

supply and venous return. A preliminary report on this work forms the basis of this paper.

Male dogs, weighing 13 to 17 kg. were anesthetized by the intravenous injection of 200 mg. per kg. of sodium barbital. Coagulation was prevented by 30 mg. of heparin per kg. The volume flow apparatus was placed in the right iliac artery, thus measuring the blood which entered the right femoral artery as well as the chief collateral arterial supply to the right leg. The systemic blood pressure was taken from one of the carotid arteries. The right superficial femoral artery and the right common iliac vein were exposed to permit ligation.

A control record was taken of the blood flow through the iliac artery. Then the superficial femoral artery was ligated and a blood pressure cannula placed in its distal end. After the rate of blood flow then reached an apparent equilibrium, the right common iliac vein was occluded. This caused a sharp fall in the blood flow of from 10 to 15 cc. per minute (a drop of 20 to 30% from the preceding level), which was associated with the expected rise in the peripheral blood pressure of the right leg. To control this result, the occlusion of the common iliac vein was released and there followed a rapid rise in the blood flow of from 10 to 20 cc. per minute. This was accompanied by a fall in the peripheral blood pressure.

We have shown then, by direct measurement, that in a healthy extremity whose blood supply has been reduced by ligation of its main peripheral artery, ligation of its venous return proximal to the point of arterial ligation causes a sharp fall in the per minute flow of blood to the extremity.

4667

Embryo-Arsenic Tumors in Rats.

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Carrell¹ by the injection of chick embryo pulp in conjunction with dilute arsenious acid obtained in fowls a tumor of sarcomatous type. The result was the same whether the embryo was mixed before injection with the arsenious acid or the two injected simultaneously at different places. White² repeated these experiments and confirmed

¹ Carrell, A., *Compt. rend. Soc. de Biol.*, 1925, xciii, 1083.

² White, A. W. M., *J. Cancer Res.*, 1927, xi, 111.

the results. Askanazy³ transplanted rat embryo into grown rats and added Fowler's solution to their drinking water. In each of 2 series in which arsenic was used one rat was found to have a tumor of a malignant character. In one, the examination was made 13 and in the other 15 months after the embryo transplant. In the experiments of Carrell and of White the tumors developed as early as the ninth day and rather frequently in the fowls receiving the injections. From the results obtained in these investigations it appears that the response in the rat as compared with fowls is slower and less certain. The aim of our experiments was the investigation in rats of some of the variable factors, especially sites of injection and ages of embryos, which might explain slow and uncertain results.

Experiment I. The usual procedure with minor variations has been to draw much of the embryo into a syringe fitted with a short needle having 1 mm. lumen and at once to draw dilute arsenious acid to the 2 cc. mark. Of this suspension 0.5 to 1 cc. was injected. The time elapsing from removal of living embryo to injection was under 5 minutes. One of us (McJunkin) injected the testicles of 7 rats with a suspension of 3 mm. embryos in 1-150,000 arsenious acid. Six weeks later there was found in the testicle of one rat a minute opaque focus which microscopically consisted chiefly of cysts filled with cornified material. No trace of the embryo injection was found in the other testicles.

Experiment II. (a) 5 rats. Embryos measured 3 mm. and the arsenious acid was 1-1000. The suspension was injected into a ligated segment of one uterine horn. Forty days later the inner surface of the ligated uterus was smooth and contained none of the cells injected. (b) 5 rats. A duplicate of (a) except that embryos measured 10 mm. and the dilution of the arsenious acid was 1-25,000. After one month there was none of the transplanted embryo found either grossly or microscopically.

Experiment III. 11 rats. Embryos at term. Tissues tough and much of the aspirated part was liver, spleen and brain. Arsenious acid 1-25,000. Injection into the glutei muscles. Four months later the rats were killed and no evidence of the injected cells was found.

Experiment IV. 12 rats. Embryos 3 mm. Arsenious acid 1-50,000. 1 cc. of suspension injected into the right thigh with much of it passing into the loose intermuscular and subcutaneous tissue. The rats were killed after 122 days and tumors found in 2. Both were in the subcutaneous tissue over the muscles injected. The smaller (11x7x7 mm.) was a teratoma consisting chiefly of bone

³ Askanazy, M., *Verhandl. d. Deutsch. Path. Gesellschaft*, 1926, 182.

and cartilage and presenting little evidence of active growth. The larger (18x8x7) was a soft mass in the groin attached to the muscles beneath. Histologically the growth consisted of a single type of tissue and was made up of large and small glands lined with a single to several layers of columnar epithelium which was actively proliferating. In many places several mitoses were found in single high lens fields. Some of the glands were considerably distended. The cystadenoma had invaded a small lymph node attached to the edge of the mass but no distant metastases were found.

Experiment V. 10 rats. Embryos 10 mm. long. Arsenious acid 1-50,000. Six of the rats also received arsenic in their drinking water. Autopsy in 108 days. Of the 4 rats not given arsenic in the drinking water 3 showed teratomata consisting of bone, cartilage and epidermal cysts situated either between the muscles or in the subcutaneous tissue. Of the 6 getting arsenic in the drinking water 2 showed teratomata: 1 small and the other 42x9x7 mm. The larger one in addition to bone and cartilage contained many cysts distended with cornified material, sebaceous glands and hair follicles.

The uterus is unfavorable for the growth of embryonic cells treated with arsenic. Apparently the arsenic-treated embryonic tissue grows more readily in the subcutaneous and intermuscular tissue than in testicle. The best results were obtained by injecting into the intermuscular tissue young embryos mixed with a 1-50,000 arsenious acid. Of the 50 rats in only one was there a tumor of single cell type with changes suggesting malignancy. It was a cystadenoma. The rôle of the arsenic in the production of these tumors was not determined.

In a very recent report Begg and Cramer⁴ state that they have been unable to confirm the results obtained by Carrel and they are of the opinion that the experimental fowl tumors of Carrell, White and others may have been caused by a contamination of one or another of the materials inoculated with the virus of Rous sarcoma No. 1.

⁴ Begg, A. M., and Cramer, A., *The Lancet*, 1929, ccxvii, 697.