

imals which received a minimum of 130 minutes per port. Following irradiation, glucose tolerance tests were made weekly for periods of 3 to 5 weeks. In no instance did the fasting blood sugar or the tolerance curve indicate that the treatment had been beneficial within this period. The fasting blood sugar remained between 300 and 600 mg. %, the animals did not become hypersensitive to insulin as do hypophysectomized-depancreatized dogs, and the insulin dosage was not reduced.

This work is being continued with larger doses of X-rays, and a histological study is being made of the pituitary and other irradiated areas of the brain, and also of the thyroid, adrenals, and gonads to determine the effects of the irradiation.

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Effects of Brain Cautery on Fetal Development in the Rat.

E. L. COREY. (Introduced by H. E. Jordan.)

From the Physiological Laboratory, University of Virginia Medical School.

The primary purpose of this study is to determine whether the fetus can survive extensive damage to the brain, and the possible effects of brain injury on subsequent growth and development. Previous studies have been almost entirely confined to observations on teratological (anencephalic) human material (Preyer,¹ Bruns *et al.*,² Nañagas,³ Marcus and Nickman⁴).

Destruction of portions of the fetal brain (rat*) was accomplished by means of the electric cautery. No repair was found necessary other than suture of the maternal body wall (Nicholas⁵). Fetuses recovered from the uterus or taken at birth subsequent to such procedure were examined as to behavior, measured, weighed

¹ Preyer, W., *Specielle Physiologie des Embryo*, 1885.

² Bruns, I., Cranen, A., and Ziehen, Th., *Hand. d. Nerven. Krankh. im Kindesalter*, Berlin, 1912.

³ Nañagas, J. C., *Am. J. Anat.*, 1925, **35**, 455.

⁴ Marcus, J. H., and Nickman, E. H., *Arch. Pediat.*, 1930, **47**, 739.

* The rats used in this study were obtained through the generosity of the Wistar Institute of Anatomy and Biology.

⁵ Nicholas, J. S., *Anat. Rec.*, 1925, **31**, 385; *Proc. Soc. Exp. Biol. and Med.*, 1926, **23**, 436.

and placed at once in 5% formalin preparatory to microscopic study of the injured area. Unoperated litter-mates served as controls. A series of control experiments involved (a) injection of carbon ink into the ventricles of the brain, and (b) extensive cautery of an extremity. Seventy fetuses from 21 litters comprise the experimental material, and 36 fetuses from 10 litters were used in the control experiments.

Of the 70 operated fetuses ranging between 11 and 37 mm. of crown-rump length at operation, 40 survived until term or were recovered alive from the uterus 1, 2, 3, 4, 5, or 6 days following cautery. The remainder were either aborted (2) or partially resorbed. At term (39 to 42 mm.) 11 fetuses died *in utero* and none of the animals survived parturition more than 24 hours. The rat fetus may survive brain cautery until term regardless of the stage of development at which the operation is performed.

Living operated fetuses recovered from the uterus or those born dead or alive present certain distinct gross abnormalities (aside from cranial malformations attributable to cautery *per se*): an enlarged and protruding tongue, thickened body contour with heavy neck and jaw and an abnormally shortened rostral region. The maxillae are more markedly affected than the mandibles. There is little if any repair of the injured area although the general vascularity appears unimpaired.

All living fetuses recovered from the uterus or those born alive exhibit spontaneous (*i. e.*, non-specifically induced) movements indistinguishable from those shown by their litter-controls. The application of tactile stimuli by bristle or needle elicits no marked difference in response when applied to operated and control fetuses from the same litter, although the strength of the response appears weakened and the reactions sluggish in the operated fetuses. These results indicate that the cerebral cortex of the fetus cannot be extensively involved in the production of fetal movements either spontaneous or induced. It is suggested, however, that the cortex may be necessary for (quantitatively) normal movement. Both operated fetuses and their litter-controls show vigorous respiratory movements and the ability to squeal.

Crown-rump length and weight were selected as criteria for a comparison of the rate of development of the operated fetuses with that of their litter-controls. It was found that the operated fetuses average 8% below the controls in crown-rump length and 10% below the normal fetuses in weight. The lesser crown-rump length of the operated animals may possibly be due to the pronounced

abnormality of the head region, and the figure obtained (-8%) is perhaps of little significance. The relatively small difference (-10%) in body weights may likewise be of only slight significance since the apparent retardation in growth shown by the cauterized fetuses could be attributed to tissue lost at operation, together with faulty development in the region of cautery. Nevertheless, the fetuses showing the greater weight discrepancy when compared with their litter-controls are those operated at the earlier stages. Thus litters 1, 8 and 16, operated at crown-rump lengths of 12, 11 and 10 mm. respectively, show smaller body weights when compared with their litter-mates by 25, 24, and 23%. That these are the youngest fetuses operated, and that they show the most pronounced apparent retardation of development may not be wholly without significance. The results are summarized below.

Number of litters used, 21. Number of fetuses operated, 70.

Days in uterus after operation: range, 1 to 6; average, 4.

Operated fetuses surviving until term, 40.

Crown-rump length of operated fetuses at operation: range, 11 to 37 mm.; average, 21 mm.

Crown-rump length of operated fetuses on recovery from uterus. range, 21 to 41 mm.; average, 36 mm.

Crown-rump length of control fetuses on recovery from uterus: range, 25 to 42 mm.; average, 39 mm.

Weight of operated fetuses on recovery from uterus: range, 1.1 to 5.7 gm.; average, 3.8 gm.

Weight of control fetuses on recovery from uterus: range, 1.4 to 5.3 gm.; average, 4.3 gm.

Microscopic study of the material reveals unilateral and bilateral destruction of the hemispheres with extensive thalamic and cerebellar injury in certain cases and section of the brain-stem at various levels above the medulla in others. No correlation could be demonstrated between post-operative survival, behavior or rate of growth and the size and location of the areas destroyed, provided the medulla remained uninjured.

The control experiments gave wholly negative results. It is interesting to note that no instances of hydrocephalus occurred following the injection of carbon ink into the brain ventricles (Weed⁶), although the presence of the ink is discernible in histological section in all cases.

⁶ Weed, L. H., *Contr. Embry. Carnegie Inst. Wash.*, 1920, No. 44, 425.