Anxiety And Its Pharmacologic Control

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"Peace be unto you." This has been an esteemed greeting from the earliest of times, and is indicative of man's great desire to obtain inner peace. However, anxiety, considered by some to be inherent in mankind, arises from time to time to disturb this state of inner peace. To reduce the frequency and severity of these disturbances man is constantly seeking additional calming measures. Reliance upon the protection of someone more powerful be that mother, spouse, or God, increases one's feeling of personal security. The measures in which we are more directly interested are those which serve to reduce the awareness of the disturbance and to reduce the physical responses to those stimuli. Frequently, new drugs are introduced as solving this problem only to fade into lesser positions later.

Probably the oldest and best liked sedative is alcohol. It is utilized much more than some realize to quiet jangled nerves. Unfortunately it is frequently habituating and has toxic side effects which are well known. The barbiturates are dispensed as if they were nearly harmless. However, here also habituation is common and close supervision and concern by the physician is necessary. Convulsions and other withdrawal reactions to barbiturates must be considered. Of the standard drugs, paraldehyde and chloral hydrate are the most desirable. Chloral hydrate is now available in a palatable liquid, 0.5 gm. capsules and tablets. Two recent additions to the long list of sedatives are methyl-prylon (Noludar) and glutethimide (Doriden) which are moderately potent and non-barbituric.

AMPHETAMINES AND RELATED COMPOUNDS

Sympathomimetic drugs and central nervous system stimulants are usually neglected as agents for reducing anxiety on the assumption that they would only increase tension. In certain depressive states the reverse is true as the agitation is secondary to the depression. To those unfamiliar with this response it is quite surprising to see a restless, agitated patient, when given amphetamines intravenously, begin to calm down within a few minutes, to smile, and to verbalize his pleasure with the subjective mood changes. This occurs only in those depressions having a strong affective component (reactive, so-called involutional, or manic-depressive, depressed). The neurotic depressives, where the depression is only one of a group of symptoms, do not obtain such relief but often experience an aggravation of their anxiety. This difference in reacting to the amphetamines can be utilized to help differentiate between these groups. For such a test 20 mgm. benzedrine (or its equivalent) is injected intravenously early in the morning when the affective depressions are usually worst. The response should be clear within 15-30 minutes. If the medication proves effective, it might thereafter be given orally upon arising and at noon. If given later in the day, it may impair sleep. If the depression is severe, the patient should, of course, be hospitalized and probably be treated with electro-shock therapy.

Some doctors hesitate to utilize these drugs in hypertensive individuals; however, I have never seen any marked elevations of blood pressures. Quite to the contrary, the blood pressure often decreases as the agitated depression is alleviated. Likewise.

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appetite is improved rather than decreased as when amphetamines are taken by “normal” persons. This group of medications should be kept in mind and used as frequently as possible to reduce anxiety instead of barbiturates which sedate and may aggravate depressions.

AZACYCLONOL (FRENQUEL)

Frenquel is a piperdyl isomer of pipradiol hydrochloride (Meratran). It was found very effective in alleviating the experimental psychoses produced by mescaline sulfate and lysergic acid diamine. Because these experimental psychoses somewhat suggested schizophrenic episodes, it was felt that this drug might have a similar effect upon schizophrenic hallucinations and delusions. The initial work done by Fabing\(^1\) at Cincinnati was most encouraging, but few people\(^2\) have been able to duplicate his work. Rinaldi\(^3\) stated it was most helpful in acute schizophrenic episodes, in other acute transient delusional states, and in postoperative confusional states. A group of individuals using this medication met in April 1956 and were almost unanimous in finding that the oral use of this medicine to be of no avail. It was then suggested that the difficulty was in using it orally instead of intravenously. I have subsequently prescribed it intravenously and still found it to be of no avail, even when used in acute situations. All seem agreed that it is of no value in the chronic schizophrenic. It may be that this drug will prove to have some value, but at present the most that can be said is that it does not cause any deleterious side effects.

RAUWOLFIA

Rauwolfia and related compounds were introduced in 1954-1955. In institutionalized patients Rauwolfia greatly reduced hyperactivity and aggressivity. However, in the greater number of anxious persons who were managing to adjust with varying success outside of hospitals, response was not as gratifying. Marked hyperactivity and aggressivity had not been their chief problems. The drug slowed them physically and mentally without solving the underlying problems. Reduction in activity is often quite disturbing to persons who have neurotically determined needs to be very active and constantly productive or to persons who realistically must do considerable physical or mental work, such as a mother of a large family or a business executive. In addition, the drug frequently causes unpleasant nasal stuffiness and occasionally aggravates depressions. Therefore, as a drug to produce psychologic peace, Rauwolfia compounds leave much to be desired and have been totally discarded from my practice.

