

# The Treatment of Anxiety\*

JOHN H. SCHWAB AND NANCY H. MCGINNIS

*Department of Psychiatry, College of Medicine, University of Florida, Gainesville*

Rational therapy requires accurate diagnosis. When we apply this precept to anxiety a fundamental question arises. Is anxiety an illness in terms of the now be-  
rated medical model which holds that an illness has a cause, a natural history, and hopefully a cure? Or is anxiety a basic aspect of the human condition, an innate pattern of response which becomes pathological when stress, induced by physiologic and social forces, is magnified out of proportion to the original stimulus? If the latter is true, then stress and social interactions are the causative factors, the anxiety only a reaction. Logically then, the condition of anxiety can be modified by alleviating stress or changing the social environment. Although there is no definitive answer to this major question concerning the nature of anxiety, we would like to present briefly some of the present knowledge about it.

In 1921, Freud stated: "We call it [anxiety] an affective state, although we are also ignorant of what an affect is." He discussed three components of anxiety: (1) the specific feeling of displeasure, (2) acts of discharge (autonomic and endocrine functions), and (3) perceptions of these acts. Although more knowledge of biochemical and neurophysiologic mechanisms has accumulated since Freud made this observation little more is known about anxiety. Engel (1962) proposed that anxiety is

the earlier of two basic biological patterns of which depression-withdrawal is second. He says that anxiety "includes a variety of active modes of coping with stress which are designated the *flight-fight patterns* to indicate corresponding behavioral aspects (Cannon, 1939). These involve not only the biochemical and physiological preparations for flight or fight but also internal changes anticipating bodily injury." The psychophysiology of anxiety is neuroendocrinological, including activity of the limbic system and the hypothalamus, which leads to activation of the pituitary-adrenal cortical system and facilitates a wide range of metabolic processes involved in the long-term responses to injury (Engel, 1953; Ingle, 1952; Selye; 1960).

Grinker (1956) characterized the clinical manifestations of anxiety quantitatively. Mild anxiety is consonant with alertness or vigilance; it may be automatic, and the patient has little psychical or physical awareness of his anxiety. Greater quantities are manifested as episodes of recognized apprehension with physical symptoms. Thirdly, free anxiety, which may be episodic or continuous, is obviously neurotic. As the anxiety becomes more severe, disorganization of function occurs.

These are the fundamental psychiatric concepts. For the sake of completeness we should include that Berger (1962) propounds a strictly organic point of view when he says that anxiety is a "disease of the brain." In contrast, others see anxiety as a patterned re-

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sponse; neurotic symptoms are learned faulty patterns of behavior (Hall and Lindzey, 1957). Further, many theorists believe that anxiety is a constructive force, which not only acts as a danger signal to protect the organism, but also accounts for motivation and monitors behavior.

In medicine, psychosomaticists hold that excessive or sustained anxiety produces disturbances of bodily functions or structures which in turn result in organic illness. Physicians find that anxiety is a contributing factor, a correlate, or a result of many disease states. They are concerned with treating patients with acute, distressing "anxiety" attacks and those with high levels of chronic anxiety who are difficult to work with because of their general nervousness, irritability, fright, and erratic behavior.

### Incidence of Anxiety

Despite our difficulties in understanding the nature of anxiety, awareness of it is increasing in the Western world (Andresen, 1963; Finn and Husten, 1966; Rennie, 1948). Adams and Hope (1962) observe: "As a clinical syndrome, the anxiety state outranks all other problems in general medicine." Our studies (Schwab et al., 1966a, b, and c) with medical inpatients showed that 20% to 27% of them had severe anxiety. These data are in accord with Cattell and Scheier's statement (1961): "Epidemiological estimates vary . . . [but] a conservative consensus estimate would probably place 20% of the American population as needing treatment for disorders in which anxiety plays a prominent role."

### Treatment

The effective treatment of anxious patients hinges on the combined benefits of psychotherapy and medications. The limitations of psychotherapy are well known, and the limitations of drug therapy have been aptly expressed by

Goodman and Gilman (1965a): "obviously neither drugs nor other somatic treatment can give the insight to the patient that can be achieved by psychotherapy."

### Psychotherapy

We like Appel's definition of psychotherapy as quoted by Rickels (1964): "helping people to handle their feelings, motivations, and behavior more appropriately." And we should remember that psychotherapy is one of the oldest medical skills. The essence of psychotherapy is communication, and achieving the therapeutic dialogue is dependent on the relationship between the patient and the physician.

By listening, the therapist tries to obtain understanding, not necessarily agreement but rather comprehension. Either sympathetic agreement or antagonistic disagreement may produce distortions and solidify the neurotic organization. Thus, the task of the therapist is, in Wahl's words (1962) ". . . to convert apprehension to comprehension."

