalography. *Journal of Neuropsychiatry*, **5,** 475–478, 1964.

388 PITTS, F. N. and McCLURE, J. N. Lactate metabolism in anxiety neurosis. *New England Journal of Medicine*, **277,** 1329–1336, 1967.

389 POSTMAN, L. and BRUNER, J. S. Perception under stress. *Psychological Reviews*, **55,** 314–324, 1948.

390 PRAT, J. and MASANA, J. Some results of our tachistoscopic method applied to psychopharmacology. p. 398–400 in CERLETTI, A. and BOVÉ, F. J. (Eds.) *The Present Status of Psychotropic Drugs.* Excerpta Medica, Amsterdam, 1969.

391 PRICE, D. B., THALER, M. and MASON, J. W. Preoperative emotional states and adrenal cortical activity. Studies on cardiac and pulmonary surgery patients. *Archives of Neurology and Psychiatry (Chicago)*, **77,** 646–656, 1957.

392 QUARANTELLI, E. L. The nature and conditions of panic. *American Journal of Sociology*, **60,** 267–275, 1954.

393 RACHMAN, S. *Phobias. Their Nature and Control.* Charles C. Thomas, Springfield, Illinois, 1968.

394 RACHMAN, S., HODGSON, R. and MARKS, I. M. Treatment of chronic obsessive-compulsive neurosis. *Behaviour Research and Therapy*, 1971, in press.

395 RAPHELSON, A. C. The relationships among imaginative, direct verbal, and physiological measures of anxiety in an achievement situation. *Journal of Abnormal and Social Psychology*, **54,** 13–18, 1957.

396 RAYMOND, M. J., LUCAS, C. J., BEESLEY, M. L., O'CONNELL, B. A. and FRASER ROBERTS, J. A. A trial of five tranquillizing drugs in psychoneurosis. *British Medical Journal*, **2,** 63–66, 1957.

397 REYNOLDS, E., JOYCE, C. R. B., SWIFT, J. L., TOOLEY, P. H. and WEATHERALL, M. Psychological and clinical investigation of the treatment of anxious out-patients with three barbiturates and placebo. *British Journal of Psychiatry*, **111,** 84–95, 1965.

398 RICKELS, K. BAUMM, C. and FALES, K. Evaluation of placebo responses in psychiatric outpatients under two experimental conditions. p. 80–84 in BRADLEY, P. B., FLÜGEL, F. and HOCH, P. (Eds.) *Neuropsychopharmacology*, Vol. 3. Elsevier, Amsterdam, 1964.

399 RICKELS, K., BOREN, R. and STUART, H. M. Controlled psychopharmacological research in general practice. *Journal of New Drugs*, **4,** 138–147, 1964.

400 RICKELS, K. and SNOW, L. Meprobamate and phenobarbital sodium in anxious neurotic psychiatric and medical clinic outpatients. A controlled study. *Psychopharmacologia*, **5,** 339–348, 1964.

401 RICKELS, K. et al. Controlled psychopharmacological research in private psychiatric practice. *Psychopharmacologia (Berlin)*, **9,** 288–306, 1966.

