Drug Treatment of Disease

SEDATIVES AND TRANQUILLIZERS: PART I

BY

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Introduction

In considering the new sedatives and tranquillizers, it is worth remembering that it may take a year or more to learn how to use any one new drug skilfully and selectively; and all one can do is to keep a range of well-proved sedatives in use, and to look among all the new drugs for others likely to fill some of the present treatment gaps. It is certainly unwise to try one new tranquillizer after another in the hope of finding some universally applicable drug. There cannot be one, because of the number and variety of psychological reactions to life's stresses, and because of the different constitutional types of person showing them. These different types of person may all need handling in quite different ways with drugs. In this article advice will be given only on drugs which the writer has himself tried to learn how to use in as practical a manner as possible over the years. This does not mean there are not other similar ones, just as good, which may not happen to have been tried out and tested as thoroughly.

Two most important points about the giving of sedative drugs must be emphasized before discussing any of them in detail. Experiments on animals have shown that different constitutions may need quite different dosages of any drug used. In Pavlov's dogs, for instance, those with "strong excitatory" temperament often needed up to *eight* times the body-weight dose of sedative required by those with "weak inhibitory" temperament if an induced experimental neurosis was to be satisfactorily treated; until the right dose of any drug was found, the use of sedatives could often worsen rather than improve a neurotic state. It is the same with human beings.

Dosages of sedatives differ very widely in different illnesses and different constitutional types of person. This is shown, for example, in the response of the "strong excitatory" epileptic to a sedative drug such as phenobarbitone. He may thrive on 4-6 gr. (260-400 mg.) a day, given as a maintenance dose to prevent fits and to keep him in active nervous health. But a "weak inhibitory" hysterical patient may fall about and be greatly worsened by being given as little as $\frac{1}{2}$ gr. (32 mg.) of phenobarbitone twice a day. Unless these large individual differences in response to drugs are recognized, the proper use of sedative drugs can be very difficult to learn, and the results obtained with standardized dosages can be most misleading.*

The other general point to mention is the possibility of harmful addiction to all such drugs. Any drug which successfully treats anxiety and tension, especially if it also creates states of euphoria, is likely to have

strong addictive tendencies. In this article it is impossible to go into all the ethical considerations involved, but it is clearly our duty to try to confine ourselves to those drugs that do the least harm and have the least serious side-effects when from time to time they may have to be withdrawn or curtailed. To do this, it is wise to try to adhere, whenever possible, to drugs which, though they combat anxiety and tension, do not also create too much undesirable euphoria. Man's constant search for happiness can make these the hardest to give up.

The Older Sedatives

Bromides.—Before the second world war potassium bromide was one of the most widely prescribed drugs in the *British Pharmacopoeia*. In recent years, however, it has tended to become discredited and to be replaced by the barbiturates. Bromide began to fall into disrepute when the numerous cases of bromide intoxication came to be more generally recognized. Its disuse, however, may now have gone too far. Intoxication rarely occurs, except in the elderly, the arteriosclerotic, and in patients with impaired renal function. Intoxication can practically always be avoided by not prescribing it for these types of patient, and by insisting that the patient taking this medicine should also take adequate salt. There are some strong and chronic tension states in which large amounts of barbiturate are necessary to bring any real sedative relief, and this often causes severe addiction, and even greater tension when attempts are later made to lower the dose of barbiturate or to withdraw the drug. There are patients with reactive depressions and strong body-builds, and those who show explosive outbursts of anger and tension, who can still be helped better by bromide in doses of 20-30 mg. three times a day than by barbiturates. Bromide should certainly not be forgotten by the physician in search of a suitable sedative for some of his patients with chronic tension. It may also be useful in supplementing a smaller daily dose of barbiturate. It is hard to believe that the enormous vogue for the bromides over so many years was without any foundation whatever.

