SPONTANEOUS DIABETES IN A DOG.

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PLATE 41.

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Spontaneous diabetes occurring in the dog or other lower mammal is of interest on account of its rarity; and when associated with pancreatic lesions, it becomes a valuable link between the experimental diabetes of dogs and the spontaneous diabetes of man. While some pathologists believe that it occurs frequently in overfed, pet dogs, numerous published records of diabetes in animals are not readily found.

Fröhner (1) observed seven dogs in which persistent glycosuria and other clinical signs of diabetes were present, and quotes other cases observed by Schindelka, Eichhorn, Miller and Fettick (three each), and Gutzeit and Lienaux, Thiernesse, Schmidt, Wolff, Haltenhoff, Schulz and Strubing (one each). Eber (2) reported a series of twelve animals, and Lanfranchi (3) and Ferraro (4) each one; but all these occurred before Opie had demonstrated the now well known lesions of the islands of Langerhans. In four of Eber's five cases changes were noted in the pancreas; in one the organ was reduced by chronic inflammation to one-half its normal size; and in the other three, of normal size, numerous small yellowish abnormal specks were visible. It is noteworthy that the animals in all these cases were of advanced age and that the symptoms closely resembled those of human diabetes. Case reports of diabetes in other domestic animals are even rarer, though it has been found in the horse by Diickerhoff (5), Freller (6), Kruger (7), Heiss (8), Rueff (8), and Perozino (9); in the cow by Girotti (10), Ingardi (10), and Darba's (9); and in the ape by LeBlanc (9). Freller's careful study of a case of spontaneous diabetes in a horse is the only instance in which associated pancreatic lesions have been investigated by modern methods of technique. At autopsy, an interacinous pancreatitis with extensive degeneration of the islands of Langerhans was found. The type of degeneration, however, is not stated and no study of the island cells with special granule stains was made. As to the rarity of diabetes in animals Fröhner states that the two cases first observed by him were the only ones in 40,000 examinations (incidence of 0.005 per cent).
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From the clinical point of view it is noteworthy, in comparing the experimental diabetes of animals with that of man, that one of Fröhner's and one of Eber's dogs went into diabetic coma 5 and 3 days, respectively, before death. In two other animals of Eber's series, the diacetic acid test was positive on several occasions. As ketonuria has been observed by Allen in certain types of experimental diabetes in dogs, such cases form an additional link between the experimental and the spontaneous form of the disease.

Case Report.

A pet Airedale bitch, weight 19 kilos, age 9 years, after pregnancy and abortion in the spring of 1915, began to lose weight. The loss of weight was progressive, the animal was continually thirsty, ate ravenously of an unrestricted dietary, and, as in the case of Naunyn's depancreatized dogs, it was noticed that flies collected about her urine. Diabetes mellitus was suspected and it was found on collecting urine that a single drop completely reduced Fehling's solution (about 2 cc.).

Dr. A. E. Taylor kindly consented to study the animal's metabolism; but when she was placed in the strange conditions of a metabolism cage many difficulties arose which prevented detailed studies. It was found, however, that on a general diet the animal eliminated 60 gm. of sugar per day. When placed on 10 gm. of nitrogen daily (beef heart), the amount of sugar was reduced to 30 gm., a G : N ratio of 3. When fasting, the G : N ratio sank to 1.7, and the daily sugar output fell below 10 gm. At no time was there any ketonuria. It is possible that if the fast could have been continued longer the animal would have become sugar-free; but she was so obviously uncomfortable under laboratory conditions that the owner preferred to have her returned to her home where instructions that she was to be fed a carbohydrate-free diet were carefully carried out. Her clinical condition, however, steadily grew worse; sugar continued in the urine in large amounts, and after 3 months, cataracts developed in both eyes to the stage of total blindness. Abscesses and ulcers occurred on the legs and trunk, and she became greatly emaciated. A rapidly growing, freely movable, painless tumor appeared in the right side of the neck, and soon discharged watery and later bloody pus. She was chloroformed at the suggestion of her owner 6 months after the first symptoms had been noticed.
Autopsy.—Weight 10.9 kg. The pancreas was removed immediately after death and small sections (about 2 mm. thick) were placed at once in Zenker’s, formalin, and sublimate-bichromate solutions. The pancreas was found to be large, rather soft, of normal color and shape, and without any signs of old or recent inflammation or hemorrhage in or about it. Weight 33.8 gm.; length 14.5 cm.; width at head 4 cm.; at middle 3 cm. The tissue cut easily, disclosing the normal lobular arrangement, without increase of fibrous tissue. Numerous minute, ocher-yellow points (1 mm. or less in diameter) were seen through the peritoneal covering, especially near the tail, but these were less noticeable on the cut surface. Otherwise the postmortem examination showed nothing worthy of note except a tumor, 83 gm. in weight, occupying the right side of the neck at the level of the thyroid cartilage but arising apparently in the thymus gland. A similar mass 2.5 cm. in diameter was found at the base of the heart.

