

The Soufrière volcano in St. Vincent erupted from October 1971 to March 1972, as 80×10^6 m³ of basaltic andesite lava was quietly extruded inside the mile-wide crater. The eruption was largely subaqueous, taking place in the 180-m-deep crater lake, and resulted in the emergence of a steep-sided island. The mild character of the eruption and the absence of seismic activity stand in direct contrast to the highly explosive character of the eruption of 1902 to 1903.

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Year

Clinical Psychopharmacology in Its 20th Year

Late, unanticipated effects of neuroleptics may limit their use in psychiatry.

George E. Crane

The use of neuroleptic drugs (1) for the treatment of mental disorders began in the early 1950's and has increased steadily. According to one estimate (2), 250 million people had received these drugs by the end of 1970. In the last decade, hospital beds have been increasingly phased out, and, to take their place, new community mental health centers have been opened or existing facilities have been expanded throughout the nation. According to the medical profession, this new program for the treatment of the mentally ill would not have been possible without neuroleptics. Psychiatrists, sociologists, and professionals in allied fields have emphasized the advantages of maintaining the mentally ill in the community. On the other hand, it is

acknowledged that a large proportion of patients released from hospitals are incapable of meeting the demands of society. Inadequate programs for the management of these mentally handicapped persons have created new and unexpected problems, and, in an effort to solve them, the psychiatric community has become more and more dependent on the use of neuroleptic agents. One of the consequences of this reliance on psychopharmacology has been the tendency to minimize the potential danger of long-term exposure to powerful chemical agents. Thus, permanent neurological disorders have become very common among patients treated with neuroleptics, but little effort has been made to come to grips with this problem.

Use of Neuroleptic Agents

Physicians prescribe neuroleptic drugs on a long-term basis for mental disorders such as schizophrenia, psychosis due to mental deficiency, paranoid states of adulthood and senility, chronic brain syndromes, mania, hyperactivity in disturbed children, addiction to narcotics, excessive anxiety as observed in neurosis, and physical illness. The National Research Council of the National Academy of Sciences has recently reviewed the data on the effectiveness of some of the neuroleptics (3), but it has not confirmed claims that such agents are indicated for the treatment of mental conditions other than schizophrenia and related diseases. There are few schizophrenic patients now living in the United States and Europe who have not received a phenothiazine or a butyrophenone at one time or another. In the last 15 years, neuroleptic agents have replaced most forms of treatment for psychoses and other serious mental ailments. Electroshock therapy and various types of psychotherapy have survived, but the former is seldom used in institutions and the latter play a subordinate role in the total management of psychotic individuals. The fact that these drugs reduce overt psychopathology without causing excessive sedation, euphoria, or addiction explains, in part,

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use in psychiatry. Tranquillization is not a prominent feature of analytic action (4, p. 41) despite the fact that the term "tranquillizer" is used in the classification of these drugs. Neuroleptics may reduce activity and belligerent behavior, but these are secondary effects of a lessening of psychopathology. Such an effect occurs only in the early stages of drug therapy in certain susceptible individuals or when excessive doses are administered, particularly of chlorpromazine. Animal studies and biochemical research have produced further evidence that the pharmacological effects of neuroleptics are very different from those of hypnotics (barbiturates) and anxiety agents (meprobamate, diazepam).

In the clinical area, large-scale collaborative investigations by the Veterans Administration (5) and the National Institute of Mental Health (6) have proven that neuroleptics are more efficacious in schizophrenia than are other substances or conventional sedatives. Even though the conclusions of these and other studies are supported by impeccable methodology and highly sophisticated statistics, the questions remain: How many patients benefit from drug therapy? How effective are these drugs? Reports on the subject are extensive, complex, and often contradictory, but several reviews permit certain conclusions (7; 8, pp. 70-72). Investigations, with the patient's ability to remain in the community as a criterion of drug effectiveness, reveal that 70 to 80 percent of acute schizophrenics on no drugs are readmitted within 1 year, while only 20 to 30 percent receiving some form of drug therapy require rehospitalization within that year. The superiority of drugs over placebo may be somewhat higher when drug therapy is provided and when allowances are made for the failure of certain patients to adhere to the prescribed drug regime (9). However, the difference between those patients treated with drugs and those not treated with drugs decreases over time. According to one study, the difference is only on the order of 10 to 15 percent after several years (10). As to the quality of the patient's adjustment after he leaves the hospital, the results of drug therapy are even less encouraging: the majority of those who remain in the community continue to be ill and are often a burden on their families (11). Individuals re-

turned environments may be as dependent and alienated as those confined to an institution (12).

