

strontium or calcium is eliminated with the bile out of a total excretion of about 25% in bile fistula animals in a period of about 3 days.

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Radiation Effects on Nervous System and Roentgen-Pigmentation of Goldfish (*Carassius auratus*).

CHARLES DAVISON AND FRIEDRICH ELLINGER.*

From the Neuropathological Laboratory and the Radiotherapy Department, Montefiore Hospital for Chronic Diseases, New York City.

A variety of stimuli has been employed for the study of the relationship between the nervous system and the chromatophores in fish. Smith¹ was the first to produce an eruption of corial melanophores in the goldfish. During studies concerning the suitability of the goldfish for problems of experimental radiation therapy,^{2, 3, 4} one of the authors (Ellinger) made some observations on the roentgen pigmentation of goldfish.⁵ This led to the assumption of a disturbance in the chromatomotoric nerve center in the medulla oblongata as a possible cause for the observed roentgen pigmentation. This pigmentation started on the head of the fish and spread caudally. To substantiate this assumption, a histopathologic study of the central nervous system of 10 goldfish (8 of which were irradiated) has been made.

Methods. The radiation factors were: 200 kv, 30 ma (mechanical rectification); filter (a) zero, H.V.L. 6 mm Al, corresponding to 0.233 mm Cu (intensity, 230-172 r/min); (b) 0.5 mm Cu and 1 mm Al, H.V.L. 1 mm Cu (intensity, 48 r/min). The distance was

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¹ Smith, G. M., *Am. J. Cancer*, 1932, **16**, 863.

² Ellinger, F., *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 527.

³ Ellinger, F., *Radiology*, 1940, **35**, 563.

⁴ Ellinger, F., and Gross, R., *Radiology*, 1941, **37**, 717.

⁵ Ellinger, F., *Proc. Soc. Exp. Biol. and Med.*, 1940, **45**, 148.

always 50 cm (target surface of water), and the field size 15 x 15 cm. The doses, ranging from 500 to 10,000 r (measured in air), have been given in one session. For each exposure 12 fish were placed in an open Petri dish, 15 cm in diameter, covered with a single layer of gauze fixed by an elastic. For further details of the technic of irradiation the reader is referred to a previous paper.³ All the brains of those animals were embedded in celloidin, sectioned and stained by the myelin sheath and cresyl violet methods.

Results. The histopathological examination in all instances revealed most pronounced pathological changes in the medulla oblongata of the irradiated central nervous system. Three typical protocols will suffice to describe the findings:

I. *Protocol No. 883.* Goldfish 59A irradiated with 1500 r/air, (minimal lethal dose³) developed pigmentation on the 11th day and the fish was killed on the 15th day following irradiation.

Microscopic Examination. In the myelin sheath preparation, some of the myelin fibers in the diencephalon, but especially those of the medulla oblongata, disclosed slight destruction. At the periphery of the medulla oblongata these had a slight spongy appearance (Fig. 1B). Swelling and destruction of myelin fibers were detected (Fig. 1B). A few of the axis cylinders were slightly swollen, had a corkscrew appearance and bulbous terminations. In the cresyl violet preparation, in the areas of demyelination, there was a slight increase in the glia nuclei (Fig. 2A) and some extravasation of the red blood cells. The nerve cells of the medulla oblongata were diminished in number and most of these were vacuolated (Fig. 2A) or appeared as shadow cells. Complete disintegration of nerve cells was also noted (Fig. 2A). There were a few agonal hemorrhages around the central canal and ventricles.

The spinal cord disclosed a slight swelling and fragmentation of the myelin sheaths especially at the periphery. In the cresyl violet preparation, the anterior horn cells showed vacuolization (Fig. 2B) or complete destruction.

II. *Protocol No. 879.* Goldfish 49A, irradiated with 1000 r/air (sublethal dose³). Pigmentation appeared on the 17th day and the fish was killed on the 28th day after irradiation.

