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## The relation of the adrenals to tuberculin poisoning.

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A paper which we read before this society in the spring of 1910 showed that "old" tuberculin or the filtered fluid from a culture of *B. tuberculosis* caused a marked arterial depression in the dog when injected into the femoral vein. This same tuberculin if heated above 105° lost this power of depression.

We have recently found that commercial adrenalin preparations and saline extracts of the experimental dog's freshly removed adrenal gland prevented this depression when mixed with tuberculin and the mixture injected intravenously.

Samples of tuberculin, which caused marked drops in the blood pressure, when mixed with a sufficient amount of an emulsion of the dog's own adrenals and injected intravenously, caused no fall in the blood pressure, thus showing an antagonistic action between tuberculin and the adrenals. The intravenous injection of samples of tuberculin containing the active depressor substance, after the adrenals had been removed, caused a drop with a more gradual recovery to the previous pressure level, than when the adrenals had been left intact. The intravenous injection into the dog with both adrenals removed of an emulsion of its own adrenals caused a return of the blood pressure to and above the normal level.

Further light is apparently thrown on the nature of the poisons of the tubercle bacillus as found in tuberculin by the following observations.

A. Four tuberculous guinea pigs were injected with a mixture of .5 c.c. of "P. D. & Co. Adrenaline Chloride 1–1000." Three of the pigs died within 18 hours and one within 36 hours. One control, a tuberculous pig, receiving .5 c.c. tuberculin without adrenalin died within 18 hours. The other control, a normal guinea pig, receiving .5 c.c. of the adrenalin chloride "P. D. & Co. 1–1000" did not apparently suffer any harmful results or show any noticeable toxic symptoms.

Four tuberculous guinea pigs injected with a mixture of .5 c.c.

tuberculin and 2 c.c. of a 1/100 dilution of "P. D. & Co. Adrenalin Chloride 1–1000" died within 18 hours. The control, a guinea pig, infected with *B. tuberculosis*, with enlarged glands, was injected with 2 c.c. of the same diluted adrenalin solution and did not show any toxic symptoms and lived.

B. .5 c.c. of the same tuberculin used in the previous experiments heated from 106° C. to 110° C. for 1 hour killed a tuberculous guinea pig within 18 hours.

We have studied the nature of tuberculin poisoning further by injecting tuberculin into dogs after one and both adrenals have been removed. The characteristic kymograph reaction of a tuberculin injection into normal dogs is a quick fall followed by an almost equally quick rise in pressure to the previous level.

The injection of a depressing dose of tuberculin into the dogs with the adrenals removed caused a marked drop with a much delayed response in the return to the previous pressure level.

Repeated successive depressing doses, varying from .5 c.c. to 5 c.c. for each dose, of samples of tuberculin injected intravenously into several large dogs which had had both adrenals removed did not cause a drop to the base line or immediate death, but the dogs lived from 2½ to 3 hours after the removal of the adrenals.

The average life of a dog after both adrenals have been removed is about 40 hours. Little or no ether was required after both adrenals had been removed to keep the dogs anesthetized. Clotting, which after the intravenous injections of samples of tuberculin in several doses, varying from .5 c.c. to 5 c.c. for each dose, had always seriously interfered with our work with the kymograph, was entirely absent after the adrenals had been removed even when tuberculin had been repeatedly injected.

We have repeatedly injected normal dogs in order to sensitize them with 5 c.c. of crude tuberculin without apparent injury or noticeable toxic effects.

These results indicate:

A. That tuberculin is a complex substance consisting of at least two poisons, one a blood pressure depressor destroyed by heat and antagonized by adrenalin; the other a substance characterized by its fatal effects on tuberculous guinea pigs when injected sub-

cutaneously and by its stability, which resists heating to 110° C, and which is not neutralized by adrenalin.

B. It is possible that we have evidence here that the absence or the abnormal diminution of the adrenal secretion permits some of the pathogenetic action of the products and extracts of the tubercle bacillus and that their administration mixed with the whole adrenal or some part of it, in a measure overcomes their deleterious action.

C. It is possible that the neutralizing value of blood mixed with tuberculin or some other appropriate adrenal antagonist might be a valuable index of the functional condition of the adrenal glands.

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## Comparison of the blood-flow in the hands in a case with lesion of upper motor neurones (birth palsy) and in a case with lesion of lower motor neurones (infantile paralysis).

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The blood flow was calculated from the formula

$$\varphi = \frac{H}{T - T'} \times \frac{1}{S}$$

where $\varphi$ is the quantity of blood flowing through the hand in the period of observation, $H$ the heat given off to a calorimeter containing the hand, $T$ the temperature of the arterial blood coming to the hand (taken as rectal temperature),[1] $T'$ the temperature of the venous blood leaving the hand (taken as the average temperature of the water in the calorimeter[2]) and $S$ the specific heat of blood. Before being put into the calorimeter the hand was immersed for a sufficient time (usually ten minutes) in a large

[1]Observations since made on the actual temperature of the arterial blood show that in a healthy man the rectal temperature is about half a degree above that of the blood coming to the hand under the conditions of the experiments. The temperature of the arterial blood is arrived at by determining that temperature of the calorimeter at which the hand neither loses nor gains heat.

[2]That this assumption is approximately correct for a certain range of bath temperature has been shown by actual measurement of the temperature of blood issuing from one of the veins of the hand, with suitable precautions to render the loss of heat as small as possible.