From awareness of his problems comes clarification; the patient is better able to make more appropriate decisions about his life. Other fundamentals of psychotherapy are the educative and the manipulative, deriving from increased knowledge of self and environment.

Just as communication is the essence of psychotherapy, self esteem is the fulcrum on which success balances. Only with increased self esteem can the patient order his world and create healthful relationships with it.

### Medication

Medication is the second component of treatment. When tranquilizers were first introduced, it was feared that they would render the patient too comfortable for psychotherapy. Obviously, this fear has not been realized. Available

medications do not purge anxiety, but they can reduce it to manageable proportions, thereby improving personal relationships, and forestalling ego disorganization and psychosis.

### Guidelines

To obtain maximal advantages in the use of drugs, the therapist must adhere to certain principles.

1. *Little is known about their pharmacologic action.* Most of these agents act as weak sedatives. The barbiturates, of course, are depressants of the reticular formation in the brain stem. The action of meprobamate is quite similar; although no specific site of action has been identified. Hendley et al. (1954) indicated, however, that it produces some thalamic synchronization, and others have observed slow wave activity in the basal ganglia and limbic system. It may interfere with centrally mediated autonomic responses. Indirectly, by affecting conduction in the limbic system, it appears to depress the reticular formation.

According to Goodman and Gilman (1965b), the effects of chlordiazepoxide (Librium) and the related compounds diazepam (Valium) and oxazepam (Serax) are more ubiquitous than those of meprobamate and the barbiturates. Chlordiazepoxide has a central action, possible peripheral actions, and a definite sedative effect intermediate in potency between meprobamate and chlorpromazine. Like barbiturates and meprobamate, in experimental animals it blocks both conditioned and unconditioned avoidance responses.

The phenothiazines (Thorazine, Mellaril, Stelazine) appear to produce changes at many levels: the EEG is characteristic of drowsiness; arousal is diminished; there are some effects upon the limbic system and the basal ganglia; and conditioned avoidance responses are blocked without affecting the unconditioned responses. Jarvik

(1965) states that there are "several disparate views concerning the sedative action of chlorpromazine and its effects on the reticular system." Various investigators contend that it depresses, that it has a biphasic action, or even that it is stimulating. Through its depressive action on the hypothalamus, it has strong adrenergic and weak cholinergic blocking effects on the autonomic nervous system, and it acts on the endocrine system to reduce urinary gonadotropins, suppress estrous cycles, interfere with growth, induce lactation, and decrease secretion of ACTH.

2. *The dosage must be carefully individualized.* For example, some patients respond to 1200 mg of meprobamate per day, whereas others receive little benefit unless that is doubled. This is even more true of the phenothiazines; some patients improve on 100 mg of chlorpromazine in 24 hours, whereas others require many times that amount.

3. *They provide only symptomatic relief* by damping reactions and quieting inner turbulence. Thus they are only adjuncts.

4. *They are not remedies for psychosocial distress.* Too often tranquilizers are prescribed for the treatment of sociocultural dilemmas; obviously when used for these purposes the results will be poor.

5. *Negative effects occur.* Some patients react poorly to one or all of the antianxiety agents. Paradoxical reactions, to say nothing of side effects, are reported for meprobamate, the benzodiazepine compounds (such as Librium), and the phenothiazines.

6. *Knowledge of the patient's personality is essential.* DiMascio and Klerman (1960) concur with the almost universal recognition that the personality of the subject and his psychophysiological state are important modifiers of drug action. Many anxious patients cannot tolerate a slowed-down feeling; it results in clinical depression for

some and a loss of required motor activity for others. Importantly, Rickels (1964) has described the effects of the barbiturates as producing more improvement in lower socioeconomic patients who have low drive levels, low ambition, highly compliant behavior, and a strong passive-dependent character makeup. In the more intelligent, less dependent, less compliant and socioeconomically higher patient, the barbiturates are less well tolerated, producing more sedation and less improvement.

7. *The physician should restrict his use of the countless sedatives and tranquilizers available to only a few,* so that he can become familiar with their indications, side effects, and contraindications. Sainz (1964) states: "The rate at which new psychopharmacologic agents appear and old ones disappear attests only to their relative ineffectiveness." We advocate that one should switch to a new drug only when it has been proved demonstrably superior. Among the phenothiazines, chlorpromazine is still the standard against which others are measured. And, meprobamate and chlordiazepoxide have been used for so many years with so many patients that their effects and side effects are well known.

#### Clinical States

In practice, patients are seen with various anxiety states, which can be conceptualized on two dimensions: the first is the continuum from conscious to unconscious awareness of causes and dynamics; and the second is severity, ranging from the stress reaction, which may be mild, to the extreme anxiety manifested by the schizophrenic patient who is undergoing ego disorganization.