For patients residing in hospitals, the criterion of drug effectiveness is usually the number of patients requiring a resumption of therapy after the active agent has been replaced by a placebo. The results vary with age, types of symptoms, duration of the disease, methods of assessment, and length of observation. In general, studies reporting a high relapse rate for placebo-treated patients also show a considerable degree of deterioration in the drug group. Major investigations, using standard rating instruments, reveal that fewer than 50 percent of patients hospitalized for several years improve in response to neuroleptics. Yet, according to surveys of medical records, 85 percent of all hospitalized schizophrenics receive medication at any given time (13).

As with other types of chemotherapies, doses depend on a number of factors such as age, severity of symptoms, and duration of illness. Yet there is little uniformity in the dosage of neuroleptics prescribed by physicians, even within reasonably homogeneous classes of patients (14). It is not uncommon to prescribe dosages exceeding those recommended by the manufacturers. Patients who present serious management problems are most likely to receive large quantities of neuroleptics for long periods of time, although the persistence of severe psychoses would suggest that chemotherapy is not effective in such cases. Data on the drugs prescribed for patients attending clinics are not readily available, but there is reason to believe that psychopharmacological therapy is equally extensive in outpatient facilities, since the main function of these centers is to dispense drugs.

There is some justification for the continued administration of drugs to patients who, in the course of treatment, appear to become less psychotic. Therapists, however, fail to take into account the possibility of naturally occurring remissions. Thus, in many instances, the choice of a drug regime is determined more by the severity of a previous episode than by the patient's current status.

Schizophrenia and related mental diseases are often characterized by episodes of violence, self-destructiveness, or utter helplessness. Such episodes may develop suddenly, with no apparent reason, and may last from a few

hours to several years. A malfunctioning brain is not the only cause of interpersonal and social difficulties for the schizophrenic patient. The deprivation and stresses of the poverty in which this person is forced to live, whether he resides in a hospital, sheltered living quarters, or his own home, are also, in a great measure, responsible for what is often called unacceptable behavior. Many physicians, nurses, guardians, and family members who resent the patient's behavior and are threatened by potential acts of violence fail to distinguish between manifestations of illness and reactions to frustrations. Hence, drugs are prescribed to solve all types of management problems, and failure to achieve the desired results causes an escalation of dosage, changes of drugs, and polypharmacy. It is often reported that patients refuse to ingest their pills or that relatives fail to supervise the proper administration of medicines (15). Less publicized is the patient's dependence on drugs. The medical staff gains a feeling of accomplishment from the patient's adherence to a prescribed regime, while the nursing personnel and relatives, who are in more direct contact with the patient, derive a spurious feeling of security when the doctor's orders are carried out. Thus, the prescribing of drugs has in many cases become a ritual in which patients, family members, and physicians participate. Mystification, a concept developed by Lenard and associates (16), plays a certain role in the contemporary practice of psychopharmacology, inasmuch as neuroleptics are often used for solving psychological, social, administrative, and other nonmedical problems.

Drugs and Community Psychiatry

The widespread prescribing of potentially dangerous drugs has been particularly evident in the field of psychopharmacology because of its role in a rapidly expanding and changing program of mental health care. The public and the medical profession consider hospitalization of mental patients a therapeutic failure. Efforts on the part of administrators to improve the image of psychiatric institutes have been largely unsuccessful because of the chronic shortage of trained personnel and spiraling costs of medical care. When psychopharmacological agents were first introduced in the treatment of mental illness, administrators and

clinicians hoped that the phasing-out of the old-fashioned state hospitals could be accomplished in a matter of a few years. Indeed, the number of institutional beds has been reduced drastically, and some hospitals have been closed. However, institutional care is still required for chronic schizophrenics and other categories of patients who never leave the hospital and for a substantial proportion of patients who must be readmitted. To meet the demands of patient care with inadequate funds, hospitals keep recently admitted patients for only a short time. For persons requiring more extensive hospitalization, these institutions can provide only substandard psychiatric and nursing care. This situation has generated the feeling that drug therapy is indispensable.

