THE USE OF TRANQUILLIZERS IN PSYCHIATRY

By

PAUL H. HOCH, M.D.

Commissioner of Mental Hygiene, State of New York
Professor of Clinical Psychiatry, Columbia University

I SHOULD like to discuss some of the clinical aspects of the tranquillizing drugs, but without going into great detail as to the many theoretical considerations in biochemistry, physiology, pharmacology, etc. which have been ventilated so often in connection with this form of treatment.

In the last few years more and more chemical compounds have been introduced that influence mental states. The older group of drugs or sedatives were used usually to reduce emotional tension, to relieve anxiety, to induce sleep, and to eliminate excitement. Up to a point these compounds influenced mental symptomatology, but they were not very effective. The recently introduced tranquillizing drugs also have, as we will discuss later, a sedative action; but they are far more effective in the treatment of mental illness than the sedatives that formerly were used.

The number of such drugs has been growing rapidly. At this time I cannot mention all the different compounds which are now in use, and will limit myself to chlorpromazine and the Rauwolfia preparations. Many of the new compounds are variations of the above-mentioned drugs. The action radii of chlorpromazine and the Rauwolfia compounds are fairly well known today and could be used as a comparative baseline in evaluating the newer compounds. The selection of drugs to be used for treatment is still made largely on the basis of the therapist's preference rather than on particular indications. In many instances the actions of these drugs overlap. However, special considerations have to be followed in their use. For instance, in acute mental disorders where there is an excitement or a state of agitation we prefer the use of chlorpromazine because it is a quick-acting drug and therefore more effective in this particular group of patients than Rauwolfia. We feel that in the treatment of chronic patients, too, chlorpromazine is superior to Rauwolfia, but it must be mentioned that chlorpromazine produces more side reactions. This should be taken into account in some clinical situations—for instance in a patient suffering from a known liver ailment or gall-bladder disease we would prefer treatment with one of the Rauwolfia preparations.

Clinical experience shows that individual patients respond better to one drug than to another, but we have no evidence as to why this is so. Neither the psychiatric state of the patient nor the known biochemical facts regarding the action of these drugs give sufficient clues to enable us to decide why a patient responds better to one compound than to another. Statistics compiled in the State of New York and in many other places indicate that chlorpromazine is probably the most effective drug in our hands in the treatment of psychotic patients. This is followed by reserpine. Other available compounds such as Frenquel and Miltown are far less effective. Sparine (promazine) is effective though apparently milder in action than chlorpromazine, but also has fewer side effects.

Most of the information we have on the action of tranquillizing drugs relates to psychotic patients. This is not surprising, because patients with gross symptomatology are better subjects to be studied in determining the validity of drug action than the milder disorders which do not have as conspicuous a symptomatology. The investigative techniques—for instance, the double-blind method—also can be more effectively applied in a hospital setting than in a clinical or private practice. The evaluation of hospitalized patients is therefore much easier than that of patient treated in an ambulatory fashion.

Indications for the use of the tranquillizing drugs are not sharply drawn. From some publications one might assume that these drugs can be used in every condition regardless of origin, and that every psychiatric patient provided he takes the drug long enough and in sufficient doses can be cured. Unfortunately, this is not the case. Even though many patients benefit from the use of these drugs there is still a very large number of patients who do not respond. This is especially true regarding patients who have been sick for a long period of time.

All investigators agree that these drugs are most effective in psychotic patients who are excited, disturbed, tense, or anxious, and who have productive psychotic symptoms. Apathetic, driveless, non-productive patients do not respond well to tranquillizing drugs. There are exceptions, however, which occur in those patients where behind an apathetic front there is a great deal of hidden tension. As far as we know the drugs do not influence a disease or disorder; they eliminate or alleviate symptoms only; nevertheless in a large number of patients the elimination of the most disturbing and conspicuous symptoms is sufficient to enable the patient to function.