(1) The *acute stress reaction* is evidenced clinically by: agitation, restlessness, autonomic symptoms, insomnia, and visceral dysfunctions. Conscious elements are predominant; i.e., the patient is aware

of his tension and is able to describe its causes and effects. The severity is commensurate with the degree of trouble the patient is encountering. The ordinary dilemmas of human existence, i.e., problems of work and family, are the most common causes.

Psychotherapy should be directed toward helping the patient resolve the environmental stress or removing him from it. Medications may be necessary, but in these instances they should be given for only a short time because their chronic use may produce just enough relief that the patient, instead of seeking resolution, remains helplessly and symptomatically caught in a stressful situation. Barbiturates, either sodium amytal or butabarbital (30 mg three or four times a day), are useful. Sometimes adequate sedation at bedtime suffices. Of course, barbiturates have drawbacks: sedation, addictive properties, and possible use for suicide. Meprobamate (400 to 800 mg three times a day) is obviously preferable when there is any risk of suicide.

(2) Although *acute anxiety attacks* usually appear as discrete clinical syndromes, the patient is relatively unaware of the precipitating events and the dynamics. He displays overt apprehension and the symptoms of autonomic nervous system imbalance. He complains of severe dread, a fear that he is dying, or that he is afflicted by a terrifying condition. The physical symptoms include headache, an inability to concentrate, rapid heartbeat, shortness of breath, gastrointestinal distress, bizarre sensations, and generalized motor hyperactivity. Also, he may be hyperventilating, complaining of tingling of the extremities and sharp twitches of pain in the chest, and showing signs such as pallor, profuse sweating, and muscle spasms.

Clarification of the patient's physical status usually terminates the acute attack, but seldom pre-

vents its recurrence. When these patients are first seen the physician should explore possible causes incisively. If the anxious condition becomes chronic, the patient focuses on his symptoms so completely that his awareness of other stresses diminishes and valuable information cannot be obtained. Because these patients are suffering and frightened, they accept direct questioning about the quality of their interpersonal relationships, stresses at home and work, sexual activities, basic fears regarding adequacy, etc. Psychotherapy is essential because the patient is unaware of the dynamics and usually of the precipitating events.

Intravenous sodium amytal (200 to 500 mg) quickly relieves the acute attack. Meprobamate (400 to 800 mg three times a day) or chlordiazepoxide (Librium) (10 to 25 mg three times a day) alleviates the anxious condition but does not protect the patient from recurrence. Therefore, we recommend both intensive psychotherapy and medications. Side effects of the antianxiety agents (meprobamate and chlordiazepoxide) include withdrawal reactions, paradoxical reactions, and allergic conditions.

(3) *Chronic anxiety states* are persistent, the causes obscure, and the manifestations multifarious. Engel (1962) says: "The somatic symptomatology and the physiologic changes associated with anxiety set in motion a vicious cycle—the patient begins to fear the onset of the next acute anxiety attack and his perception of somatic symptoms reinforces this signal of danger." Repeated acute attacks thus lead to the chronic condition; the baseline level of anxiety between attacks is raised.

Chronic anxiety is evidenced by the patient's worried, tense appearance which is accentuated as the day goes on and the stresses and strains of activity take their toll. Although the anxious patient has difficulty going to sleep, he

feels better in the morning. In contrast, the depressed patient is generally more apathetic in the morning and brighter in the evening. Morbidly anxious patients are preoccupied with their mental and physical status, speaking freely of their symptoms, and betraying their agitation by trembling and tension. Although they describe symptoms easily, they do not know what is happening to them. If unchecked, the condition becomes progressively more severe and panic states develop.

Psychiatric referral is recommended. Because the condition is both severe and chronic, medications are usually needed to help the patient work with a psychiatrist. If the patient displays muscle tension and agitation and if his ego strength is reasonably good, meprobamate is preferred. For the patient who appears more psychiatrically ill, obsessive, and has diffuse complaints, chlordiazepoxide (Librium) is usually more effective. For the even more clinically ill patient who will require medication over a period of months, phenothiazine compounds should be used. We start with 25 mg of chlorpromazine (Thorazine) or thioridazine (Mellaril) four times a day, check for hypotensive reactions, and then increase the dosage by 50 to 100 mg every few days until the patient notices some relief or side effects appear. The most common side effects are dyskinesias, particularly parkinsonism and akathisia. Dystonia is seen only occasionally. In recent years the reports of jaundice and agranulocytosis have diminished greatly. Hyperpigmentation and photosensitivity as well as pigmentation of the cornea and lens have been reported (Redlich and Freedman, 1966). Recently Hollister (1966) noted that some patients taking chlorpromazine for many years were found at post-mortem examination to have coronary artery changes, but this has not yet been confirmed.