Community mental health centers, which are expected to take over many functions of state institutions, have not always been an unqualified success. Certain well-conducted programs in sparsely populated areas (such as the Saskatchewan Project) have provided excellent low-cost care for patients with chronic mental diseases and thus have practically eliminated the need for prolonged hospitalization (17). Other rapidly expanding mental health programs have created new burdens for the already strained medical facilities of urban areas. Recently, the New York County District Branch of the American Psychiatric Association (18) criticized the state's announced intention of restricting hospitalization of geriatric and chronic schizophrenic patients without making alternative provisions for such persons.

One of the main goals of community-oriented programs is to return hospitalized patients to their homes, but little effort has been made to study the effects that a mentally ill individual has on the psychological climate of his family. At least one study (19) has shown that the presence of such a person at home can be a source of considerable apprehension for members of his family. Physicians practicing in clinics and private offices feel obligated, and sometimes forced, to maintain the patient in the community, despite his precarious state of mind. Under these conditions, it is only natural that community mental health centers, outpatient facilities, and private practices should also rely heavily on drugs.

It has been stated often that, without neuroleptics, modern psychiatric treatment would not be possible. It is also

true that the promotion of neuroleptics for the treatment of all types of psychiatric disorders has prevented federal, state, and municipal agencies from providing adequate personnel and better facilities for hospitals and other mental health centers. Mental institutions have benefited little from the expanded support of mental health programs. They continue to be low-morale, underprivileged facilities, compared to the community health centers, which have greater resources and thus attract better trained personnel. Anyone who has had experience with the institutional atmosphere before and after the introduction of drugs knows that the understaffing, insufficient funds, poor housing, marginal food, and improper maintenance of patients' quarters are as great now as they were in the immediate postwar years.

Toxicity

Clinicians feel that the routine administration of neuroleptics is necessary in schizophrenia because responders to drugs cannot be differentiated from nonresponders on clinical grounds. It is equally difficult to predict whether or not a patient will relapse upon withdrawal of the drug. Routine administration would be justified if neuroleptics were low-toxicity agents. While a single dose of any neuroleptic is seldom dangerous, administration over a period of weeks or months causes a variety of side effects and complications (8, pp. 94-116; 20). Parkinsonism is the best known effect of neuroleptics. Often associated with parkinsonism is akinesia, which, in severe cases, is characterized by physical immobility as well as emotional indifference. This syndrome is poorly understood and often mistaken for psychomotor retardation. Some clinicians may even consider it a desirable effect because it helps control unruly behavior. In the early days of psychopharmacology, psychiatrists were accused of replacing a mechanical straitjacket with a chemical one, a criticism that is still justified when excessive doses of neuroleptics produce severe reduction of motor activity and a general loss of spontaneity.

Hypotension, drowsiness, leukopenia, jaundice, galactorrhea, photosensitivity, impotence, and excessive weight gain occur with a certain frequency. These effects, as well as parkinsonism, are reversible when the drug

is withdrawn, or they may disappear in the course of treatment. The most lethal effect is agranulocytosis, usually caused by chlorpromazine. It seems to be a rare complication, most likely to occur in the elderly during the first few months of therapy. Another serious effect is retinitis, which may result in blindness. It is caused by thioridazine but can be prevented if doses do not exceed those recommended by the manufacturer. In the early 1960's (21) deposits of metabolites of chlorpromazine in the lens and cornea, and less frequently in the skin, became a source of considerable concern, but it soon became apparent that the deposits in the eye were clinically insignificant and that the cosmetically objectionable skin pigmentation could be avoided by early recognition and change to another neuroleptic. More disturbing was the discovery that thioridazine and, less frequently, other phenothiazines may cause abnormalities in electrocardiograms (22). According to clinicians, the abnormalities are of no clinical significance and subside once the drug is withdrawn. Since most patients are on chemotherapy indefinitely, changes in their electrocardiogram may also persist indefinitely. Indications of serious heart complications and cases of sudden death have been attributed to neuroleptics. The role these agents play in cardiac disorders is still uncertain because of diagnostic difficulties and the dearth of good clinical studies.

