

DIPHtheria ANTIToxIN SOMETIMES FOUND IN THE
BLOOD OF HORSES THAT HAVE NOT BEEN
INJECTED WITH TOXIN.

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EVERY one who has undertaken the production of diphtheria antitoxin has encountered a marked difference in the behaviour of the horses undergoing inoculation. With some horses it is a matter of very little difficulty to obtain antitoxin of high potency in a comparatively short time. With others it seems impossible in any way to obtain strong antitoxin, and with others again there is such a violent reaction even with small doses of toxin that it is impossible to continue inoculation.* It occurred to me that the explanation of this might be found in the normal differences of the blood in the different animals. In order to test this, all the horses that were afterward used for the production of antitoxin for the laboratory of the Board of Health of Philadelphia were first tested as to the presence of antitoxin normally. It was, perhaps, to be expected that marked differences in this respect would be observable. I had rather expected, if there were any differences, that these would be gradual, that all horses might exhibit more or less antitoxic power in their blood. But from the results of the tests I am inclined to believe that this is not the case. There is in some cases a notable amount of antitoxin, in others it seems to be totally lacking. It seems to be present to a certain definite extent, or to be entirely absent.

In all, the blood-serum of twelve healthy horses was tested previous to injection with diphtheria toxin. Out of this number three

* This difficulty has now been entirely overcome by injecting these super-sensitive horses with antitoxin previous to and during the treatment with toxin, as recommended by Pawlowsky and Maksutow, *Zeitsch. f. Hyg.*, vol. xxi, p. 485, 1896.

were found to possess antitoxin of such strength that 3 cubic centimetres of the serum were capable of neutralizing ten times the minimum fatal dose for guinea-pigs, i. e., $1/30$ of a normal antitoxin unit. In all three horses the strength of the antitoxin seemed to be the same. The guinea-pigs injected with 3 cubic centimetres all remained alive and well; those injected with a lesser amount all succumbed promptly to the accompanying dose of toxin. Injections of blood-serum from horses not possessing normal antitoxin exerted no influence even in larger doses up to 5 cubic centimetres. The difference seems to be clearly one of quality and not of quantity, an essential difference in some constituent of the blood.

The behaviour of the horses possessing antitoxin normally in their blood presents certain points of interest on injections of toxin. These horses show much less reaction at the beginning than other horses, and it is possible to increase the doses to a certain point much more rapidly without causing alarming symptoms. After the dose has been increased till it reaches about 100 cubic centimetres or more the reaction seems to be as marked as in those horses that have had to be brought up to this dose more gradually. Experiments on two horses with antitoxin in their blood normally and two without antitoxin were begun together. One of the latter reacted so strongly that it was impossible to continue even with very small doses. The experiments on the other three horses have been continued. Up to the present time one of the horses, with antitoxin normally present, has received nearly 3 litres of toxin, the other over 4 litres, and the horse without the antitoxin normally present has received less than 2 litres, and yet they all show about the same amount of reaction at present from injections of 100 cubic centimetres of toxin. At first, when the doses were small, there was practically no reaction in the horses where the antitoxin was present normally, whereas in the other horse there was always decided reaction.

One of the horses with antitoxin normally present (the horse that has received about 3 litres of toxin) is beginning to furnish strong antitoxin, almost 1,000 units to 10 cubic centimetres. The other horse with antitoxin normally present (the horse that has received

over 4 litres) furnishes very weak antitoxin, less than 600 units to 10 cubic centimetres. The horse * that had no antitoxin normally, that had received nearly 2 litres of toxin, furnishes quite strong antitoxin, almost 1,000 units to 10 cubic centimetres. It would seem from this that the presence or absence of more or less antitoxin normally has no effect upon the ultimate production of artificial antitoxin by inoculation, but its presence enables the inoculations to be made with less risk to the animal.

It is difficult to explain the presence of antitoxin normally in the blood of horses. Wassermann † found antitoxin in the blood of healthy persons, who claimed never to have had diphtheria, but he inclined to the belief that these persons at some period must have suffered from unrecognized diphtheria. Orłowski ‡ also found diphtheria antitoxin in the blood of children who had presumably never suffered from diphtheria, and he found it also in the blood of convalescents, as others had done. Orłowski does not accept Wassermann's explanation, because he does not find that the age of the children has anything to do with the presence of normal antitoxin, and, moreover, he finds that the antitoxin present after convalescence disappears. #

* This animal has since died.

† Wassermann, Die Immunität Gesunder gegenüber Diphtherie. *Deutsche med. Wochenschr.*, 1894.

‡ Orłowski, Ueber die antitoxischen Eigenschaften des Blutserums bei Kindern. *Deutsche med. Wochenschr.*, 1895.

Cobbett (Contribution to the Study of the Serum Therapeutics of Diphtheria, etc. *The Jour. of Path. and Bact.*, vol. iii, No. 4), in an article which appeared since the above was sent in for publication, has also found that there is a definite amount of antitoxin present normally in the blood of some horses. He furthermore finds that, if there is no antitoxin in the blood, injection of the latter into guinea-pigs rather increases than diminishes the action of diphtheria toxin.