

tated blood varies with the state of the circulation, being least when the animal is in shock. The destruction of 2 leaflets, in such acute experiments, is fatal in from 30 to 60 minutes. These curves were obtained from dogs anesthetized with chloretone and heparinized after exposure of the great vessels.

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Effects of Daily Pituitary Heterotransplants on an Hypophysectomized Puppy.

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Recent results obtained by Smith and Engle¹ by daily hypophyseal homeo and heterotransplants in mice and rats led to an investigation of the effect of daily injections of fresh rabbit pituitary gland on an hypophysectomized puppy. Aschner² published striking photographs of hypophysectomized puppies of various ages which had remained infantile in appearance and size until sacrificed.

Evans and Long³ found that fresh anterior lobe fluid given intraperitoneally to immature rats produced gigantism. Later, this extract was found to stimulate hypophysectomized rats to normal growth but failed to affect their sex glands. Smith,⁴ using fresh pituitary glands of rats, was able completely or in large measure to cure the disabilities arising from hypophysectomy in immature rats. Smith and Engle⁵ were able to induce precocious sexual maturity both in immature and in hypophysectomized rats, in 2 animals within 36 hours, by these fresh daily transplants. By means of the intracranial approach of Dandy and Reichert⁶ a total hypophysectomy was performed on a 6 weeks old female puppy and the base of the brain in the infundibular region cauterized by heat. This animal was constantly kept with her control litter mate, also female. After months of observation, she remained infantile, failed

¹ Smith, P. E., and Engle, E. T., *Am. J. Anat.*, 1927, xl, 159.

² Aschner, B., *Arch. f. d. Ges. Physiol.*, 1912, cxlvi, 1.

³ Evans, H. M., and Long, J. A., *Anat. Rec.*, 1921, xxi, 62.

⁴ Smith, P. E., *J. Am. Med. Assn.*, 1927, lxxxviii, 158.

⁵ Smith, P. E., and Engle, E. T., *Proc. Soc. Exp. Biol. and Med.*, 1927, xxiv, 561.

⁶ Dandy, W. E., and Reichert, F. L., *Bull. Johns Hopkins Hosp.*, 1925, xxxvii, 1.

to grow, retained the puppy face and hair, failed to erupt permanent teeth and exhibited infantile genitalia, indicative that a total hypophysectomy had been performed.

Six months after hypophysectomy when 7½ months old, weighing 4.2 kilos and when the control had attained adult size and weighed 9.3 kilos, fresh whole rabbit's hypophysis was given subcutaneously every day by the technic described by Smith and Engle.¹ Within 48 hours the vulva were definitely swollen and within 3 days became so greatly distended as to protrude 3 cm. from the body. This marked swelling of the external genitalia has now persisted for over 2 months while the control whose external genitalia have remained of normal size has never been in heat. A vaginal secretion appeared after about 2 weeks but she did not attract a male dog until the 18th day when coitus was attempted.

The weight of the experimental puppy remained stationary for the first 2 months, then began to increase, although adipose tissue in the groin definitely disappeared during the first 2 weeks of giving the transplants.

During this 2 months' period of treatment, measurements of the long bones outlined by the X-ray have shown no growth in the control, and an increase in length of the tibia and femur of only 1 cm. each in the operative animal.

The permanent teeth appeared during the 3rd to 5th month in the control, while even at the age of 7 months the hypophysectomized puppy still had all of the first denture. Within a month after the beginning of the injection therapy these teeth dropped out and were replaced by the permanent set.

The experimental animal showed a marked change in behavior, with increased activity, attentiveness and playfulness appearing early in the first week of treatment.

In the 3rd week the soft, downy texture of the coat began to change to a coarser and longer coat of hair.

This heterotransplant treatment has readily produced the characteristic stimulation of the genital system, and has led to maturity of other systems, while skeletal growth was so far but moderately affected. The latter might be attributed to the fact that an interval of 6 months existed between the time of hypophysectomy and the initiation of the replacement therapy during which time the control had attained maturity.

Further experiments are in progress to determine the effect of transplants on puppies soon after hypophysectomy.