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Protective Action of Mercury and Lead Salts Against Procaine Convulsions.*

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Recently Beutner, Landay and Lieberman[1] reported that hydroxy mercuri-methoxy-propyl carbamyl phenoxy acetate (salyrgan) will act as an anticonvulsant drug. They found that salyrgan prevented the usual procaine convulsions if the two drugs are mixed prior to the injection. They also noted that if the salyrgan is injected separately before that of procaine, it afforded no protective action against the procaine. They concluded from these experiments that the "anti-convulsant" action of salyrgan is not through a renal diuretic action but rather by virtue of a "tissue diuretic" action, *i. e.*, decreased cellular permeability.

A series of experiments was performed in our laboratory in which the following intramuscular injections were made into guinea pigs: (1) procaine alone, (2) procaine and salyrgan into separate areas of the body, (3) procaine and salyrgan mixed before the injection, (4) procaine and mercuric chloride mixed before the injection, and (5) lead nitrate and procaine mixed before the injection.

Results. Our experiments confirm Beutner, *et al.*, that salyrgan will protect an animal against procaine convulsions if the 2 drugs are mixed before being injected, but not if the 2 drugs are injected separately in different regions of the body. In 17 experiments performed on as many guinea pigs, 150 mg per kilo of procaine (10% solution) were injected intramuscularly into the right rear leg. Sixteen of the animals showed violent convulsions, from which they recovered in 15 to 40 minutes. In 12 experiments 20 mg per kilo of a 10% solution of salyrgan were injected intramuscularly and immediately following 150 mg of procaine per kilo were injected intramuscularly into the opposite extremity. All of these animals had convulsions which were as severe and lasted as long as those in which procaine was injected alone. In another series of 10 experiments the same quantities of procaine and salyrgan per kilo were

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1 Beutner, R., Landay, J., and Lieberman, A., PROC. SOC. EXP. BIOL. AND MED., 1940, 44, 120.

mixed and injected intramuscularly. In not a single experiment did the animal have a convulsion.

In our experiments it was noted that when salyrgan and procaine are mixed a white precipitate is produced. In the quantities used in these experiments, *i. e.*, 20 mg salyrgan per 150 mg procaine, the precipitate does not persist but redissolves upon agitation. If, however, the quantity of salyrgan is increased to 75 mg per 150 mg of procaine, a permanent white precipitate is produced. It appears from this that salyrgan and procaine are incompatible, the mercury in the salyrgan molecule probably acting as an alkaloidal precipitant.

A series of similar experiments was performed on guinea pigs in which an inorganic mercury salt was substituted for the salyrgan. In 10 experiments in which 150 mg of procaine (10% solution) and 3 mg mercuric chloride (1% solution) per kilo were injected separately into different areas of the animal, convulsions were noted in every instance. However, in 31 experiments in which the same quantities of procaine and mercuric chloride were mixed prior to the injection, mild convulsions were noted in only 8 of the animals. It was noted also that small quantities of mercuric chloride when added to a 10% procaine solution produce a white precipitate, which redissolves upon agitation. Larger quantities, as with the salyrgan, will produce a permanent white mercury-procaine precipitate.

Lead nitrate was found to be nearly as effective as mercuric chloride in protecting against procaine convulsions. In 12 experiments 150 mg of procaine (10% solution) and 10 mg lead nitrate (5% solution) were mixed in a test tube and injected intramuscularly into guinea pigs. In these experiments only 5 of the 12 animals had convulsions.

From these experiments we conclude that salyrgan, mercury chloride and lead nitrate protect against procaine convulsions by virtue of their alkaloidal precipitating properties. The mercury-procaine and lead-procaine compounds are probably absorbed too slowly to produce convulsions. Intravenous injections of salyrgan-procaine and lead-procaine mixtures are equally as toxic as pure procaine solutions.