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The so-called permanent polyuria of experimental diabetes insipidus.

By E. B. TOWNE.

[*From the Laboratory of Surgical Pathology, Stanford University Medical School, San Francisco, Cal.*]

Several types of operative damage to the pituitary body or to the tuber cinereum of the dog cause a polyuria which lasts about three days. A few observations of more enduring polyuria have been reported. In Crowe, Cushing and Homans's[1] Obs. 34 (partial removal of the anterior lobe and separation of the stalk) the polyuria was still present when the animal was killed six months after operation. Camus and Roussy's[2] dog "Moustachu" was putting out large amounts of urine when killed in the seventh month. Autopsy showed that the tuber cinereum had been punctured and that the stalk had been divided. Matthews[3] twice produced polyuria by introducing through the sphenoid bone a piece of gutta-percha tissue which impinged on the posterior lobe, stalk and tuber cinereum. One experiment lasted nine weeks before the animal was killed. Camus and Roussy[4] reported two dogs with "permanent diabetes insipidus" which were still alive ten and twelve months after the production of a lesion intended to involve only the tuber cinereum. Bailey and Bremer,[5] who produced small lesions of the tuber cinereum, said that in three dogs "the polyuria was permanent." The experiments lasted ten days, six weeks and four months respectively; in the third animal the posterior lobe had been detached from the infundibulum.

The matter at issue is whether the polyuria is due to suppression of the secretion of the pars intermedia, or to injury of a hypothetical nerve center in the tuber cinereum, or to some other

[1] Crowe, Cushing and Homans, *Johns Hopkins Hosp. Bull.*, 1910, xxi, 127.

[2] Camus and Roussy, *Presse méd.*, 1914, xxii, 517.

[3] Matthews, *Arch. Int. Med.*, 1915, xv, 451.

[4] Camus and Roussy, *Comptes Rendus de la Soc. de Biol.*, 1920, lxxxiii, 764; ibid., 901; ibid., 1578.

[5] Bailey and Bremer, *Arch. Int. Med.*, 1921. xxviii, 773.

cause. The average length of life in the eight observations summarized above was five months. It has been assumed in some of these experiments that the polyuria was permanent. I have made observations which bear on the question of permanency.

Dog 4; female, weight 6,135 gm., about 6 months old, had an average daily output of 140 c.c. of urine. Jan. 5, 1920, under ether anesthesia, the pituitary gland was exposed by Paulesco's technic, and an incision was made through the tuber cinereum which opened the third ventricle and completely separated the stalk and gland from the base of the brain. The output of urine rose for three days to about 600 c.c., dropped to 200 c.c. for the following four days, and rose to 1,000 c.c. on the ninth day. From that time until Apr. 1, the output was always above 1,000 c.c. except when it was reduced for a day by injection of pituitary extract. The largest amount was 1,450 c.c. on Feb. 26. From Apr. 1 to May 22 the output varied between 800 and 500 c.c., always tending downward. On June 5 it reached 250 c.c. and remained there until June 24, when the animal was killed. The polyuria had lasted about 20 of the 24 weeks after operation, and during that period her weight rose to 1,250 gm. She was always active and well, but did not come in heat.

At autopsy there was a marked increase in adipose tissue. The uterus and ovaries were infantile. The thyroid and adrenals were microscopically normal. The ovaries showed ova in every stage of development. A block from the floor of the third ventricle, including the tuber cinereum and the attached pituitary gland, was cut in serial sections. The scar of the operative incision was at the lower margin of the optic chiasm anteriorly and at a slightly lower level posteriorly. To this extent the floor of the third ventricle had been reformed by connective tissue without ependymal lining. All of that portion of the pars intermedia which covers the tuber cinereum and the neighboring base of the brain (Tilney's pars tuberalis) had been detached with the stalk. The pars anterior appeared normal, with about the usual proportion of chromophile and chromophobe cells. The pars nervosa was atrophic and invaded by cells of the pars intermedia type. Surrounding the altered pars nervosa was an empty space which, from the evidence of a few sections, had been filled with colloid

material. Outside this space was a zone of pars intermedia cells. Posteriorly these cells were separated from the base of the brain by scar tissue, but anteriorly, at the point where the connective tissue portion of the floor of the ventricle joined the normal floor, there was no intervening scar tissue. Here a mass of pars intermedia cells, continuous anteriorly with pars anterior cells, had invaded the base of the brain so that the cells lay immediately under the ependymal lining. The majority of these cells were chromophobe and arranged in alveoli containing colloid, but among them were occasional eosinophiles similar to those in the adjacent anterior lobe.

In other experiments I have produced polyurias that ended in the third, fourth or fifth month, but sections have shown that the stalk division had not been made sufficiently high to detach all the pars tuberalis cells from the base of the brain, and that this epithelium had proliferated above the scar. Only in Dog 4 were all of these cells detached with the gland. The sections of this animal are interpreted as meaning that the anterior and superior portion of the pars intermedia reunited with the uninjured floor of the third ventricle without any intervening scar tissue, so that there was nothing to prevent pars intermedia products from passing into the ventricle, if that be the method of secretion.

I am not ready to interpret these findings as they effect the question of the cause of experimental polyuria. They indicate that a stalk division high enough to detach all epithelium from the base of the brain and completely destroy the tuber cinereum does not necessarily result in a permanent polyuria, and that the true permanency of previously reported results of such experiments is open to question.