Chloral.—This is another drug which has also had a long innings because of its excellent sleep-producing qualities, but which is now tending to be replaced by the barbiturates. However, with the increasing tendency to barbiturate dependence so often seen at the present time, and because of the craving that can be aroused by too injudicious a use of the short-acting barbiturates, the writer is finding that chloral still has a valuable role as an alternative sedative to the barbiturates, especially to avoid the building up of tolerance to barbiturates so that sedation may be given over long periods of time. Chloral should generally be given in doses of $\frac{1}{2}$ -1 $\frac{1}{2}$ drachms (1.7-5.2 ml.) of the *B.P.* mixture, and it can sometimes be used to supplement smaller doses of longer-acting barbiturates, each enhancing the effect of the other.

Paraldehyde.—Paraldehyde is now less useful than formerly as a sedative and tranquillizer. It is an exceedingly valuable drug, and still has its limited place in helping to cope with the withdrawal symptoms of the alcoholic, especially in the "strong excitatory" and confused patient. But it is a bad sedative for routine use because of its unpleasant smell and its consequent social drawbacks. It acts quickly, effectively, and safely in an emergency. But where routine administration of paraldehyde has been indicated in the past, the giving of one of the new tranquillizers such as chlor-

*This is in fact one of the outstanding faults of most of the double-sampling tests of to-day. Moreover, neuroses and psychoses may get lumped together in such tests, and often more misinformation than information is gained about the skilled use of a drug being tested. As a good example of this, many schizophrenics are now thriving and having their symptoms held at bay with doses of chlorpromazine that may have to be as high as 300-500 mg. a day. On this dosage they are also possibly able to do a full day's work. Every doctor has other neurotic and depressive patients who complain of a marked worsening of their symptoms when more than 25 mg. of the same drug is given three times a day for comparatively short periods.

promazine, together with smaller amounts of other sedatives is now often preferable, especially for the elderly. It does, however, still have a real place in the efficient sedation of physically ill and restless patients in hospital. Because it can be obtained freely without prescription, it is not advisable to give it out too liberally in general practice, especially to the alcoholic, the compulsive barbiturate addict, and all the other potential seekers after chemical euphoria and temporary oblivion, in particular the hysterical psychopaths. Doses of 1-4 drachms (3.5-14 ml.) can be safely prescribed by mouth, and it is worth remembering that 2-4 drachms (7-14 ml.) can be injected intramuscularly when necessary in an emergency.

Barbiturates.—The long- and short-acting barbiturates have now become the main standby of physician and psychiatrist alike. And they are often the sedative of choice both for the neurotic and for the normal patient. In general, the barbiturates are much cheaper than the newer tranquillizing drugs. However, the short-acting barbiturates have more addictive dangers than, say, the bromides, and this is possibly because they are often more efficient drugs for the purposes for which they are prescribed. The enormous range of barbiturates, and the number of different preparations of each, make it impossible to learn to use anything like all the possibly valuable ones. A clinician should choose for himself a few selected long-acting and short-acting barbiturates and learn how to use and vary these in his many different types of patient. Barbitone sodium, for instance, still seems to be an excellent long-acting sedative when given in doses of 5-15 gr. (0.32-1 g.) at night. It is often the drug of choice in depressive states, when early waking is much more of a problem than is getting to sleep at night. Long-acting barbiturates also seem to have less addicting and tension-creating qualities on withdrawal than do the shorter-acting ones. Phenobarbitone can be a satisfactory daily sedative for neurotic patients, in doses of $\frac{1}{2}$ gr. (32 mg.) three times a day to 1 gr. (65 mg.) twice a day, and many of the patients who used to be kept on bromides three times a day are now being maintained on this drug.

The short-acting barbiturates, of which sodium amylal and quinalbarbitone are good examples, can be very good indeed in relieving tension during the day and in bringing about sleep at night. The trouble is that they are often too efficient, and it is becoming more and more clear to the writer that short-acting barbiturates, when taken continuously over long periods, can perpetuate states of tension as well as relieve them. Great relief may be obtained for an hour or two after taking these short-acting barbiturates, but tension is soon created again, and further short-acting barbiturates are then demanded. Once the total dosage of amylal has reached 9 gr. (0.6 g.), or of quinalbarbitone 6 gr. (0.4 g.), in the 24 hours a vicious circle of self-perpetuating tension has often been created. The writer has seen some patients who have had one, two, or three modified leucotomies for relief of unbearable tension and who have turned out later to be barbiturate addicts. Their tension has finally subsided or been greatly reduced once this fact has been recognized and their drugs withdrawn or altered. When patients come to doctors complaining of states of chronic persistent tension, or a marked increase in recent tension for which they are demanding short-acting barbiturate medication, it should never be forgotten that addiction to and a previous unwise prescribing of such barbiturates may be the cause rather than the cure.

