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THE USES OF AND POISONING BY THE BARBITURATES

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The topic of this paper was chosen with the realization that the barbiturates are too widely used at present and are far too easily obtained by the general public. The writing was stimulated by attendance on a patient with severe barbiturate intoxication, associated with a toxic psychosis following the self administration of a large amount of a particular barbiturate.—EDITOR.

The barbiturates comprise a large group of compounds which act to depress the central nervous system and are derived from the same parent substance. They are sold as tablets or in capsules or solutions. This group of drugs finds wide use as sedatives, anesthetics, and in the prevention or treatment of convulsions. The action of all the barbiturates is essentially similar, differing only in speed of action, duration of effect, and rapidity of excretion. Some of these compounds are excreted in the urine while others are destroyed by the liver. Generally speaking, the rate of excretion is slow and is about at its height on the second day. With some of the compounds, excretion continues into even the fourth day after the poisoning. Because of this, the barbiturates commonly have a cumulative action on the body—that is, since their rate of excretion is slow, successive doses will build up their concentration within the body.

The barbiturates are without doubt the most popular sedative at present, and their use is becoming an ever increasing problem. They are used chiefly by people with an emotional crisis which has produced nervousness, tension, anxiety, and disturbances in the sleep (1). Judicious use of the barbiturates in the above situations for short periods of time is medically justified. However, the use of these drugs in a chronic neurotic disorder is in almost all cases to be condemned.

STATISTICS ON USAGE

There have been a series of studies emphasizing the importance of the increasing use of the barbiturates. In one of the earlier reports covering the five year period from 1932-1936, barbiturates were found to be responsible for 4.2% of all suicides, excluding gases. Overall, in this series, the barbiturates were used in 0.66% of all suicidal attempts (2). In the study of the admissions of twelve large city hospitals in the period 1928-1937, 643 admissions out of a total of 1,254,464 were due to barbiturate poisoning. Of these, 47 or 7.3%
proved to be fatal (3). Supporting further the contention that the use of the barbiturates has been increasing steadily is the information that there were approximately 550,000 pounds of the barbiturates produced in 1945 as against 230,000 pounds manufactured in 1936 (4). Most recent figures indicate that over 2,000 tons are being sold annually (12). Then, too, comes the information from the National Office of Vital Statistics that generally there has been a steady increase in the number of suicidal and accidental deaths caused by the barbiturates. There is one interesting exception to the above generalization. In those states where laws governing the sales of these drugs have been passed, a leveling off or, in some cases, an actual decrease in the number of deaths has been recorded.

Acute Intoxication

Acute intoxication occurs when quantities of the drugs in an amount greater than five times the usual oral sedative dosage are consumed. Generally speaking, anything in excess of four grams may be considered toxic. Acute intoxication, itself, may be the result of a therapeutic overdose, of a deliberate suicidal attempt, of an accidental overdose, or of an attempted homicide (5). It is pertinent in this regard to remember that the stupefied, confused individual in the so-called state of "automatism" due to a small overdose of the drug may take still further amounts of the drug. This of course will add to the intensity of the drug's effect.

Signs and Symptoms of Acute Intoxication

The signs and symptoms of acute barbiturate intoxication include mental confusion, drowsiness, a drop in blood pressure, varying degrees of coma, increased pulse rate, moist skin, pulmonary edema, and most important of all varying degrees of respiratory depression (2). In addition, the patient may exhibit moderately enlarged pupils (or less often small pupils), and a skin rash. Skin eruptions generally are said to be the most common reaction of the body to the barbiturates (12). Thirty-three per cent of the patients also have nausea and vomiting. Rarely a patient may present the picture of acute delirium. In this acute organic reaction due to the interference of the barbiturates with normal functioning of the brain, one sees typically a waxing and waning of consciousness, confusion, apprehension, hallucinations, and illusions. Neurological signs and symptoms of barbiturate intoxication include a to-and-fro movement of eyes, slurred speech, tremors of the tongue,
lips, and fingers, unsteadiness of gait, and inability to stand upright with the eyes closed (6).

**Pathological Findings and Diagnosis**

The findings at autopsy are not characteristic nor diagnostic. The organs appear congested with blood, and there may even be small hemorrhages around blood vessels of the brain or other organs. The heart is reported to be dilated in a large number of cases.

Diagnosis is dependent among other things upon—learning that a drug was taken, or that the person was found unconscious in a room with an empty container that had been used for barbiturates. Physical examination will reveal a patient in deep coma or stupor, with diminished rate and depth of respiration, and pupils which are moderately enlarged or less often smaller than normal. In addition, the patient will have a decreased blood pressure and decreased (or rarely, elevated) temperature. The physical examination and medical laboratory procedures will aid in excluding other causes of stupor or coma such as those due to diabetes, "stroke," or alcoholic intoxication (7).

By chemical analysis of blood or urine samples it is found that the barbituric acid derivatives are the commonest poisons which can be extracted with immiscible solvents from acid solution (8). They can be extracted from acidic aqueous solutions by shaking with ether in which they are soluble. The ethereal extract can be decolorized and purified when necessary by shaking with a small amount of animal charcoal and filtering. They are also removed from ethereal solution by shaking with a very dilute caustic soda solution, which distinguishes them from certain other sedatives, such as sulphonal, trional, and open chain ureides.

