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Toxicity of Solutions of Cocaine Hydrochloride of Various Ages.

DAVID T. CARR AND HIRAM E. ESSEX.

From the Division of Experimental Medicine, Mayo Foundation, Rochester, Minn.

Although cocaine hydrochloride is a very useful drug, it is also very toxic. The frequency of untoward reactions has been decreased by premedication with one of the barbiturate series of drugs but recent reports^{1,2} indicate that fatalities still occur following the use of cocaine. Several clinicians³⁻⁶ have found that no serious reactions occurred when they used an absolutely fresh solution of the drug and this has been our clinical experience.

Regnier, David and Joriot⁷ have reported that solutions of cocaine hydrochloride that were 6 months to several years old were more toxic to roots of white lupine seedlings than were fresh solutions but we have been unable

to find a report of any investigation on animals of the relation between the age and the toxicity of solutions of cocaine hydrochloride. Consequently the following experiments were done.

Method and Results. Using sterile precautions, 1% solutions of cocaine hydrochloride in sterile distilled water were made and placed in stoppered bottles of clear glass. The solutions were kept at room temperature (75° to 95°F) exposed to daylight but not to the direct rays of the sun.

Healthy adult rabbits of both sexes were used; their weights varied from 1.5 to 4.0 kg. It was determined that the intravenous injection in 10 seconds of 10 mg of cocaine hydrochloride per kilo of body weight, a 1% solution being used, was always followed by a generalized convulsion and fairly frequently by death. This dosage and technic of injection were followed throughout this experiment.

The fresh solution of cocaine hydrochloride was used during the first hour after it was prepared. The toxicity of this solution was compared with that of solutions one week, one month and 3½ months old. It seemed wise to compare the lethal effects, as the accurate

¹ Derbes, V. J., and Englehardt, H. T., *J. Lab. and Clin. Med.*, 1944, **29**, 478.

² Shumaker, H. B., Jr., *Sur.*, 1941, **10**, 134.

³ Gardner, J. A., *J. Urol.*, 1923, **10**, 509.

⁴ Braasch, W. F., quoted by Hirschfelder, A. D., and Bieter, R. N., *Physiol. Rev.*, 1932, **12**, 190.

⁵ Emmett, J. L., *Local Anesthesia of the Urethra and Bladder*; in Lundy, J. S., *Clinical Anesthesia*, Philadelphia, W. B. Saunders Co., 1942, 195.

⁶ Moersch, H. J., personal communication.

⁷ Regnier, Jean, David, Robert, and Joriot, Robert, *Comp. rend Soc. de biol.*, 1937, **125**, 1012.

TABLE I.
Toxicity of Solutions of Cocaine Hydrochloride.*

Age of solution	Rabbits	Deaths	Mortality rate %
Fresh	76	15	19.7
1 wk	87	25	28.7
1 mo	36	9	25.0
3½ "	10	1	10.0

* The drug was injected intravenously in 10 seconds in the dosage of 10 mg per kilo of body weight, a 1% solution being used.

grading of convulsions seemed impossible (Table I). It will be seen that there was not a demonstrable difference in the toxicity of the solutions of various ages. There was no evidence that the sex or the weight of the rabbits had any influence on the mortality rate. Neither was there any evidence that the fresh solution of cocaine hydrochloride became more toxic during the hour-long period that it was being used.

These results do not support the clinical impression that fresh solutions of cocaine hydrochloride are less toxic than older ones. However, it has been shown that sensitivity to cocaine hydrochloride varies among members of the animal kingdom, the monkey be-

ing much more sensitive than the rabbit.⁸ It seems probable that the human being is even more sensitive. If this is true, then it seems possible that small differences in toxicity which could not be detected in the rabbit might be of real significance in human beings. Therefore, even though the older solutions of cocaine hydrochloride did not cause a higher death rate in rabbits, it should not be concluded that old solutions of cocaine are entirely safe for human beings. In view of the clinical reports cited in the earlier part of this paper, it would seem wise to use fresh solutions of cocaine exclusively in clinical work.

Summary. The toxicity of solutions of cocaine hydrochloride of various ages (less than one hour, one week, one month and 3½ months) was studied in rabbits, the drug being given intravenously in the dosage of 10 mg per kilo of body weight. The mortality rates following injections of solutions of cocaine of various ages showed no significant differences.

⁸ Tatum, A. L., and Collins, A. H., *Arch. Int. Med.*, 1926, **38**, 405.

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Protection of Dry Bacteria by Fat Against Cationic Detergents.

OTTO RAHN.

From the Laboratory of Bacteriology, N. Y. State College of Agriculture, Cornell University, Ithaca, N. Y.

Klarmann and Wright¹ have shown that quaternary ammonium compounds cause an agglutination of bacteria and precipitate them against the walls of the test tube. This causes a very coarse and irregular distribution and explains the irregular results obtained by every investigator trying to evaluate the germicidal efficiency of these compounds.

It is not clear, however, why the bacteria in these clumps die more slowly than those

which remain singly in suspension. In order to prove whether these detergents are strongly adsorbed on the surfaces of bacteria, 1 g of baker's yeast was suspended in 100 ml of a 100 ppm solution of Zephiran (dimethylbenzyl alkyl ammonium chloride, also known as Roccal), the yeast removed by centrifugation, and the surface tension of the clear solution measured by the drop number method (Table I.) Nearly 20 ppm of the Zephiran had been adsorbed on the cells. This amount indicates a multimolecular adsorption layer. Bentonite particles in 1000 ppm Zephiran

¹ Klarmann, E. G., and Wright, E. S., *Soap and San. Chem.*, 1946, **22**, 125.