402 RICKELS, K. et al. Tybamate—a perplexing drug. *American Journal of Psychiatry*, **125,** 320–326, 1968.

403 RITTER, B. Treatment of agoraphobia with contact desensitisation. *Behaviour Research and Therapy*, **7**, 41–45, 1969.
404 RITTER, B. The use of contact desensitisation, demonstration-plus-participation and demonstration alone in the treatment of aerophobia. *Behaviour Research and Therapy*, **7**, 157–164, 1969.
405 ROBBINS, P. R. Some explorations into the nature of anxieties relating to illness. *Genetic and Psychological Monographs*, **66**, 91–141, 1962.
406 ROBEY, W. H. and BOAS, E. P. Neurocirculatory asthenia. *Journal of American Medical Association*, **71**, 525–529, 1918.
407 ROBIN, A. A. Pecazine ("Pacatal") compared with amylobarbitone sodium in anxiety states. *Journal of Mental Science*, **105**, 1064–1069, 1959.
408 ROBINSON, J. T., DAVIES, L. S., KREITMAN, N. and KNOWLES, J. B. A double-blind trial of oxypertine for anxiety neurosis. *British Journal of Psychiatry*, **111**, 527–529, 1965.
409 ROGERS, C. R. *Client-centred Therapy*. Houghton Mifflin Company, Boston, 1951.
410 ROGERSON, H. L. Venereophobia in the male. *British Journal of Venereal Disease*, **27**, 158–159, 1951.
411 ROTH, M. The classification of affective disorders, p. 9–47 in *Symposium on Treatment of Depression*. Appelbergs Botryckeri, Uppsala, 1968.
412 ROTH, W. F. and LUTON, F. H. The mental health programme in Tennessee. *American Journal of Psychiatry*, **99**, 662–675, 1943.
413 RUBIN, H. and TOWNSEND, A. H. The Taylor manifest anxiety scale in differential diagnosis. *Journal of Clinical Psychology*, **14**, 81–83, 1958.
414 RUBIN, L. S. Autonomic dysfunction as a concomitant of neurotic behavior. *Journal of Nervous and Mental Diseases*, **138**, 558–574, 1964.
415 RUBIN, S. E. and LAWLIS, G. F. Factor analysis of the 122 item fear survey schedule. *Behaviour Research and Therapy*, **7**, 381–386, 1969.
416 RUNQUIST, W. N. and ROSS, L. E. The relation between physiological measures of emotionality and performance in eyelid conditioning. *Journal of Experimental Psychology*, **57**, 329–332, 1959.
417 RUNQUIST, W. N. and SPENCE, K. W. Performance in eyelid conditioning related to changes in muscular tension and physiological measures of emotionality. *Journal of Experimental Psychology*, **58**, 417–422, 1959.
418 RUSSELL, R. W. A comparative study of "conflict" and "experimental neurosis". *British Journal of Psychology*, **41**, 95–108, 1950.
419 SACHS, A. *The Jail Diary of Albie Sachs*. Harvill Press, London, 1966.
420 SACKS, B., FENWICK, P. B. C., MARKS, I., FENTON, G. W. and HEBDEN, A. Paper to U.K. EEG Society, London, January, 1971.
421 SAINSBURY, P. and GIBSON, J. G. Symptoms of anxiety and tension and the accompanying physiological changes in the muscular system. *Journal of Neurology, Neurosurgery and Psychiatry*, **17**, 216–224, 1954.
422 SAMPSON, H. and BINDRA, D. "Manifest" anxiety, neurotic anxiety, and the rate of conditioning. *Journal of Abnormal and Social Psychology*, **49**, 256–259, 1954.
423 SARASON, I. G. Effect of anxiety, and two kinds of motivating instructions on verbal learning. *Journal of Abnormal and Social Psychology*, **54**, 166–171, 1957.
424 SARASON, I. G. Test anxiety, general anxiety, and intellectual performance. *Journal of Consulting Psychology*, **21**, 485–490, 1957.
425 SARASON, I. G. Effects on verbal learning of anxiety, reassurance, and meaningfulness of material. *Journal of Experimental Psychology*, **56**, 472–477, 1958.
426 SARASON, I. G. Empirical findings and theoretical problems in the use of anxiety scales. *Psychology Bulletin*, **57**, 403–415, 1960.