**Treatment**

The treatment may be divided into immediate primary therapy administered by those first on the scene, and definitive secondary treatment by the physician.

The immediate treatment is concerned primarily with maintaining respiration, since these drugs have a more or less specific effect of decreasing that vital function. In the process of getting the patient to the hospital, one may administer artificial respiration if that is deemed necessary. Sadove, Gordon *et al.*, have recently reported on studies of artificial respiration in barbiturate poisoning (15). They concluded that all of the newer push-pull methods of artificial respiration and the Eve Rocking Method are superior to the Schafer prone
pressure method. The pulmotor apparatus may be used quite effectively while enroute to the hospital.

The most important definitive treatment of acute intoxication includes washing out the stomach. Some discount the importance of this procedure, but Davison is convinced it is advantageous (2). He claims that since the barbiturates decrease intestinal movements, the drug is retained longer within the gastrointestinal tract. Therefore, he recommends a thorough stomach washing using water and dilute potassium permanganate followed by an enema to evacuate the bowels. Oxygen should be administered if there is an indication for it, and any obstruction to breathing should be eliminated. Stimulants such as picrotoxin or metrazol are very useful in more profound cases. These stimulants are especially indicated when the patient is completely without reflexes, when a patient is unconscious longer than forty hours, when a patient shows markedly decreased respiration even after the administration of oxygen and carbon dioxide, or in a patient in whom there is a marked drop in blood pressure. Glucose solution intravenously is used to supply the body with nourishment and fluid, and to increase the urine output. Ephedrine may also be used in an attempt to raise the blood pressure if preceding measures have not accomplished this. Penicillin is administered prophylactically to guard against secondary lung infection. A retention catheter is inserted in cases with urinary retention.

A relatively new technique of treating acute barbiturate intoxication is that of using non-convulsive electro-stimulation by means of the Reiter apparatus (10). This is used in association with stimulants, moderate amounts of normal saline intravenously, prophylactic antibiotics, and good nursing case. Its chief value is in combating depression of the brain centers that control respiration.

PROGNOSIS AND COMPLICATIONS

The degree of danger to the patient, as in other acute intoxications, is dependent upon the patient's previous state of health, the amount of drug consumed, and the adequacy of treatment. The immediate prognosis is good as long as respiration and blood pressure are maintained. The main causes of death are as follows: failure of heart or respiration, pneumonia, or cerebral edema (13). Another complication is the accumulation of waste substances in the blood due to inadequate kidney function which in itself is due to partial circulatory collapse. During convalescence, the patient is extremely restless and unless
watched may rub the skin off of portions of the body by "purposeless" movements. Hoarseness and sore throat may result from the emergency procedures employed.

**CHRONIC INTOXICATION**

Chronic intoxication with the barbiturates is an addiction in the true sense of the word. A patient who has taken these drugs continuously over a long period of time develops tolerance, emotional dependence, and a degree of physical dependence (14). Chronic intoxication occurs most commonly in patients with neurotic disorders who use the drugs merely as a "crutch." It must be remembered that the excessive use of the barbiturates is probably determined by the type of personality concerned, in the same way as are chronic alcoholism and other forms of drug addiction (11).

The patient who is suffering from chronic intoxication may become dull, lethargic, and irritable. He may develop chronic paranoid tendencies and undergo intellectual deterioration. Among the neurological signs and symptoms seen are dizziness, wobbly, drunken gait, to-and-fro movement of the eyes, tremors, and slowness and thickness of speech. There may be a seeing and hearing of things that do not exist, and false ideas and beliefs of all types, with mood variations from well-being to depression.

Diagnosis is chiefly by means of the history and those methods mentioned under the diagnosis of acute intoxication.

Treatment must be carried out in a hospital where the patient can be kept under close supervision. The first part of the treatment consists of gradual withdrawal of the drug over a period of two to four weeks. During this period a definite withdrawal syndrome will be seen. Among the signs and symptoms are weakness, inability to sleep, tremor, great anxiety, loss of appetite, nausea and vomiting, weight loss, increased pulse rate and respiration, and convulsive seizure. In some cases, a psychosis may develop. Following withdrawal of the drug, the patient is started on a course of rehabilitation and psychotherapy.

**SUMMARY**

A survey of the literature reveals that the use of the barbiturates is reaching alarming proportions. Acute intoxication generally occurs when amounts in excess of four grams are consumed. The patient with acute intoxication exhibits a varying degree of confusion accompanied by physical and neurological signs. The findings at autopsy may be
quite widespread throughout the body. Diagnosis is dependent upon history of taking the drug and upon laboratory tests. Treatment is chiefly concerned with maintenance of respiration and blood pressure.

The type of patient most likely to be a victim of addiction is discussed. The treatment of addiction that is used at the Government Hospital at Lexington, Kentucky, is briefly outlined.

CONCLUSIONS

1. The use of the barbiturates should be restricted to patients suffering from acute emotional upset. Generally speaking, prolonged use is dangerous.

2. Acute intoxication may be the result of therapeutic overdose, a deliberate suicidal attempt, an accidental overdose, or an attempted homicide.

3. Immediate treatment consists of artificial respiration and of the use of the pulmotor apparatus in the more severe cases.

4. The stomach should be washed out by a physician if the patient is seen within three hours after taking the drug.

5. Chronic intoxication is an addiction in the true sense of the word, exhibiting tolerance, and emotional and physical dependence.

BIBLIOGRAPHY