(4) Anxiety is also evidenced clinically by *neurotic behavior and attitudes*, and a host of *characterologic defenses*, particularly by patients who have little awareness of their anxiety. Interpersonal relationships suffer. These manifestations of anxiety appear so intangible that the physician is reluctant to refer the patient for psychiatric consultation until more obvious difficulties appear. The neurotic behavior includes emotional lability, erratic and inconsistent attitudes, and impaired communication—especially between patient and physician. This may be so great that the physician and his patient are unable to agree about the severity of the illness or the necessity for particular types of treatment.

We found that highly anxious medical patients hold distorted views of the severity of their illnesses, maintain negative feelings (even flagrant dislike) for hospitalization, and distrust their physicians. They display manifold characterologic defenses: irritability, suspicion, lack of cooperation, and passive-aggressive activities (Schwab et al., 1966a).

When anxiety is expressed through these defenses, the severity is variable; the defenses become an integral part of the character structure so that the person lives with the reputation of being troublesome. But more severe anxiety states develop when he is stressed by medical illness or one of life's catastrophes.

In these patients medications have little value; the defenses bind the anxiety, and the patients consider their personality symptoms to be ego-syntonic. Psychotherapy also has limited effectiveness until the patient's interpersonal difficulties multiply.

(5) Overwhelming anxiety is a conspicuous symptom of *schizophrenic reactions*, particularly the acute undifferentiated type. These patients show many of the classic signs of schizophrenia: they are

vague, their thinking is autistic and highly personalized, ambivalence and indecisiveness are obvious, their affect is one of fright and suspicion, and of course they may be hallucinatory or delusional. They are not aware of the sources of their anxiety, or their description is so incoherent that they cannot communicate with others. In the milder forms, misdiagnosis is common. For example, Lynn (1964) found that of 133 patients referred for psychiatric consultations to the Indiana University Medical Center, 34 schizophrenic patients had been either misdiagnosed or inadequately treated.

The schizophrenic patients with less severe disorders respond well to psychotherapy that emphasizes specificity, concreteness, and current realities. Phenothiazines are the only medications which are really beneficial. Ambulatory schizophrenic patients require 200 to 500 mg of chlorpromazine (Thorazine) per day for many months. When the medication is discontinued it should be reduced gradually over a period of months.

(6) Newer concepts of mental illness now recognize *admixture of anxiety and depression*. Once they were rigidly differentiated as entities, but now we know a patient may appear at any point on the continuum ranging from so-called "pure" anxiety, through complex reactions which manifest both anxious and depressive elements concurrently, to the more classical, obvious, retarded depressive state.

Many of these patients respond to the newer antidepressant medications, particularly those which exert some phenothiazine-like action. Amitriptyline (Elavil) (10 to 25 mg three or four times a day) or nortriptyline hydrochloride (Aventyl) (20 to 100 mg daily) are recommended. Several British investigators (Sargent, 1962; Sargent and Dally, 1962) have reported on the successful use of MAO inhibitors for the treatment of patients showing anxiety as a

prominent feature of their illness; however, we have had no experience with them in the treatment of these patients. These various antidepressants should not be used in combination and can be used in tandem only if there is a 7 to 14 day drug-free interval between them.

It is impossible to generalize about psychotherapy for these patients. Some are benefited; many are not. Each case must be individualized.

### Conclusions About Drug Therapy

Evaluating the tranquilizing agents is complicated for a number of reasons; the literature is filled with inconsistencies.

First, the end result is often a non-specific, "feeling better," which defies quantification.

Second, selected patient samples are used for much of the research. In this respect, Rickels (1964) found that conscious and unconscious attitudes toward physicians differ greatly in lower social class patients visiting a medical clinic, as compared with middle social class patients visiting a psychiatric clinic. Moreover, the physician, usually a member of the middle or upper social class, is better able to understand and treat patients with similar backgrounds and aspirations than patients from the lower social classes. Yet, this latter group is frequently in even greater need of help.

Third, drug response varies with the motivation of the subject (DiMascio and Klerman, 1960). Financial remuneration, counterphobic defenses, and wishes to establish contact with psychiatric personnel motivate subjects who take part in drug studies.

Finally, most clinical trials are conducted for only four to six weeks. We have found that many anxious patients will improve on any medication during the first few weeks. Yet many reports of the ef-

ficacy of these medications are derived from such brief studies.

Notwithstanding these difficulties, when properly used, the psychopharmacologic agents have benefited many patients. And, just as importantly, the use of our relatively crude compounds of the 1960's lends hope that we are just on the threshold of a biochemical and psychopharmacologic era in which our knowledge of the physiology of the brain will become exact, the mechanics underlying mental illness will be revealed, and definitive drugs for treatment will be found.

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