

bromophenol-blue complexes. In six myasthenic patients given neostigmine by mouth, less than 5 per cent of the drug was excreted in the urine unchanged, while six similar patients given pyridostigmine by mouth excreted 2 to 16 per cent of this drug. On the other hand, two myasthenic patients given neostigmine intramuscularly excreted up to 67 per cent of the drug in the urine. It would appear neostigmine is partially metabolized in the alimentary tract and that it is less readily absorbed than pyridostigmine. (*Nowell, P. T., Scott, C. A., and Wilson, A.: Determination of Neostigmine and Pyridostigmine in the Urine of Patients with Myasthenia Gravis, Brit. J. Pharmacol. 18: 617 (June) 1962.*)

POTASSIUM DEPLETION The weight of available clinical and experimental evidence does not support the thesis that prolonged administration of benzothiadiazine drugs produces a significant depletion of body potassium, other than an initial transient phase. Renal compensatory mechanisms subsequently lead to readjustments, so that the chronic hypokalemia which may be present represents a deviation from the normal intracellular-extracellular potassium concentration gradient and not a total depletion. It is a relatively benign state, except for its possible potentiation of digitalis toxicity. Deliberate routine supplementation of potassium intake over long periods of therapy with benzothiadiazine drugs is unjustified. (*Weller, J. M.: Potassium Depletion and Benzothiadiazine Drugs—A Source of Over-Concern?, Amer. Heart J. 63: 842 (June) 1962.*)

INTRAMUSCULAR SUCCINYLCHOLINE The intramuscular injection of 0.75 mg./kg. succinylcholine chloride, dissolved in water, to ten conscious human subjects caused, within five minutes, an average 70 per cent decrease in grip strength and a 40 per cent decrease in vital capacity. Both parameters returned to control values within 15 minutes. The intramuscular injection of 4 mg./kg. succinylcholine, dissolved in water, to ten lightly anesthetized subjects caused apnea in nine within an average time of two minutes and 35 seconds. The average duration of apnea was 14 minutes and 41 seconds, and respiratory tidal volume returned to control values within

an average time of 30 minutes and 19 seconds. The same dose of succinylcholine, dissolved in saline, caused apnea in only three of ten anesthetized subjects in four minutes and 13 seconds. The development of the maximum decrease of respiratory tidal volume in the remaining seven subjects was delayed beyond ten minutes and averaged 60 per cent of control. The average duration of the respiratory depression was 33 minutes and 33 seconds. The differences between succinylcholine dissolved in water and dissolved in saline are probably due to different speed of absorption. The intramuscular administration of a 4 mg./kg. succinylcholine dissolved in water to a cirrhotic patient with low plasmacholinesterase activity caused apnea of 51 minutes and respiratory depression of 80 minutes duration. (*Foldes, F. F., and others: Experimental Studies with Intramuscular Succinylcholine in Conscious and Anesthetized Subjects, Der Anaesthetist, 11: 144 (May) 1962.*)

BARBITURATE METABOLISM Paper chromatographic studies of urine and plasma in 18 dogs showed different metabolic pathways for n-methyl-butobarbital and n-methylthio-butobarbital. While n-methyl-butobarbital is detoxified by side chain oxidation and demethylation, the n-methylated thiocompound is metabolized by destruction of the barbituric acid ring. The faster recovery after n-methylated thiobutobarbital, in contrast to thiobutobarbital is explained on this particular pathway of detoxification, rather than redistribution factors. (*Frey, H. H.: Untersuchungen über das Schicksal eines N-methylthiobarbiturates im Organismus, Arch. Int. Pharmacodyn. 134: 175 (Nov.) 1961.*)

NEUROMUSCULAR BLOCKADE AND EEG Sleep may be the result of deafferentation of the cortex, with resulting electrocortical synchronization. Desynchronization is characteristic of the awake state. The administration of neuromuscular blocking agents should reduce afferent impulses from muscles, tendons, and joints, and should predispose to somnolence. Somnolence and electrocortical synchronization were produced by the intravenous administration of Flaxedil, or Flaxedil plus barbiturate. Intracarotid injection did not have the same effect, showing that this