hearts of elasmobranchs, and Johnston also studied the effects of some members of this group on the excised hearts of terrapin, no one seems to have made an extensive comparative study of the effects of the barbiturates on the excised hearts of frogs. . . . [In] 388 experiments . . . different concentrations of the barbiturates were tested on 64 excised frog hearts. . . . From [the] results it seems possible to divide the barbiturates studied into three groups, 1) those with marked cardiac depression; ortal and seconal, 2) those with moderate depression; amytal, pentobarbital and neonatal and 3) those with mild toxic effects; butisol, phenobarbital, evipal, vinobarbital and barbital. . . . All of the barbiturates studied depress the activity of the excised frog heart but they vary in the degree of this effect. A given concentration of one barbiturate such as ortal sodium or seconal sodium may cause complete stoppage of the heart whereas the same concentration of another barbiturate such as barbital, vinbarbital, evipal, butisol or phenobarbital may produce no noticeable change in either the rate or the height of contractions.” 2 references.

J. C. M. C.


"The indiscriminate use of sedatives and narcotics in the aged is undesirable. . . . In general, the lower level of liver and kidney functions which play such an important role in the breakdown and elimination of these drugs is responsible, in part at least, for the relatively poor tolerance to narcotics in the aged. Careful selection of a drug in proper dosage is desirable. The 'rule of thumb' that children and the aged do not tolerate large dosage is to be respected. . . . Long-acting drugs, such as phenobarbital and barbital, depend on the kidney for excretion. It is important, therefore, to know the functional capacity of these organs before barbiturates are given. Impairment of either organ may cause a cumulative toxic effect from the use of the drug. . . . Paraldehyde, a central nervous system depressant, has a wide margin of safety and should be used more often. . . . Chloral hydrate, which is inexpensive and effective, is readily absorbed by the gastrointestinal tract and is detoxified in the liver and excreted by the kidney. It produces sound sleep. Used as a sedative or soporific, it is given in a dosage of 3/10 to 1 gm. Its unpleasant taste may be overcome by diluting it with milk, water or syrup of orange. The drug is contraindicated in severe liver, renal or cardiac disease.

"Official U.S.P. preparations of bromides are potassium bromide, calcium bromide, sodium bromide and ammonium bromide. Combinations of sodium, potassium and ammonium salts may be useful for chronic sedation. The average dose is 1 to 2 gm. twice daily. In the presence of dehydration, debilitation, prostration, and impaired renal function, the preparation should be used with extreme caution because bromide intoxication can easily develop. . . . Morphine should be given subcutaneously in small doses. . . . Morphine should be used judiciously in patients who have debilitation, myxedema, anemia or pulmonary emphysema. Secondary effects from its action may be delayed for several hours to days. Larger doses cause mental confusion, respiratory depression, anorexia, vomiting and ileus. Codeine sulfate is about one-sixth as potent as morphine and is largely excreted in the urine. . . . Dilaudid has the same margin of safety as morphine. . . . Pantopon has no ad-
vantage over morphine sulfate and is more expensive. . . . Demerol has a fairly good range of safety and it rarely depresses respiration. Untoward effects are dizziness, nausea and vomiting, weakness and syncope. Tremor and convulsions may occur when doses are excessive and repeated often. Demerol is a good substitute for morphine; therefore, it should have wider use in the aged." 3 references.

J. C. M. C.


"According to the theory of narcosis proposed by Quastel and associates narcotics exert their effect by inhibiting certain metabolic processes in brain required for the metabolism of carbohydrate, upon which brain is largely dependent. . . . The site of action of narcotics has not been determined. . . . Accepting Quastel's results there are two possible positions where narcotics may exert their inhibition—(I) by blocking the transfer of H from cozymase to flavoprotein and (II) by blocking the transfer of electrons from flavoprotein to cytochrome b. If the inhibition occurs at I in the above scheme one would expect to find an accumulation of reduced cozymase (coenzyme I) in the presence of narcotic. One would also expect to find that the transfer of hydrogen from reduced cozymase by flavoprotein in some suitable hydrogen acceptor was blocked by the addition of narcotics.

"If the above scheme represents a complete picture of the metabolic pathway in brain and if the block does not occur at I, by the process of elimination it must occur at II. There still remains the possibility, however, of another step in place of, or in addition to cytochrome b, between flavoprotein and the rest of cytochrome system. Further information on the position of the block may be obtained by determining the effect of narcotics on an enzyme requiring the cytochrome system but not cozymase. Such a system is that found in yeast, which oxidized lactic acid. In contrast to the animal lactate enzyme which requires cozymase the yeast lactate enzyme does not require a coenzyme but transfers hydrogen by means of the dehydrogenase and the cytochrome system. If such a system is inhibited by narcotics it would be inferential evidence that the narcotic block was not at I, and that it could occur at II. The line attack outlined . . . was pursued.

"It has been found that reduced cozymase did not accumulate during the carbohydrate metabolism of brain in the presence of nembutal; and that the reaction

reduced cozymase + methylene blue flavoprotein → cozymase + leuco methylene blue

was not affected by nembutal.

"These results indicate that the block was not at the position suggested as the first possibility. The oxidation of lactate by yeast was also found to be inhibited by nembutal. The fact that the yeast lactate enzyme, which unlike the enzyme in animal tissues does not require cozymase for activity, was inhibited, is further evidence that cozymase is not involved, and that the block occurs at cytochrome b or at some as yet unidentified step having properties similar to cytochrome b. We suggest that the narcotic may act by binding the reduced flavoprotein with cytochrome b (or other intermediate) and that the affinity of narcotic for this complex is greater than for the succinic dehydrogenase-cytochrome b complex which is not affected by low concentrations of narcotics." 23 references.

J. C. M. C.