427 SARASON, I. G. and PALOLA, E. G. The relationship of test and general anxiety, difficulty of task, and experimental instructions to performance. *Journal of Experimental Psychology*, **59,** 185–191, 1960.
428 SARASON, S. B. The measurement of anxiety in children: some questions and problems. p. 63–79 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.
429 SARASON, S. B., DAVIDSON, K. S., LIGHTHALL, F. F., WAITE, R. R. and RUEBUSH, B. K. *Anxiety in Elementary School Children*. Wiley, New York, 1960.
430 SARASON, S. B. and GORDON, E. M. The test anxiety questionnaire: scoring norms. *Journal of Abnormal and Social Psychology*, **48,** 447–448, 1953.
431 SARASON, S. B., HILL, K. T. and ZIMBARDO, P. G. A longitudinal study of the relation of test anxiety to performance on intelligence and achievement tests. *Child Development Monograph*, Serial No. 98, **29,** No. 7, 1964.
432 SARGANT, W. *Battle for the Mind*, Pan Books, London, 1957.
433 SAVILL, T. D. *Clinical Lectures on Neurasthenia*. Williams Wood, New York, 1899.
434 SCHACHTER, J. Pain, fear, and anger in hypertensives and normotensives. A psychophysiological study. *Psychosomatic Medicine*, **19,** 17–29, 1957.
435 SCHACHTER, S. The interaction of cognitive and physiological determinants of emotional state. p. 193–224 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.
436 SCHERBEL, A. L. Preliminary evaluation of chlordiazepoxide. Double blind study with observations on its effects in various diseases. *American Practitioner (Philadelphia)*, **12,** 273–281, 1961.
437 SCHERER, M. W. and NAKAMURA, C. Y. A fear-survey schedule for children (F.S.S.-F.C.): a factor analytic comparison with manifest anxiety (CMAS). *Behaviour Research and Therapy*, **6,** 173–182, 1968.
438 SCHNEIRLA, T. A. Aspects of stimulation and organisation. In: Approach/withdrawal processes underlying vertebrate behavioural development. p. 2–75 in LEHRMAN, D. S., HINDE, R. A. and SHAW, E. (Eds.) *Advances in the Study of Behaviour*, Vol. 1. Academic Press, London, 1965.
439 SCHNUR, S. Cardiac neurosis associated with organic heart disease. *American Heart Journal*, **18,** 153–165, 1939.
440 SCHULTZ, D. P. *Panic Behavior*. Random House, New York, 1964.
441 SCHULTZ, J. H. and LUTH, W. *Autogenic Training*. Grune and Stratton, New York, 1959.
442 SCHURR, P. H. Leucotomy. *British Journal of Hospital Medicine*, **2,** 1712–1715, 1969.
443 SCHWARTZ, B. J. An empirical test of two Freudian hypotheses concerning castration anxiety. *Journal of Personality*, **24,** 318–327, 1956.
444 SCOTT, R. B. *Price's Textbook of the Practice of Medicine*. Oxford University Press, London, 1966.
445 SEEHERMAN, R. Evaluation of tybamate in the clinical management of anxiety. *Delaware Medical Journal*, **36,** 213–216, 1964.
446 SHAGASS, C. and NAIMAN, J. The sedation threshold as an objective index of manifest anxiety in psychoneurosis. *Journal of Psychosomatic Research*, **1,** 49–57, 1956.
447 SHEARMAN, R. W. Response-contingent CS termination in the extinction of avoidance learning. *Behaviour Research and Therapy*, **8,** 227–239, 1970.
448 SHEPHERD, M., COOPER, B., BROWN, A. C. and KALTON, G. *Psychiatric Illness in General Practice*. Oxford University Press, London, 1966.
449 SHIELDS, J. *Monozygotic Twins Brought Up Apart and Brought Up Together*. Oxford University Press, London, 1962.

450 SIDMAN, M. Some technical problems in evaluating the behavioral effects of drugs. p. 162–169 in VOTAVA, Z., HORVATH, M. and VINAR, O. (Eds.) *Psychopharmacological Methods*. Pergamon, Oxford, 1963.

451 SIEGMAN, A. W. Cognitive, affective, and psychopathological correlates of the Taylor manifest anxiety scale. *Journal of Consulting Psychology*, **20,** 137–141, 1956.

452 SIEGMAN, A. W. The effect of manifest anxiety on a concept formation task, a nondirected learning task, and on timed and untimed intelligence tests. *Journal of Consulting Psychology*, **20,** 176–178, 1956.

453 SLATER, E. and SHIELDS, J. Genetical aspects of anxiety. p. 62–71 in LADER, M. H. (Ed.) *Studies of Anxiety*. Royal Medico-Psychological Association, London, 1969.