Although the drugs may be used on a large group of patients simultaneously, this does not mean that the patients should not have an individual psychiatric and mental examination and that the psychiatric symptoms should not be properly appraised. If this rule is not followed, many patients will not benefit who otherwise may have responded well and complications will be overlooked. It is also essential to pay attention to what other psychiatric attention or treatment the patients needs in addition to the drug treatment.

Referring to the special psychiatric disorders I would like first to discuss schizophrenia, in which these new compounds are most effectively applied. They are used here in three different ways, in the treatment of acute hospitalized schizophrenics, chronic hospitalized schizophrenics, and schizophrenic out-patients.

Today the use of tranquillizing drugs in acute schizophrenia is widespread in the in-patient services, but less is known about their value in the out-patient services or the offices of physicians in private practice. Statistics available today indicate a drop in the admission of schizophrenic patients. In our experience there are some acute cases of schizophrenia that respond well to tranquillizing drugs and it has been possible to treat them outside hospital. However, this is only possible when proper supervision is organized in co-operation with the relatives. Where such supervision cannot be obtained and where the environment is not willing or able to co-operate, ambulatory treatment is not possible. We also feel that depressed and anti-social patients should be treated in hospital. Generally speaking, in cases where the higher dosages of tranquillizing drugs have to be used the patients are best treated in hospital, but once the maintenance dose is established these patients can be returned to ambulatory treatment. We feel that the main contribution of the drugs at present is the shortening of the patient's stay in hospital.

The tranquillizing drugs are widely advocated in the treatment of chronic schizophrenic patients. Undeniably the excellent results can be maintained for many years in cases that have not responded to other forms of treatment. Our observations on a large number of patients would indicate that about 10 to 15 per cent. of the patients improve to such a degree that they are able to return to the community. Many other patients show improvement in behaviour and are easier to care for, but must still remain in a hospital. In many chronic schizophrenic patients it is possible to influence the gross symptomatology and especially to reduce and eliminate the hallucinations and other psychotic manifestations. Many of these patients, however, still show adaptational difficulties in work, social, and sexual spheres. The tranquillizing drugs do not influence uniformly all the symptoms of schizophrenia. Symptoms such as anxiety and aggression are influenced most effectively and reliably; disorganization of thinking is less influenced.

The different forms of schizophrenia all respond to the tranquillizing drugs, but to varying degrees. The paranoid and catatonic forms respond best and the hebephrenic and simple forms less well. The tranquillizing drugs are also used in depressed types of schizophrenia, where they have some influence on the psychosis itself, but generally not on the depressive manifestations. In such patients a combination of tranquillizers with an anti-depressant should be used. These drug combinations, however, are not ideal, and we still feel that electroshock is the best treatment. In the pseudo-neurotic form where a great deal of anxiety is present the tranquillizing drugs are not generally able to reduce the symptoms.

The tranquillizing drugs are used in the treatment of the manic-depressive psychoses. Some feel that the phenothiazine derivatives can be used effectively in cutting short severe manic states if the drug is given by injection. Later on when the patient quietens down he is transferred to oral medication. In milder manic attacks the treatment can be omitted. Manic patients quieten down fairly rapidly under the influence of chlorpromazine, but there are exceptions which do not respond, or show a recurrence of manic manifestations when the drug is reduced or withdrawn.

The drugs are not effective in depressions. This applies to patients suffering from reactive as well as neurotic depressions. The only exceptions are agitated depressions, where the drug may cut short the agitation even though the depression remains uninfluenced. It must be emphasized that the tranquillizing drugs not only do not help depressed patients, but can aggravate existing depressions and even precipitate depressions in those formerly free.

It is not known how far the preventive use of tranquillizing drugs between attacks will prevent recurrence.

Tranquillizing drugs are used in arteriosclerosis and senile psychoses where they have a beneficial effect on the patients' behaviour and in controlling delusions and hallucinations. These drugs calm the patient without interfering too much with the patient's behaviour. Many of these patients formerly had to be sedated, but the sedatives even though calming the patient interfered with consciousness. The newer tranquillizing drugs do not have this effect, and it is commonly seen that the patient's confusional state instead of being aggravated is improved. The drugs, of course, have no influence on the intellectual impairment of these organic states, but they have a strong influence on the mental processes most likely to occur, because some emotional interference is removed. The tranquillizing drugs are also used in acute organic states such as delirium and have a beneficial effect if hyperactivity and agitation are present. Here

again their use is preferable to that of sedative drugs, because they do not interfere with consciousness, but rather reduce than reinforce confusional symptoms.