The variety and number of side effects would suggest that a certain amount of caution and selectivity be exercised in the use of neuroleptics. The fact that the existence of these complications is fairly well known and reasonably well documented in package inserts and in the general literature seems to indicate that clinicians are willing to take a certain amount of risk in prescribing drugs for a serious disease such as schizophrenia. (The attitude of the physicians, drug companies, and government agencies toward tardive dyskinesia, however, is more difficult to explain in terms of contemporary medical standards.) \ \

Tardive Dyskinesia

In the late 1950's, an unusual syndrome was observed in seven patients receiving phenothiazines (23). It consisted of slow, rhythmical movements in the region of the mouth, with protrusion of the tongue, smacking of

izarre muscular activity. Physical examinations of patients receiving drug therapy revealed not only the mouth, but practically all parts of the body could be affected by motor disorders, such as myoclonus, chorea, and athetosis. Overweight of the spine and neck, shift of weight from foot to foot, and abnormal postures indicated that coordination of the various segments of the axial musculature was affected. Less frequently, the syndrome resembled in every respect known neurological diseases, such as Huntington's disease, dystonia musculorum deformans, and postencephalitic damage (24). In milder cases, particularly when only the distal parts of the extremities are affected, tardive dyskinesia is of little clinical significance, but moderate to severe involvement of the region of the mouth creates considerable embarrassment as well as distress. The condition may be disabling when breathing or motor coordination is seriously impaired, or when it simulates known neurological diseases. The syndrome is called tardive dyskinesia because it manifests itself months or years after the initiation of drug therapy. Some clinicians also refer to it as persistent dyskinesia because it continues unchanged for years after all medication is removed.

The number of patients so afflicted cannot be ascertained. In mental hospitals, 2 or 3 percent of all patients exhibit some motor disorder consistent with tardive dyskinesia, but the percentage may rise to over 50 among patients over age 60 who have been exposed to neuroleptics for 3 years or longer. The frequency with which this disorder occurs in patients receiving neuroleptics in clinics and private offices is less well known. Neurologists claim that it is not uncommon.

Country, Government,

Physicians

In 1967, there was a considerable amount of evidence to indicate that tardive dyskinesia was caused by neuroleptics, that it occurred in at least 5 percent of patients exposed to drugs for several years, and that it could be induced in young adults as well as in older patients, regardless of diagnosis. Years later, many physicians are not aware of this problem or seem

to be ignorant of it. A common sight in all wards of hospitals where drugs are administered routinely for long periods of time. Lack of clinical information cannot explain this ignorance of a major health problem—more than 100 papers reporting 2000 cases of tardive dyskinesia have been published since 1957. The diagnosis offers no major difficulties, nor are special techniques of examining patients or laboratory procedures required. Tardive dyskinesia becomes more pronounced after drugs are withdrawn, a fact that skeptics have used to question its existence as a clinical entity. [This seemingly paradoxical phenomenon can be explained in terms of known mechanisms of synaptic transmission (25).]

Only recently have drug companies and government agencies shown some interest in this major health problem. Before 1971, package inserts devoted one sentence to the description of permanent neurologic effects of these drugs. This short communication did not describe the manifestation of tardive dyskinesia, but emphasized, incorrectly, its rarity and likelihood to occur only in elderly or neurologically predisposed individuals. One company (Squibb, manufacturer of Prolixin) has included a paragraph on persistent neurological manifestations but, like other drug companies, has avoided using the term "tardive dyskinesia." Like most terms in medical practice, it leaves much to be desired, but it has been accepted by most clinicians who are familiar with this drug effect. In 1972, Smith Kline and French made a number of changes in the package inserts of three drugs (Thorazine, Stelazine, and Compazine) to include a fairly detailed description of lasting neurologic effects under the heading "Persistent Tardive Dyskinesia." The Food and Drug Administration held a meeting on 15 May 1972 (26) to discuss means of informing physicians of the danger of tardive dyskinesia. Since then, it has urged manufacturers of neuroleptics, other than Smith Kline and French, to update information on tardive dyskinesia in the package inserts of their products. Nevertheless, the 1973 edition of the *Physicians' Desk Reference* (27), which is the most popular source of information on drugs, fails to show any change with regard to neurological effects in 12 of the 17 neuroleptics available for prescription use. This may give the clinician

dated are safer than the remaining 5. Drug manufacturers also neglect to include items describing tardive dyskinesia in check lists of the side effects of drugs to be used in research on human beings. Many new drugs are still tested on chronic psychiatric patients with a history of prolonged exposure to neuroleptics.

