ventricular extrasystoles arising from one focus. Intravenous doses of 50 mg./Kg. precipitated violent clonic convulsions in the animals and increased the heart rate to nearly double the control value, the respiration being of the shallow spasmodic type. The electrocardiogram exhibited multiple ventricular ectopic beats arising from at least two foci. In each instance it appeared that the respiratory effects preceded slightly the cardiac effects. In one case, an electrocardiogram was taken 24 hours after the animal had recovered from a 50 mg./Kg. dose, and the record was entirely normal.

These effects on cardiac function and respiration were demonstrable shortly after oral doses of polypropylene glycol 425 had been given to anesthetized dogs, and are indicative of the rapidity with which this compound is absorbed from the gastrointestinal tract. A dose of 50 mg./Kg. was not sufficient to elicit them in two cases. However, at a dose of 0.1 Gm./Kg. an increase in heart rate, together with a change in the contour of the electrocardiogram, was detectable within as little as three minutes. About 10 minutes after administration of the dose, premature ventricular beats from multiple foci became evident. Following an oral dose of 0.5 Gm./Kg., another dog went into convulsions within three minutes. The heart rate increased from an initial value of 130/min. to 250/min. at four minutes after dosing, and frequent ventricular extrasystoles showed on the electrocardiogram.

Polypropylene glycols 1025 and 2025 in oral doses as high as 1 Gm./Kg. and 5 Gm./Kg., respectively, produced no appreciable effect on the electrocardiogram within the 15 minutes following the dose, during which the record was taken at frequent intervals.

Dipropylene glycol injected intravenously at a dose of 0.77 Gm./Kg. (undiluted) had no appreciable effect on the electrocardiogram; however, a dose of 50 mg./Kg. did precipitate further premature ventricular contractions in an animal that was recovering from a total intravenous dose of 60 mg./Kg. of polypropylene glycol 425.

Mechanism of Action: Effects of the Polypropylene Glycols on Certain Enzymatic Reactions.—Since the acute effects of overdosage with the lower polypropylene glycols appear to be mediated by the central nervous system, a study of the manner in which these compounds act on some enzyme systems of brain tissue was undertaken. Rat brain homogenate was used as the source of enzymes, and the conventional Warburg technic was employed to determine gaseous exchange. Anaerobic glycolysis was measured by the method of Utter, Wood, and Reiner,[10] and the oxidadation of glucose by the procedure of Reiner.[11] Succinic dehydrogenase and cytochrome oxidase activities were determined by the method of Schneider and Potter,[12] cholinesterase by the method of Mazur and Bodansky,[13] and urease by the procedure of Potter.[14] With a single exception, only one concentration of each compound was tested, namely, 5×10^{-3}M as based on the final volume in the reaction flask.

Under the above conditions none of the three polypropylene glycols exerted any effect on the rate of anaerobic glycolysis or cholinesterase activity. Similarly, no effect was observed when they were added to a test urease system. Polypropylene glycol 425 produced no inhibition of the succinoxidase system, although under the same conditions polypropylene glycols 1025 and 2025 caused 41 and 52 per cent inhibition, respectively. An increase in the concentration of polypropylene glycol 425 to 1.2×10^{-2}M has no effect on the activity of the system.

Only polypropylene glycol 2025 was investigated with respect to the cytochrome oxidase system. Again at the 5×10^{-3}M final concentration it inhibited the activity of the enzyme to the extent of 25 per cent.

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