Histology of the Pancreas.—The acini are well filled with zymogen, in some places so densely packed that these areas have an almost homogeneous reddish appearance (hematoxylin and eosin) with the acinous cells much obscured. In a few areas are collections of small round cells with localized increase of fibrous tissue, but these changes are not sufficiently numerous or extensive to be important. The blood vessels are normal. Striking abnormalities, however, are found in the islands of Langerhans. Not only are they scarce, but every island shows degeneration of one or more kinds (Fig. 1). The most obvious change, easily visible in almost every island, is the typical hydropic degeneration of one or more cells. Similar hydropic cells are prominent, either singly or in groups of three or four, in the interacinous spaces. These are probably miniature islands of Langerhans. As we did not have the necessary stain, the tissues fixed in sublimate-bichromate solution were sent to Mr. Walter B. Martin, of the Johns Hopkins Medical School, who kindly prepared sections stained with neutral azo-violet, to bring out the alpha and beta granule cells of the islands of Langerhans. Although the fixative did not penetrate for any great depth into the tissue, he was able to observe the changes in the islands fairly well, and reports as follows:
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"The islets show complete degeneration of the beta cells, although remnants of these cells still are apparent in some of the islands as red staining areas. The alpha cells are also undergoing degeneration, but this has not progressed so far as in the others. The outline of the alpha cells can be made out, their nuclei are intact, and in a number of cases, the blue granulation is still quite distinct. Some of the islets are made up entirely of alpha cells undergoing degeneration."

Although some of the island cells have a hyaline appearance, the typical hyaline degeneration of Opie (11) and Weichselbaum (12) is not present. On the other hand, certain localized areas of fibrous tissue, especially those containing one or two isolated hydropic cells, show that in many cases whole islands have been replaced by fibrous tissue.

Histologic examination of the growth in the neck shows it to be a sarcomatous tumor of the thymus. The second tumor is a metastasis of the same in a lymph node. Thyroid, pituitary, adrenals, spleen, and liver show nothing of importance histologically, except extreme fatty change in the last named organ.

SUMMARY.

The picture is one of a true diabetes mellitus, first attracting attention after miscarriage. Although the G : N ratio sank from 3 : 1 on 10 gm. of nitrogen to 1.7 : 1 after 3 days' fasting, the disease progressed steadily in spite of a long continued carbohydrate-free diet. Together with the usual complications of diabetes, a malignant tumor of the thymus developed, so that after 5 months' observations a slow death was forestalled by chloroform. The most striking feature at autopsy was the large, apparently normal pancreas, which exhibited histologically marked changes in the islands of Langerhans, extreme hydropic degeneration and exhaustion of granules, involving both alpha and beta cells, but especially the latter, and replacement of some islands by fibrous tissue.

BIBLIOGRAPHY.

EXPLANATION OF PLATE 41.

Fig. 1. Degenerated island of Langerhans. a, two cells showing extreme hydropic degeneration; b, normal island cells with alpha granules; c, two cells with beta granules that have escaped destruction. (In very few islands of this pancreas are these cells to be found.) d, island cells showing beginning hydropic degeneration; e, pancreatic acinus with lumen and apices of acinus cells filled with zymogen; f, fibrosis, involving most of the island; g, pancreatic acinus in which zymogen granules have failed to take the stain.

Fixation, sublimate-bichromate. Stain, Martin's azo-fuchsir-neutral violet.
(Krambhaar: Spontaneous Diabetes in a Dog.)