454 SMITH, G. M. and BEECHER, H. K. Amphetamine sulfate and athletic performance. 1. Objective effects. *Journal of the American Medical Association*, **170,** 542–557, 1959.

455 SMITH, M. E. and CHASSAN, J. B. Comparisons of diazepam, chlorpromazine and trifluoperazine in a double-blind clinical investigation. *Journal of Neuropsychiatry*, **5,** 593–600, 1964.

456 SOKOLOV, E. N. *Perception and the Conditioned Reflex*. Pergamon Press, Oxford, 1963.

457 SOLZHENITSYN, A. I. *The First Circle*. Collins, London, 1968.

458 SPENCE, J. T. and SPENCE, K. W. The motivational components of manifest anxiety: drive and drive stimuli. p. 291–326 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.

459 SPENCE, K. W. Anxiety (drive) level and performance in eyelid conditioning. *Psychological Bulletin*, **61,** 129–139, 1964.

460 SPENCE, K. W. and FARBER, I. E. Conditioning and extinction as a function of anxiety. *Journal of Experimental Psychology*, **45,** 116–119, 1953.

461 SPENCE, K. W., FARBER, I. E. and TAYLOR, E. The relation of electric shock and anxiety to level of performance in eyelid conditioning. *Journal of Experimental Psychology*, **48,** 404–408, 1954.

462 SPENCE, K. W. and GOLDSTEIN, H. Eye-lid conditioning performance as a function of emotion-producing instructions. *Journal of Experimental Psychology*, **62,** 291–294, 1961.

463 SPENCE, K. W. and TAYLOR, J. Anxiety and strength of the UCS as determiners of the amount of eyelid conditioning. *Journal of Experimental Psychology*, **42,** 183–188, 1951.

464 SPENCE, K. W. and TAYLOR, J. The relation of conditioned response strength to anxiety in normal, neurotic, and psychotic subjects. *Journal of Experimental Psychology*, **45,** 265–272, 1953.

465 SPIELBERGER, C. D. On the relationship between manifest anxiety and intelligence. *Journal of Consulting Psychology*, **22,** 220–224, 1958.

466 SPIELBERGER, C. D. The effects of manifest anxiety on the academic achievement of college students. *Mental Hygiene*, **46,** 420–426, 1962.

467 SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.

468 SPIELBERGER, C. D. The effects of anxiety on complex learning and academic achievement. p. 361–398 in SPIELBERGER, C. D. (Ed.) *Anxiety and Behavior*. Academic Press, New York, 1966.

469 SPIELBERGER, C. D., GORSUCH, R. L. and LUSHENE, R. E. *Manual for the State-Trait Anxiety Inventory*. Florida State University, Tallahassee, Florida, 1968.

470 SPIELBERGER, C. D. and KATZENMEYER, W. G. Manifest anxiety, intelligence, and college grades. *Journal of Consulting Psychology*, **23,** 278, 1959.

