

Photos: Pfizer

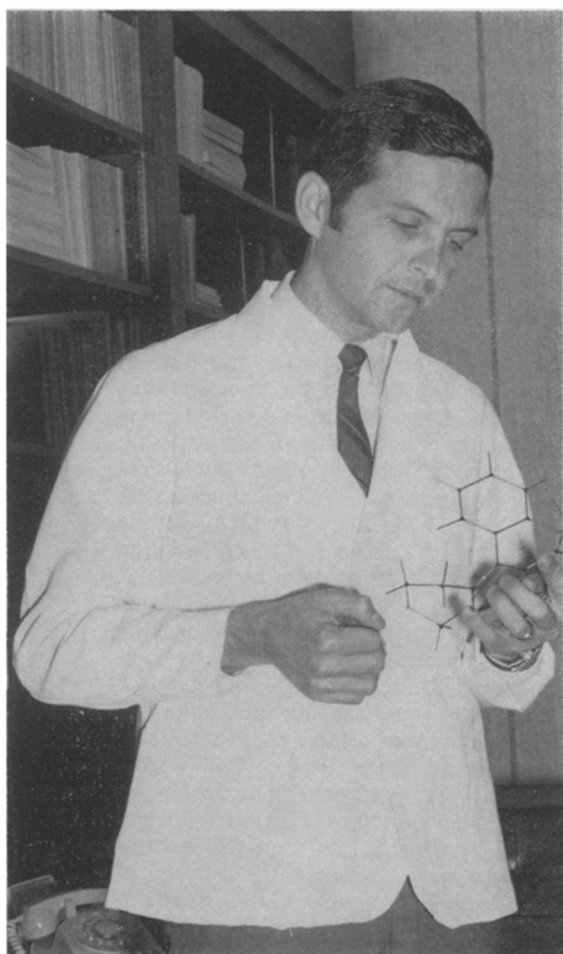
Variations in psychotropic drug structure (right) led to versatile drug.

PSYCHOPHARMACOLOGY

Highs, lows and both

A drug that combats anxiety and depression may aid in treating patients who have both

by Jeanne Bockel



Pfizer's J. R. Tretter and drug model.

It is becoming increasingly apparent that anxiety and depression, though separate symptoms, are intimately intertwined in emotional illness. However, when prescribing, physicians are hard pressed to know whether the patient has anxiety masquerading as depression, or depression with prominent features of anxiety. Treating one without aggravating the other is a constant source of concern.

Drugs with fixed combinations—tranquilizers for anxiety and antidepressants for depression—can be unsatisfactory; the dosages cannot be regulated to match the intensity of symptoms. The alternative, prescribing the two drugs separately, is equally difficult; it can become a complex, involved procedure often leading the patient to emotional highs and lows.

Development of a new drug by manipulating its structure to give it both antianxiety and antidepressant properties would seem to solve the problem. However, the structure of psychotropic drugs is a vague area, and more often than not the activity cannot be determined by the structure but must be demonstrated by experiments with patients.

Most psychotropic drugs are tricyclic compounds with a side chain. With tranquilizers, the middle ring has a sulfur and nitrogen attached, and with the antidepressants, the middle ring is seven-membered. Side chains, similar

in most, improve penetration of the drug into the brain.

A step in the right direction is a new drug, Sinequan (doxepin hydrochloride), produced by Charles Pfizer and Co. It has both antianxiety and antidepressant properties. How big a step it represents has still to be demonstrated.

The drug, modified from other psychotropic agents, has a different nucleus but shares structural features with both tranquilizers and antidepressants. The first of a class of chemical compounds called dibenzoxepines, the drug was recently approved by the Food and Drug Administration.

Pfizer is offering the drug for treatment of anxiety or depression if they exist alone, or both when they exist together—which is usually the case. In more than 50 clinical studies involving nearly 2,000 patients over a five-year period, Pfizer reports, of patients with coexisting anxiety and depression, 83 percent showed slight to marked response; with anxiety prominent, 84 percent showed improvement; with depression prominent, 81 percent exhibited some improvement.

According to Dr. D. N. Cannarsa, medical director of Charles Pfizer Laboratories, doxepin for the first time allows the physician to treat virtually the entire range of psychoneurotic anxiety-depression symptoms with a single agent.

But Pfizer's view is not yet universally accepted.

Even though the drug is effective in cases of mixed anxiety and depression, Dr. Daniel Efron of the National Institute of Mental Health in Chevy Chase, Md., says in cases where one symptom is dominant, manipulation of dosages of several drugs for each individual case might still be best. "Physicians can play with ups and downs, which are at most minor, compared with some conditions themselves," he says. Other NIMH scientists agree that the drug, though effective, cannot compete clinically with combining drugs.

Nevertheless, according to Dr. Blaine McLaughlin of the University of North Dakota in Grand Forks, the quick action and low toxicity of the drug do offer a solution to the general practitioner who must deal quickly, safely and effectively with anxiety or depression, or both.

One advantage of doxepin is its apparently low toxicity compared to other psychopharmaceuticals.

Dr. Frank J. Ayd Jr., a private practitioner in Baltimore, agrees that if doxepin remains as nontoxic as it appears to be, it may become one of the most widely prescribed psychotherapeutic drugs. □