In spite of the widespread use of the drugs in the United States, our knowledge about their effectiveness, however, is not too well documented in their use with psychoneurotic patients. Some such patients with tension, phobic manifestations respond to the drugs; others with a similar symptomatology do not. Why one patient responds and the other is refractory is unknown and we have no biochemical clues as to how this occurs. Some neurotic patients undoubtedly benefit from these drugs, and in our experience it does not reduce or limit their ability to participate in psychotherapy.

I do not want to go into a lengthy discussion of dosages, but should like to call attention to the fact that the individual dosages must be worked out. There are patients with very similar symptomatology who need for instance 100 mg. whereas, other patients need 1,000 mg. or more. In the United States there is a more or less uniform procedure to increase the dosage to the extent needed to eliminate the patient's symptoms. Some physicians increase the dosage rate rapidly, while others follow a slower course. There are adherents to techniques that prefer large doses, whereas others feel that they can get along with relatively less. We feel that a generalization of small or high dosages should be used with the recognition of the fact that individual patients respond differently to the drug and the drug has to be adapted to the particular patient's need. The usual technique is to raise the level to control the patient's symptoms, leave the patient on that dosage level, and then gradually reduce the drug or eliminate it altogether if the patient shows a gratifying response. We usually start out with 25 mg. three times a day and then work it up, if necessary, to 1,500 mg. daily. There are therapists who have used much higher dosages than this. In reserpine we usually adminster between 3 and 5 mg. These dosages do not apply automatically to all available drugs.

The duration of treatment is often a matter under discussion. We feel that a patient should be treated for several months and preferably with two or three compounds if he does not respond. If a patient does not respond within a few weeks to one compound, it is advisable to change. Some patients for instance respond better to one drug than to another. But there are patients who do not respond satisfactorily to any of the available drugs. The maintenance dosage has to be individualized. Patients who receive maintenance drug treatment should be seen frequently by their psychiatrists or physicians to have this dosage adjusted. Many patients will need a long-range treatment, and some will have to be kept on a maintenance dosage for many months and sometimes longer or the symptoms will re-appear. Once the patient is comfortably established, the medication should be reduced or eliminated altogether. The tranquillizing drugs are used either alone or in conjunction with other psychiatric therapies. Some patients seemingly have enough ego strength and are able to function well if the drug eliminates the most disturbing features of the emotional disorder. Others need other psychiatric therapy in addition. This can be in the form of milieu therapy, group therapy, or individual therapy. Many patients under the influence of the drug become more co-operative and are more ready and willing to discuss their adaptational problems. This, of course, would indicate that they would like to have a therapist with whom they can discuss some of their problems. Some therapists feel if the patient's symptoms are reduced or completely eliminated by the drug they have no incentive to undergo psychotherapy. This is especially noted in those patients suffering from the

psychoneuroses. We have not had such an experience and feel that patients who have conflicts will seek psychiatric help to resolve them.

I cannot discuss at length here the complications produced by the tranquillizing drugs. Fortunately they are not very serious and usually can be controlled by withdrawal of the drug. I should like to call attention here to the fact that in addition to physical complications such as jaundice, skin conditions, agranulocytosis and Parkinsonism, these may also be psychic complications which should be watched for. In some patients the drugs can produce peculiar feelings of depersonalization, depression, and lethargy. Occasionally new psychotic manifestations may develop. These complications are not serious and can be dealt with by changing the dosages or by switching the patient from one drug to another.

