FDA-ACNP

COMMITTEE ON ANTI-ANXIETY DRUGS

# SELECTION OF PATIENTS

Prepared by: Samuel Guze, M.D.
Washington University
School of Medicine

Without careful attention to the selection of patients, satisfactory evaluation of the results of treatment is well nigh impossible. A properly designed treatment study should minimize the risk that the results will reflect pre-treatment characteristics of the patients rather than the effect of the treatment itself. In other words, the experimental and control groups must be carefully matched on those variables known, or suspected, to influence outcome. Often, however, sufficient data about variables that influence course and outcome are not available.

While there are now a large number of follow-up studies of patients with depression, few provide consistent answers to the question: Which factors are associated with course and prognosis? Early age of onset and a history of manic attacks seem to be associated with more recurrences and long-term disability. But adequate systematic data are not available about the effect on course and prognosis of sex, race, socioeconomic status, family history of depression or alcoholism, presence of delusions or hallucinations, presence or absence of certain life situations or stresses, etc. The situation with regard to anxiety reactions is even less satisfactory. There are only a few follow-up studies, and there has been considerably less agreement about the definition of the disorder.

Nevertheless, available data suggest that the following are useful guides for designing studies of treatment of anxiety neurosis and depression.

1. Anxiety neurosis is a common syndrome that characteristically includes recurrent anxiety attacks and one or more of the following symptoms between anxiety attacks: nervousness, palpitation, breathlessness, chest pain, dizziness, fatigue, and headaches. Anxiety attacks are brief sudden episodes of marked apprehension or dread, frequently of impending death, associated

with shortness of breath, palpitation, sweating, dizziness, and weakness. Anxiety neurosis typically begins in the teens or twenties and rarely manifests itself for the first time after the age of 35. It is a chronic, persistent disorder of variable severity. The symptoms in any given patient wax and wane over the years. Psychiatric hospitalization is infrequently necessary.

2. Some anxiety neurotics experience episodes of depression; others do not. These depressions may be symptomatically indistinguishable from those seen in patients with affective disorders without anxiety neurosis, but the suicide risk seems to be low. The episodes of depression, when present, do not seem to affect the long term course and prognosis of the anxiety neurosis. Experience suggests that the history of anxiety symptoms should precede those of depression by at least two years before the case should be considered one of anxiety neurosis complicated by depression.

3. Depressions are also frequent. They characteristically include feelings of sadness, discouragement, and hopelessness, with a variable number of the following symptoms: anorexia, weight loss, insomnia (especially early morning awakening), constipation, impaired concentration, reduction in pep and energy, loss of interest in usual activities, diminished sex drive, self-blame and self-derogation, strong guilt feelings, thoughts of death, and suicidal preoccupation. Apathetic speech and behavior, or restlessness and agitation, and certain delusions or hallucinations are seen in some patients. Depressions typically last for months, usually remit completely, but may recur at variable intervals. While depressions may begin at any age, the majority do not start until early middle age or later. Depressions vary greatly in their duration and intensity, frequently require psychiatric hospitalization, and carry a strong risk of suicide.

4. Anxiety attacks and symptoms are seen in some patients with depression. In these patients, the anxiety symptoms are present only during the period of depression and subside as the depression remits. The presence of anxiety symptoms does not seem to affect the severity or duration of the depression. Sometimes, anxiety symptoms and depression begin at about the same time, or it is difficult to tell which started first. The course and outcome of most such patients is apparently similar to that of uncomplicated depression.

5. Anxiety symptoms and episodes of depression may be seen in many other psychiatric disorders, including hysteria, obsessional neurosis, schizophrenia, alcoholism, and sociopathy, but such patients are excluded from the present discussion.

6. We are left, therefore, with four possible groups of patients: a) those with anxiety neurosis who do not experience episodes of depression, b) those with anxiety neurosis who experience episodes of depression during the course of the anxiety neurosis, c) those with episodes of depression without the accompanying symptoms of anxiety neurosis, and d) those with episodes of depression complicated by the symptoms of anxiety neurosis during the course of the depression. These four groups should be handled separately in studies of treatment. That is, experimental and control patients should be stratified so that therapeutic effects can be assessed for each group of patients separately.

7. Specific criteria for each diagnosis should include a) the number or combination of diagnostic symptoms that must be present, b) criteria for scoring individual symptoms as present or absent, and c) the minimum duration of symptoms to be considered significant.

8. Feighner et al, Arch. Gen. Psychiat. 26: 57-63, 1972, provide one possible way to fulfill 7a and 7b. At least one year for anxiety neurosis and one month for depression are proposed for 7c.