

produced experimentally in a clean bird by feeding a part of the material direct from the other. Although I have not been able to find the specific organism in an egg before hatching, the observations recorded above indicate that very young birds acquire quail disease through eggs infected with the specific organism and layed by carriers of the infection.

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**Procaine Base Dissolved by Means of CO<sub>2</sub> and Its Mode of Action.\***

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It is well known that the local anesthetic power of procaine hydrochloride or related local anesthetics is augmented by the addition of sodium bicarbonate or other alkaline salts. This effect is readily explained through the stronger action of the uncombined procaine base which is liberated from the salt by sodium bicarbonate, etc. However, only an unknown part of the procaine base is thus liberated since chemical equilibrium exists between procaine HCl and sodium bicarbonate and the resultant products.

The use of procaine base as such in a water soluble form became possible through the observation that procaine loosely combines with CO<sub>2</sub>, thus being rendered water soluble, probably as a carbonate. On account of the rapid diffusion of CO<sub>2</sub> in the tissues, this solution can be expected to act as if the procaine base was dissolved as such.

Such a solution of procaine can be made as follows: 2 to 5 g of procaine base are suspended in 100 cc of water which is warmed to, or very slightly above, the melting point of the base (59°C). A steady stream of CO<sub>2</sub> is conducted through the mixture which is shaken vigorously. Further heating is avoided so long as the procaine is still a liquid, since above 60°C the solubility of CO<sub>2</sub> in water is too slight. Should procaine crystals appear, the suspension is reheated to the melting point. CO<sub>2</sub> is rapidly absorbed and the procaine goes into solution.

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With a procaine solution prepared in such a manner, the following experiments were performed by Dr. H. Wastl† at the suggestion of the writer :

(1) The incidence of convulsions in guinea pigs was tested. As previously shown by Beutner and Miley,<sup>1</sup> guinea pigs usually survive procaine and other convulsants, the incidence of convulsions being indicative of the convulsive power of any given local anesthetic. From Dr. Wastl's observations the following data were figured through graphic interpolation:

100 mg per kg procaine base	convulsions in all injected animals (136 of them) (direct observation)
100 mg per kg procaine as hydrochloride	convulsions in about 87% of the injected animals (calculated by graphic interpolation)
50 mg per kg procaine base	22.2% convulsions
50 mg per kg procaine as hydrochloride	22% convulsions

It appears, therefore, that the central convulsive action of procaine is not very different whether it is dissolved as a hydrochloride or, in looser combination, by means of CO<sub>2</sub>. Evidently while passing through the blood stream, procaine is liberated nearly to the same extent no matter whether it is combined with HCl or with CO<sub>2</sub>.

(2) In another series of experiments the local anesthetic effect on the cornea of the rabbit was tested. It was found to be much greater for procaine dissolved by CO<sub>2</sub> than for procaine hydrochloride. This is to be expected in view of the scarcity of buffer material present on the cornea. It was found that a solution of procaine hydrochloride containing 0.5% of the base when instilled on the conjunctiva anesthetized in 4.5 minutes (average of 6 observations). When procaine was dissolved in CO<sub>2</sub> at the same concentration, anesthesia occurred much faster, *viz.*, in 1.2 minutes (average of 6 observations). With 0.25% procaine as hydrochloride anesthesia occurred in 5.6 minutes (average of 6 observations); with 0.25% procaine dissolved in CO<sub>2</sub>, in 3.8 minutes (average of 6 observations).

As to be expected, these figures show that the topical effect of procaine CO<sub>2</sub> combination is considerably larger than that of the hydrochloride and corresponds to that of the free base.

*Summary.* A method of dissolving procaine base by means of CO<sub>2</sub>

† The writer wishes to thank Dr. H. Wastl for her careful observations from which the above figures are calculated.

<sup>1</sup> Beutner, R., and Miley, G. P., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 279. Compare also Beutner, R., and Wastl, H., *Scientific Proc. Am. Soc. for Pharm. and Exp. Ther.*, Thirtieth Annual Meeting, Toronto, Ontario, Canada, April 26-29, 1939.

is presented. The solution thus formed is only slightly more convulsant than procaine hydrochloride but considerably more anesthetic on topical application.

## 10912

**Effect of a High Fat Diet on Carbon Dioxide Combining Power of Blood Plasma.**

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Stewart, Gaddie and Dunlop<sup>1</sup> in a series of experiments on human subjects studied the carbon dioxide combining capacity of plasma with relation to blood fat content during and after exercise. They found that total lipid content varied inversely with the blood carbon dioxide combining power. These investigators believed that the carbon dioxide combining power was responsible for the changes in the blood fat content because changes in carbon dioxide combining capacity preceded the changes in fat content.

Since the subjects were not fed a high fat diet, nothing can be learned concerning the effect of an excessive amount of fat in the plasma on the CO<sub>2</sub> combining power. Van Slyke, Sendroy, Hastings and Neill<sup>2</sup> have shown that carbon dioxide is much more soluble in lipemic plasma than in normal plasma. Accordingly, even if the alkaline reserve of a lipemic blood sample were decreased, this might not be apparent from the carbon dioxide combining capacity as ordinarily determined from whole plasma.

During the past year, a group of investigators at this university conducted an experiment in which they fed students meals consisting chiefly of fried foods and pastries. Since such a diet is obviously high in fat content, we believed that information concerning the influence of fat in the diet on the carbon dioxide combining power of plasma might be obtained by studying the blood of these subjects. Permission was therefore granted us to draw the samples necessary for conducting the present investigation.

<sup>1</sup> Stewart, C. P., Gaddie, R., and Dunlop, D. M., *Biochem. J.*, 1931, **25**, 733.

<sup>2</sup> Van Slyke, D. D., Sendroy, J., Jr., Hastings, A. B., and Neill, J. B., *J. Biol. Chem.*, 1928, **78**, 784.