PHENOTHIAZINE COMPOUNDS

 Probably the best known member of this group today is chlorpromazine (Thorazine). Initially, there was optimism concerning its curative abilities. Subsequent critical controlled studies have shown that it is very helpful in controlling agitation and combativeness but that it is otherwise rather ineffective in either psychotic or neurotic individuals. Side reactions, including jaundice, allergic reactions, parkinsonism, and aggravated depressions occur in up to 25 per cent of treated patients making it too dangerous for use except in special cases. A new analogue, Compazine (proclorperazine), is just being introduced with claims of lower toxicity. From my limited observations Compazine is much less potent and relatively ineffectual in disturbed patients. It may be helpful in mild anxiety states.

Another member of this group is promazine (Sparine) in which the chlorine
Tranquilizing Drugs

radical has been omitted. This drug is available in tablets of 25 mgm., 50 mgm., and 100 mgm. and in an injectable form for either intravenous or intramuscular administration. I have also been using this medication in a capsule form made up so that one cannot tell the difference between any of these strengths nor of a corresponding placebo. According to animal experimentation, it was expected that larger doses of this drug than of chlorpromazine would be necessary, but I have found it of about equal effectiveness milligram for milligram. The dosage is not fixed and patients have been maintained on as much as 800 mgms. daily for five months without untoward effect. However, increasing the dosage beyond 400 mgm. per day usually does not prove worth-while.

Twenty-two patients suffering from many types of nervous disorder, mostly chronic psychoneuroses, were given promazine. Of the twenty-two, thirteen appeared to be helped, but seven of these felt just as well on a placebo. Of the six who could be said to have been helped by the medication, three were suffering acute disturbances with marked hyperactivity. aranoid delusions in two of these three were not relieved by the medication, but were relieved by electro-shock therapy. Among the other three persons helped was a chronic obsessive-compulsive housewife with a great deal of tension. She stated, “The medicine slows me down, relaxes me — I don’t drive myself so.” However, she continued to have many of her other complaints. Another obsessive person retained her obsessions but was less jittery. And finally, a disorganized ambulatory schizophrenic woman became more relaxed and more effective. Three patients developed weird “hysterical” symptoms upon taking the drug and also upon taking the placebo, so that nothing can be said concerning the efficacy of the medication in these individuals. Previously I have seen the hypomanic behavior of a manic-depressive executive decreased to a point where he was able to continue his normal duties. In such cases, the dosage must be adjusted frequently according to the severity of the hypomania.

Promazine has also proven helpful in quieting the acutely psychotic hyperactive individual, the acutely disturbed alcoholic, and the drug addict during the period of removal from the drug. Occasionally it will also be helpful in the more chronic disturbances. This drug will potentiate barbiturates so that their concomitant use must be watched closely. The drug also causes hypotension. Here it should be noted that epinephrine should not be used to alleviate this, but rather nor-epinephrine. So far, somnolence has been the only side reaction and this may be controlled by reducing the dosage. Promazine appears to be more desirable than Chlorpromazine and the results appear comparable.

MEPROBAMATE

On radio, television, and in various publications Meprobamate has been described as “the happy pills”; never has a drug been so widely demanded by the populace. It has been advertised to relax skeletal muscles, to produce a mild anticonvulsant activity, and primarily to tranquilize without sedating. Our experience with psychiatric patients fails to indicate that such enthusiasm is warranted. We have found it too mild to control effectively acutely disturbed individuals. In 10-15 per cent of the chronic anxiety or tension states, obsessional neuroses, or conversion reactions we did find it helpful but the majority of patients do not show any more improvement than with a
They may improve temporarily only to have their symptoms return shortly and to discover that, like the many other remedies they have tried, Meprobamate is not solving their problems and giving peace.

Meprobamate has so far been free of serious side reactions. An occasional patient may developed some dermatologic response, complain of blurring of vision, or complain of being too drowsy (despite the statement that they “tranquilize without sedating”). On rare occasions, patients have reacted with increased excitement. With large overdoses a person becomes completely flaccid and deeply comatose for as long as forty-eight hours. If an adequate airway is maintained and fluid balance is preserved, he will, with no other treatment, gradually return to normal. There has recently been a report indicating that the drug may be definitely habit forming in a small per cent of users and lead to excessive self-medication, somnolence, or a state resembling intoxication. Some of these persons have exhibited mild withdrawal symptoms when the medication was withdrawn. This does indicate that supervision is necessary when giving this medication. Certainly, it is a drug that might be tried, but with the knowledge that only a small per cent are really going to benefit.

Summary:

New medications to reduce anxiety are appearing daily. The clinical responses to a few of these are reported. None of these drugs are cures but may be useful crutches. The patient should always be evaluated to determine if psychotheraphy might not be more helpful in a curative direction.

BIBLIOGRAPHY