471 SPIELBERGER, C. D., LUSHENE, R. E. and McADOO, W. G. Theory and measurement of anxiety states. Chapter 10 in R. B. CATTELL (Ed.) *Handbook of Modern Personality Theory*. Aldine, Chicago, 1971.
472 SPIELBERGER, C. D., WEITZ, H. and DENNY, J. P. Group counseling and the academic performance of anxious college freshmen. *Journal of Counseling Psychology*, **9**, 195–204, 1962.
473 SPLITTER, S. R. A new psychotropic drug: evaluation of tybamate in the treatment of anxiety and tension states. *Psychosomatics*, **5**, 292–294, 1964.
474 SPRENGER, J. and KRAMER, H. *Malleus Maleficarum* (Translated by SUMMERS, M.). Folio Society, London, 1968.
475 STAMPFL, T. G. and LEVIS, D. J. Essentials of implosive therapy: a learning-theory-based psychodynamic behavioural therapy. *Journal of Abnormal Psychology*, **72**, 496–530, 1967.
476 STERNBACH, L. H., RANDALL, L. O., BANZIGER, R. and LEHR, H. Structure-activity relationships in the 1-4 benzodiazepine series. p. 237–264 in BURGER, A. (Ed.) *Drugs Affecting the Central Nervous System*. Vol. 2. Dekker, New York, 1968.
477 STERNBACH, R. A. *Principles of Psychophysiology*. Academic Press, New York, 1966.
478 STRAUSS, H. Clinical and electroencephalographic studies: the electro-encephalogram in psychoneurotics. *Journal of Nervous and Mental Diseases*, **101**, 19–27, 1945.
479 SUWANA, A. B. Effect of cultural change in anxiety in women in Thailand. *Australian and New Zealand Journal of Psychiatry*, **3**, 267–270, 1969.
480 SWENSON, W. M. Attitudes towards death among the aged. *Minnesota Medicine*, **42**, 399–402, 1959.
481 TAFT, R. The validity of the Barron ego-strength scale and the Welsh anxiety index. *Journal of Consulting Psychology*, **21**, 247–249, 1957.
482 TAN, B. K. Physiological correlates of anxiety. A preliminary investigation of the orienting reflex. *Canadian Psychiatric Association Journal*, **9**, 63–71, 1964.
483 TAN, E., MARKS, I. M. and MARSET, P. Bimedial leucotomy in obsessive-compulsive neurosis: a controlled serial enquiry. *British Journal of Psychiatry*, **118**, 155–164, 1971.
484 TAN, E. S. The symptomatology of anxiety in West Malaysia. *Australian and New Zealand Journal of Psychiatry*, **3**, 271–276, 1969.
484a TAYLOR, D. H. Drivers' galvanic skin response and the risk of accident. *Ergonomics*, **7**, 439–451, 1964.
485 TAYLOR, J. A. The relationship of anxiety to the conditioned eyelid response. *Journal of Experimental Psychology*, **41**, 81–91, 1951.
486 TAYLOR, J. A. A personality scale of manifest anxiety. *Journal of Abnormal and Social Psychology*, **48**, 285–295, 1953.
487 TAYLOR, J. A. and SPENCE, K. W. The relationship of anxiety level to performance in serial learning. *Journal of Experimental Psychology*, **44**, 61–64, 1952.
488 THORPE, W. H. *Learning and Instinct in Animals*. Methuen, London, 1956.
489 TILLICH, P. *The Courage to Be*. Yale University Press, New Haven, 1952.
490 TOBIN, J. M., LORENZ, A. A., BROUSSEAU, E. R. and CONNER, W. R. Clinical evaluation of oxazepam for the management of anxiety. *Diseases of the Nervous System*, **25**, 689–696, 1964.
491 TURNER, P. *Clinical Aspects of Autonomic Pharmacology*. Heinemann, London, 1969.
492 TURNER, P., GRANVILLE-GROSSMAN, K. L. and SMART, J. V. Effect of adrenergic receptor blockade on the tachycardia of thyrotoxicosis and anxiety state. *Lancet*, **2**, 1316–1318, 1965.