Despite these objections, the short-acting barbiturates can still be some of the most useful drugs we have at our disposal. They can be especially helpful in patients who have developed recent phobias of going out in the street, travelling by train, going in an aeroplane, or tackling any special new situation because of the anxiety aroused. But they should be used only occasionally and not as a routine in such anxiety-creating situations. Sodium amylal 1-3 gr. (65-200 mg.) or quinalbarbitone $\frac{1}{2}$ -1 $\frac{1}{2}$ gr. (50-100 mg.) may be given one hour before the patient tackles the phobia. Another of the new tranquillizers, meprobamate, also seems to be helping this particular group, and therefore may

be able to replace the short-acting barbiturates in some cases. But the other new tranquillizers, such as chlorpromazine, have not proved at all useful in this particular group of patients, who can often be so difficult to help.

One of the most popular combinations of drugs in recent years has been the giving of small doses of amylal and dexedrine together in the form of "drinamyl." One tablet only is taken in the morning at 8 o'clock and possibly again at lunch-time. The combination is of the greatest value as a tranquillizer in some mild depressive and tension states, but it is of no value in deep depressions, and can make patients with severe anxiety states more anxious. Because of the euphoria it creates this combination is in great demand by the chronic neurotic patients and should be prescribed sparingly. Those patients who benefit most by it should also be advised not to use the drug on at least two days in the week, so as to avoid tolerance to it being established too quickly.

Intravenous Use of Barbiturates.—The sedative value of barbiturates given intravenously can be great in certain psychiatric emergencies. If, following an accident or a shock of some sort, the doctor is called to see somebody who has suddenly lost the use of an arm, or voice, or is showing sudden onset of other hysterical symptoms, the slow intravenous injection of a short-acting barbiturate, such as sodium amylal or pentothal, to a point of relaxation and euphoria, combined with the use of immediate and strong suggestion by the doctor, will often break up and resolve the whole acute hysterical picture, and continued sedation for a few more days may then keep it broken up. In the last war the rapid treatment of acute hysterical reactions by the use of intravenous barbiturates has saved an enormous amount of pensionable chronicity since, and there is still a place for this valuable first-aid method in civilian practice to-day. Once hysterical or acute anxiety reactions are allowed to get fixed for even hours, let alone days, they can become much more difficult to get rid of again later.

(To be concluded)

PRIORY CHURCH OF ST. JOHN OF JERUSALEM

RE-DEDICATION BY ARCHBISHOP OF CANTERBURY

The Priory Church of St. John, Clerkenwell, heavily damaged by a German air raid on the night of May 10-11, 1941, and now restored, at a cost of £80,000, not only as the church of the Order of St. John of Jerusalem but also as the Order's assembly hall, was re-dedicated by the ARCHBISHOP of CANTERBURY, Prelate of the Order, on October 17. The DUKE of GLOUCESTER, Grand Prior of the Order, opened a memorial cloister and garden commemorating those members of the Order of St. John and of the St. John Ambulance Association and Brigade who lost their lives in the 1914-18 and 1939-45 wars. The church's crypt (Fig. 2), which escaped war damage, is one of the finest examples of 12th-century church building in London.

The original church of St. John Baptist was the chapel of the 12th-century Priory of Clerkenwell; it had a choir, which forms the present building, and a round nave larger than that of the Temple church and believed to have been destroyed in Wat Tyler's revolt of 1381—its outline is now traced in the roadway. Just after 1500 Prior Thomas Docwra constructed the large perpendicular windows of the choir and made other improvements, and the present Docwra family have given the wrought-iron gates which lead to the new memorial cloister.

The restored building is divided into three main sections—the church, with its crypt; the guard house; and the war memorial cloister and the staircase hall. The guard house contains a robing-room and vestibule and makes a striking entrance to the cloister (Fig. 3). Here an ancient piece of stonework found on the site has been incorporated in the