

to antitoxic action does not appear warranted because other substances such as normal serum (heated to 61°C.), eosin, phenol, mercuric chloride, and sodium carbonate have a similar effect.

Conclusions. Sulfanilamide causes a slight, almost negligible, inhibition of the hemolytic activity of streptococcal and staphylococcal hemotoxin. More marked inhibition of streptococcal hemolysin is produced by prontosil II, normal rabbit serum, rabbit serum heated to 61°C., eosin, phenol, mercuric chloride, and sodium carbonate. The administration of sulfanilamide *in vivo* or its addition to serum *in vitro* does not enhance the inhibitory effect of rabbit serum upon streptococcal hemolysin. Prontosil I was found to have no inhibitory effect upon streptococcal hemolysin.

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Protective Effects of CaCl₂ Against Procaine Convulsions in Guinea Pigs.*

R. BEUTNER AND G. P. MILEY.

From the Department of Pharmacology, Hahnemann Medical College of Philadelphia.

In order to protect animals against the convulsions from high doses of procaine-HCl, an addition of CaCl₂ was found to be effective. Guinea pigs, which *rarely* succumb to procaine convulsions, are more suitable for such studies than rabbits, which were formerly used by Beutner, Prusmack, and Miller¹; rabbits almost invariably die from procaine convulsions. Guinea pigs, however, can be injected repeatedly with convulsant doses. In the case of procaine, just as with various other previously observed convulsant drugs,² numerous observations are necessary to determine the average convulsant dose.

As controls, 55 guinea pigs received 159 injections of 100 mg. per kilo, as 10% solution, of procaine-HCl *alone*. This means that each of these 55 pigs was injected at least twice and some as many

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¹ Beutner, Prusmack, and Miller, *J. Pharm. and Exp. Therap.*, 1936, **57**, 114.

² Lennox, Nelson, and Beetham, *Arch. Neurol. and Psych.*, 1929, **21**, 625; *Proc. Physiol. Soc. of Philadelphia*, 1937, **12**, 10.

as 5 times. Of these 159 injections 138 resulted in convulsions, an incidence of 86.7%. Only 2 of all these animals died.

Forty-eight guinea pigs received 139 injections of 100 mg. procaine-HCl and 100 mg. CaCl₂. These two salts were mixed before injection in a solution containing 10% of each by volume. Previous to the CaCl₂-procaine-injections the animals had all received one or several injections of procaine alone, the same animals being used which were used as controls. Only 19 convulsions occurred in this series of 139 procaine-CaCl₂ injections, an incidence of 14.6% as contrasted with the 86.7% incidence obtained after procaine alone.

If a mixture of procaine and CaCl₂ was injected into guinea pigs which had had *no* previous injection of any kind, a somewhat higher incidence of convulsions was seen. We used only 10 animals in this series and gave them 30 injections of 100 mg. procaine-HCl plus 100 mg. CaCl₂, mixed before the injection as described above. In this series 12 convulsions occurred, or an incidence of 40% as contrasted with 86.7% from procaine alone. The protective effect of CaCl₂ is therefore manifest.

No protective effect of CaCl₂ was observed if CaCl₂ was first injected and followed by procaine-HCl a few minutes later; 12 guinea pigs were used for these experiments; all except one had convulsions, whereupon the experiment was discontinued. It appears that a mixing of the procaine-HCl and the CaCl₂ before the injection is essential for the protective action of CaCl₂.

We also tried to obtain a protective action by stimulating the calcium metabolism of guinea pigs by feeding them the drug AT 10, highly concentrated vitamin D, along with a diet rich in calcium. But this did not influence the incidence of convulsions after procaine at all; it remained at least as high, *viz.*, 90%, as after procaine given to a normal guinea pig; 12 animals were used in this series.

Conclusion. CaCl₂ injected intramuscularly in a mixed solution with procaine-HCl protects guinea pigs against convulsions ordinarily produced by injection of procaine-HCl alone.