493 TYSON, V. Two trials with a new psychotherapeutic drug in the treatment of anxiety. *Practitioner*, **204**, 306–309, 1970.
494 UHLENHUTH, E. H., CANTER, A., NEUSTADT, J. O. and PAYSON, H. E. The symptomatic relief of anxiety with meprobamate, phenobarbital and placebo. *American Journal of Psychiatry*, **115**, 905–910, 1959.
495 UHR, L., POLLARD, J. C. and MILLER, J. G. Behavioral effects of chronic administration of psychoactive drugs to anxious patients. *Psychopharmacologia*, **1**, 150–168, 1959.
496 ULETT, G. A., GLESER, G., WINOKUR, G. and LAWLER, A. The EEG and reaction to photic stimulation as an index of anxiety-proneness. *Electroencephalography and Clinical Neurophysiology*, **5**, 23–32, 1953.
497 VANDENBERG, S. G., CLARK, P. J. and SAMUELS, I. Psychophysiological reactions of twins: hereditability factors in galvanic skin resistance, heartbeat and breathing rates. *Eugenic Quarterly*, **12**, 7–10, 1965.
498 VAZUKA, F. A. and McLAUGHLIN, B. E. Chemotherapy of symptoms of chronic anxiety states and other neurotic disorders. *Psychosomatics*, **6**, 73–78, 1965.
499 VENABLES, P. H. and MARTIN, I. (Eds.) *Manual of Psycho-physiological Methods*. North-Holland, Amsterdam, 1967.
500 von GEBSATTEL, V. E. Die Welt des Zwangskranken. *Monatschrift fur die Psychiatrie und Neurologie*, **99**, 10–74, 1938.
501 WALK, R. D. Selfratings of fear in fear-evoking situation. *Journal of Abnormal and Social Psychology*, **52**, 171–178, 1956.
502 WALKER, L. The prognosis for affective illness with overt anxiety. *Journal of Neurology, Neurosurgery and Psychiatry*, **22**, 338–41, 1959.
503 WATSON, J. P., GAIND, R. and MARKS, I. M. Prolonged exposure: a rapid treatment for phobias. *British Medical Journal*, **1**, 13–15, 1971.
504 WATSON, J. P. and MARKS, I. M. Relevant and irrelevant fear in flooding—a cross-over study of phobic patients. *Behaviour Therapy*, in press, 1971.
505 WEARN, J. T. and STURGIS, C. C. Studies on epinephrin. I. Effects of the injection of epinephrin in soldiers with "irritable heart". *Archives of Internal Medicine*, **24**, 247–268, 1919.
506 WEATHERALL, M. Tranquillizers. *British Medical Journal*, **1**, 1219–1224, 1962.
507 WEBB, J. T., MILLER, M. L. and FOWLER, R. D. Validation of a computerized MMPI interpretation system. p. 523–524. *Proceedings 77th Annual Convention of the American Psychiatric Association*, 1969.
508 WEIL, A. A. Ictal emotions occurring in temporal lobe dysfunction. *Archives of Neurology*, **1**, 87–97, 1959.
509 WEINER, S. et al. Effect on anxiety of increasing the plasma hydrocortisone level. *Psychosomatic Medicine*, **25**, 69–77, 1963.
510 WELCH, L. Human conditioning and anxiety. *Annals of the New York Academy of Sciences*, **56**, 266–272, 1953.
511 WELCH, L. and KUBIS, J. The effect of anxiety on the conditioning rate and stability of the PGR. *Journal of Psychology*, **23**, 83–91, 1947.
512 WELCH, L. and KUBIS, J. Conditioned PGR (psychogalvanic response) in states of pathological anxiety. *Journal of Nervous and Mental Diseases*, **105**, 372–381, 1947.
513 WELSH, G. S. An anxiety index and an internalization ratio for the MMPI. *Journal of Consulting Psychology*, **16**, 65–72, 1952.
514 WENAR, C. Reaction time as a function of manifest anxiety and stimulus intensity. *Journal of Abnormal and Social Psychology*, **49**, 335–340, 1954.
515 WESSMAN, A. E. and RICKS, D. F. *Mood and Personality*. Holt, New York, 1966.
516 WEST, E. D. and da FONSECA, A. F. Controlled trial of meprobamate. *British Medical Journal*, **2**, 1206–1209, 1965.

