

years of age. On the other hand, it was enormously prevalent and severe in females from twenty to forty, somewhat less prevalent, but nearly always mild, in children of both sexes from two to ten years, and almost equally prevalent in old people of both sexes. The greatest pellagra morbidity was observed among persons engaged in housework or remaining at home without occupation, indicating that the causative agent or agencies are present in or near the home. Nevertheless, the women mill workers suffered as much as, or even more than, the housekeepers of the same age when due regard is given to the total number of persons thus engaged.

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The vascular response in poisoning from diphtheria toxin.

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From recent work it would appear that neither the heart nor the vaso-motor center is the chief factor responsible for the circulatory changes in diphtheria toxin poisoning. The work we have to report is the result of an attempt made to determine what this factor is.

We have studied first the reactions of the larger blood vessels in poisoned animals. This was done in the following manner: At the height of the poisoning, at a time when the blood pressure was extremely low, the animal was killed, sections of various arteries removed and placed in cold Ringer-Locke solution, where they were kept until ready for use. For comparison sections of arteries from an unpoisoned animal were removed and preserved. A strip of artery from the poisoned animal and one of similar size from the corresponding artery of the normal animal were then prepared, placed in a vessel containing fresh oxygenated Locke's solution, and attached to an apparatus for recording contraction and relaxation. To the solution was then added either adrenalin 1 : 1,000,000; barium chlorid 1 gm. : 255 c.c., or amyl nitrite (.1 to .3 c.c. in 250 c.c.) and the contraction or relaxation of the

artery strips recorded. Allowing for individual variations, the results we obtained from a considerable number of experiments showed that there was no appreciable difference in the reaction of the arteries of the poisoned and unpoisoned animals. Both series gave the same contraction from adrenalin and barium and corresponding relaxation from the nitrite. We conclude therefore that neither the vaso-motor mechanism nor the muscle tissue in the larger arteries are affected to an appreciable extent by diphtheria toxin.

In poisoned animals gastro-intestinal symptoms are prominent. These consist of vomiting and severe diarrhoea. A post-mortem examination of the intestines and other organs shows that striking changes have occurred. The pathological picture of the small intestine shows marked injection of the small blood vessels, arterioles and venules as well as the capillaries. The epithelium shows early coagulation necrosis. In the liver the capillaries show a widespread destruction. There are seen small islands of liver tissue surrounded by pools of blood. In the spleen and kidney also there is seen marked congestion of the terminal arteries.

These structural changes in the different organs are highly significant, and the engorgement of the mesenteric vessels would offer a sufficient explanation for the low blood pressure. We have, however, further studied the reaction of these vessels. A loop of intestine, with its blood supply intact, was placed in a plethysmograph and connected to a calibrated recording tambour. Adrenalin chlorid 1 : 10,000 in Ringer's solution was then quickly run into the plethysmograph, thus bathing the intestine, connection with the tambour made and the change in the intestinal volume recorded. The difference in the decrease in volume in a normal loop, contrasted to that occurring in the intestine of an animal given toxin is very striking. Calculated as cubic millimeters decrease in volume per centimeter of intestine, the average decrease in normal loops was 10.17 cm., the extremes being 15.04 and 5.91. The average decrease in poisoned loops was 1.81 cm. the extremes being 4.73 and 0.57.

In view of the marked structural changes in the smaller blood vessels, and of the failure of these to respond in the normal way to adrenalin we conclude therefore that the chief factor concerned

in the circulatory collapse in poisoning from diphtheria toxin is the arteriole and capillary dilatation.

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The influence of feeding upon acidosis in the phlorhizinized dog.

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Experiments have been reported by Geelmuyden¹ and by Baer² in which they fed protein to dogs under the influence of phlorhizin, and noted a marked drop in the quantity of acetone bodies eliminated in the urine. Lusk³ has called attention to the fact that the animals used by Geelmuyden and by Baer in their experiments were for the most part, only partially phlorhizinized, and that their results might be explained on the assumption that the protein ingested gave rise to dextrose which was burned in the organism.

In five experiments which we have carried out upon dogs phlorhizinized according to the method of Coolen, we have found a drop of from fifty to ninety per cent. in the quantity of acetone and of oxybutyric acid eliminated, following the ingestion of moderate amounts of protein. A determination of the glucose to nitrogen ratio in the urine showed that the fall in acidosis cannot be accounted for by ascribing it to sugar burned in the organism.

Since acidosis in the phlorhizinized dog can be practically abolished by such an apparently unrelated factor as the ingestion of protein it is obvious that caution should be used in interpreting results of acidosis studies upon phlorhizinized animals.

¹ Geelmuyden, *Zeitschr. f. physiol. Chem.*, 26, p. 381, 1898.

² Baer, *Arch. f. exp. Pathol. u. Pharm.*, 51, p. 271, 1904.

³ Lusk, *Ergebnisse der Physiologie*, 1912, XIII, p. 371.