Physicians and nurses who must deal directly with hospitalized patients are firmly convinced that most patients would become unmanageable if the use of drugs were discontinued. Those employed in noninstitutional mental health centers fear that they may be forced to give up programs responsible for keeping patients in the community. These apprehensions do not seem justified—it was never suggested that the use of neuroleptics should be abandoned. The question is not whether these drugs should be used for specific ailments, the question is whether the current practices of administering these drugs are medically sound. The indiscriminate and excessive use of potentially dangerous drugs for all schizophrenic patients (and for nonpsychotic subjects) is certainly not justified medically. Periodic assessments of therapeutic and unwanted effects are essential. Unquestionably, more selective prescribing of drugs will put new demands on hospitals, outpatient facilities, and private practitioners. Similarly, reduction or discontinuation of drug therapy will create conflicts with families and administrators and may also arouse fears of lawsuits, since the use of chemotherapy is accepted procedure for the treatment of psychosis. [The risk of being sued for not recognizing tardive dyskinesia until it is too late will increase considerably, as demonstrated by recent court cases (28).] Rehospitalization may be necessary in some cases. Since many communities have established centers for the management of psychiatric crises, these facilities may have to expand their services for the management of such emergencies.

Investigators and clinicians claim that knowledge of tardive dyskinesia is inadequate and that much more research is needed in order to deal with this problem effectively. So far, little effort has been made to carry out the necessary long-term studies on the onset and evolution of neurological and other cumulative effects of drugs. During the last 2 years, some 20 papers

(29) have been published on the treatment of tardive dyskinesia, even though the majority of clinicians continue to ignore the existence of this complication. It is also revealing that most of the drugs that are responsible for neurologic side effects are being tested for the suppression of tardive dyskinesia. With a few exceptions (2, pp. 297-310; 30), little has been written on the prevention of permanent neurologic effects by a more judicious use of psychoactive agents. This is another indication of how dependent the medical community has become on chemical agents.

Until now, only a few independent investigators have carried out clinical studies on tardive dyskinesia. The problem has become of such a magnitude and complexity that drug companies and certain government agencies will have to take the initiative. A more responsible attitude toward the risks involved in long-term treatment with neuroleptics may necessitate a change in the priorities of drug research and a reallocation of funds. Education of the medical profession and the public by improving package inserts and by mailing informative material to all physicians is essential, but certainly insufficient. The neglect of a serious health problem for so many years has deeper roots than mere ignorance of facts. The problem of tardive dyskinesia should be viewed as

another example of large-scale and inefficient application of a potentially useful technical discovery without consideration for its long-term effects on the individual and his environment.

References and Notes

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Energy Conservation through Effective Utilization

Energy consumption could be reduced by improved efficiency of utilization in buildings and in industry.

Charles A. Berg

There are indications that the demand for energy in the United States will soon outstrip both power generating capacity and fuel supply.

The basic problems in energy supply

can be divided as follows. In the immediate future (1972 to 1980) the most important problem appears to be inadequate power generating capacity. In the distant future (the year 2000

and beyond) the basic problem is availability of fuel or of energy in another form, such as solar or geothermal energy. In the intermediate time range (1972 to 2000) the conservation of energy by means which do not damage the functioning of the economy could well be the most important consideration.

There are two main approaches to solving the problem of providing sufficient energy for future needs: either the supply of energy can be increased, or the demand for energy can be reduced. However, these approaches are not independent of each other. For example, a decrease in the demand for energy caused by curtailing industrial electrolytic processing could adversely affect the capacity to increase the energy supply by causing shortages of electrical conductor material. Such interactions between supply and demand must be considered and