517 WESTPHAL, C. Ueber Zwangsvorstellungen. *Archiv für Psychiatrie und Nervenkrankheiten*, **8**, 734–750, 1877.
518 WESTROPE, R. M. Relations among Rorschach indices, manifest anxiety, and performance under stress. *Journal of Abnormal and Social Psychology*, **48**, 515–524, 1953.
519 WHEATLEY, D. Comparative effects of propranolol and chlordiazepoxide in anxiety states. *British Journal of Psychiatry*, **115**, 1411–1412, 1969.
520 WHEELER, E. O., WHITE, P. D., REED, E. W. and COHEN, M. E. Neurocirculatory asthenia (anxiety neurosis, effort syndrome, neurasthenia). *Journal of American Medical Association*, **142**, 878–888, 1950.
521 WHITE, P. D. and JONES, T. D. Heart disease and disorders in New England. *American Heart Journal*, **3**, 302–318, 1928.
522 WICKERT, F. (Ed.) Psychological research on problems of redistribution. Army Air Forces Aviation Psychology Program, Research Report No. 14. Washington, D.C. 1947.
523 WILLIAMS, D. The structure of emotions reflected in epileptic experiences. *Brain*, **79**, 29–67, 1956.
524 WILSON, G. D. Social desirability and sex differences in expressed fear. *Behaviour Research and Therapy*, **5**, 136–137, 1967.
525 WING, L. Physiological effects of performing a difficult task in patients with anxiety states. *Journal of Psychosomatic Research*, **7**, 283–294, 1964.
526 WINKEL, G. H. and SARASON, I. G. Subject, experimenter, and situational variables in research on anxiety. *Journal of Abnormal and Social Psychology*, **68**, 601–608, 1964.
527 WINOKUR, G. and HOLEMAN, E. Chronic anxiety neurosis: clinical and sexual aspects. *Acta Psychiatrica Scandinavica*, **39**, 384–412, 1963.
528 WITTENBORN, J. R. Comments on the selection and use of symptom rating scales for research in pharmacotherapy. *International Review of Neurobiology*, **7**, 279–295, 1964.
529 WITTENBORN, J. R. *The Clinical Psychopharmacology of Anxiety*. Thomas, Springfield, Illinois, 1966.
530 WOLPE, J. *Psychotherapy by Reciprocal Inhibition*. Stanford University Press, Stanford, 1958.
531 WOLPE, J. and LANG, P. J. A fear survey schedule for use in behaviour therapy. *Behaviour Research and Therapy*, **2**, 27–30, 1964.
532 WOOD, P. Effort syndrome. *British Medical Journal*, **1**, 767–772, 805–811, 845–851, 1941.
533 WOODS, E. F., RICHARDSON, J. A., RICHARDSON, A. K. and BOZEMAN, R. F. Plasma concentrations of epinephrine and arterenol following the actions of various agents on the adrenals. *Journal of Pharmacology and Experimental Therapeutics*, **116**, 351–355, 1956.
534 YAP, P. M. Anxiety reactions among Western expatriates in a plural society. *Australian and New Zealand Journal of Psychiatry*, **3**, 339–342, 1969.
535 YERKES, R. M. and DODSON, J. D. The relation of strength of stimulus to rapidity of habit-formation. *Journal of Comparative and Neurological Psychology*, **18**, 459–482, 1908.
536 YOUNG, J. P. R. *An Investigation of Auditory Evoked Potentials in Male Twins*. Unpublished M.D. Thesis, University of Cambridge, 1971.
537 ZAPELLA, D. G. and WODINSKY, A. Diazepam, phenobarbital and placebo in the treatment of psychiatric patients. *Diseases of the Nervous System*, **28**, 30–34, 1967.
538 ZBOROWSKI, M. Cultural components in response to pain. *Journal of Social Issues*, **8**, 16–30, 1952.
539 ZIEGLER, F. J. and IMBODEN, J. B. Contemporary conversion reactions: II. A conceptual model. *Archives of General Psychiatry*, **6**, 279–287, 1962.

540 ZIEGLER, F. J. and RODGERS, D. A. Contemporary conversion reactions: III. Diagnostic considerations. *Journal of the American Medical Association*, **186,** 307–311, 1963.

541 ZUCKERMAN, M., LUBIN, B., VOGEL, L. and VALERIUS, E. Measurement of experimentally induced affects. *Journal of Consulting Psychology*, **28,** 418–425, 1964.

542 ZUKIN, P., ARNOLD, De V. G. and KESSLER, C. R. Comparative effects of phenaglycodol and meprobamate on anxiety reactions. *Journal of Nervous and Mental Diseases*, **129,** 193–195, 1959.

AUTHOR INDEX

The number in italics refers to the number of the reference on pages 158–183 in which the author's name appears.

SUBJECT INDEX