The mode of action of the tranquillizing drugs is still obscure and most of our treatment knowledge is empirical. There are hints that the reticular substance and mid-brain region are implicated, but details as to their relation to emotional and mental disorders are controversial. Our therapeutic approach should not be looked upon too critically because it is empirical, since progress in medicine has been achieved most impressively on an empirical level. Of course, we all hope that the present investigations in neuropharmacology will elucidate some of the causes of different mental disorders and clarify the action of these drugs.

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DISCUSSION

By **Dr. M. A. Partridge**

It is always a pleasure to hear Dr. Hoch, and now that he is a Sultan of the Psychoses with 125,000 patients under his clinical tutelage, it is more than ever a privilege to have the opportunity of learning from his experience. I am not the best person to open a discussion of his paper, because I have in my practice neither the opportunity nor patients of suitable type for the sort of extensive

trials that are necessary for the general assessment of tranquillizing substances.

The fashionable complaint today is tension, and the exasperating phrase "I'm all tensed up" is frequently used by patients who show no objective evidence of tension at all, and tranquillizers are even sometimes asked for by patients who do not recognize that somatic anxiety symptoms are sometimes a normal physiological response. There would seem to be various reasons for the increasing trend, as it appears to be, towards seeking freedom from anxiety symptoms. Among these is the fact that we live in an age of technology during which the often spectacular technical achievements encourage the belief, especially among Americans, that to every problem there must be a technical solution. These ideas are not discouraged by the great drug firms whose remedies, breeding like rabbits, insist on their diseases; and they are enhanced by the greater dissemination of medical knowledge, as well as by the activities of journalists who write up their own experiences of drugs, or those of others at secondhand. It is as though behind the frequent applications for help that one receives there lies a wish to avoid the less pleasant aspects of emotion rather than to forego emotion as a whole. This effect is not achieved by tranquillizers, which in my experience are in general unhelpful in neuroses. In this connection mention may be made of the recent experiment conducted at St. George's Hospital in which six substances (four tranquillizers, amytal, and a placebo) were given to a series of neurotic patients over a period of two weeks each, under an ingenious statistical arrangement by which each acted as the others' control. The results were of interest in that the only significant effect on neurotic symptoms was exerted by amytal.

In general, and as regards all conditions, I feel that I could dispense with Benactyzine, Sedaltin, Pacatal, Oblivon, and Anxine, and who now remembers Myanesin (mephenesin) and Seconesin—at any rate in psychiatric practice?

For practical purposes, that leaves us with meprobamate (Equanil or Miltown), reserpine (Serpasil), and chlorpromazine (Largactil). With regard to the first, I have been unimpressed, though my younger colleagues believe that in some instances it is symptomatically useful in patients who have shown an only partial recovery from endogenous depressions with lingering anxiety features. Of reserpine, I have practically no direct knowledge but there seems no doubt that it is of value in mental hospital practice for the reduction of agitation and excitement, while the fact that it is liable to produce attacks of melancholia, usually, it seems, between the fourth and sixth month of its first administration, renders it a substance of great theoretical interest. As to chlorpromazine, again there seems no doubt that in mental hospital practice it is of great value also in allaying agitation and excitement, particularly in senile cases, and particularly in deliria. I myself have found it superior to other methods of treatment in only one condition, namely paranoid schizophrenia, and particularly in the well-preserved type of paraphrenic who tends to be so resistant to other measures. Contrary to the views that Dr. Diethelm expressed yesterday, I have not found it valuable in depressive cases, with one possible exception, but in view of the remarks that have been made at these meetings I may have to revise my views, not for the first time.

If this brief dismissal of the subject seems hasty and ill-considered, it must always be kept in mind that even if the value of tranquillizers is confined mainly to chlorpromazine and reserpine, these nonetheless represent a real advance, and if the value of these is again confined to the treatment of excitement, agitation and paranoid schizophrenia, it is a real gain that they work at all, while the possibility of further contributions to knowledge arising from their

further study is also a real one. Dr. Hoch's indications and figures as to the cancellation, because of the improvement wrought by these substances, of planned mental hospital projects, and of the vastly improved atmosphere that has come about in the mental hospitals under his charge, are so impressive as to speak for themselves.