Microscopic Examination. The vegetative nerve cells of the medulla oblongata were slightly decreased in number but rich in iron pigment. Some of these, however, showed minor changes, such as shrinkage, occasional chromatolysis and shadow-like appearance. There was no marked increase in the glia nuclei and no extensive proliferation of the vessels. In other sections throughout the central

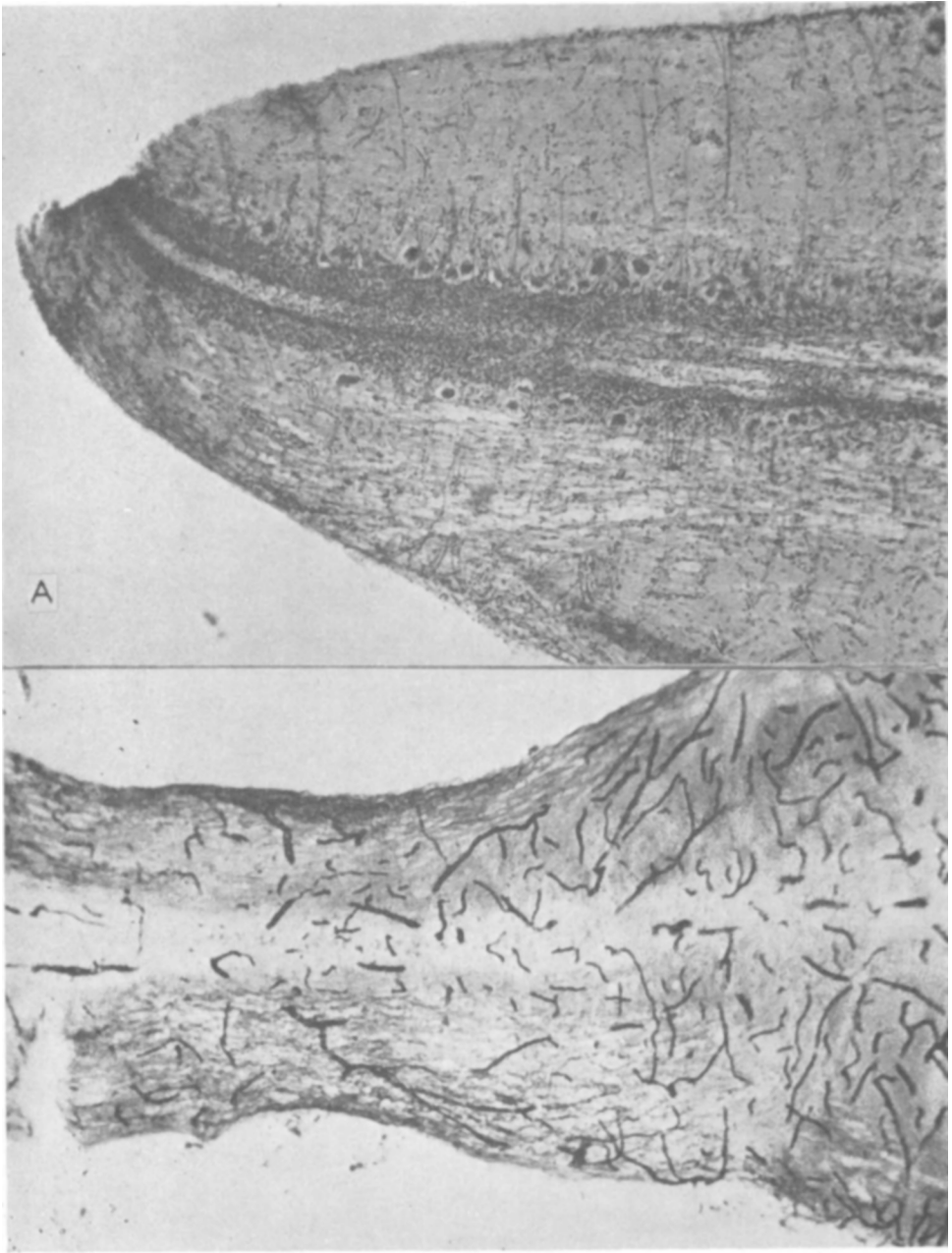


FIG. 1A.

Medulla oblongata of an unirradiated fish. Notice the normal number of nerve cells of the medulla oblongata.

FIG. 1B (Bottom).

Medulla oblongata of a fish irradiated with 1500 r. Note: Slight status spongiosus, swelling and destruction of the myelin sheaths at the periphery of the medulla. Disappearance of the characteristic nerve cells. Myelin sheath, $\times 100$.

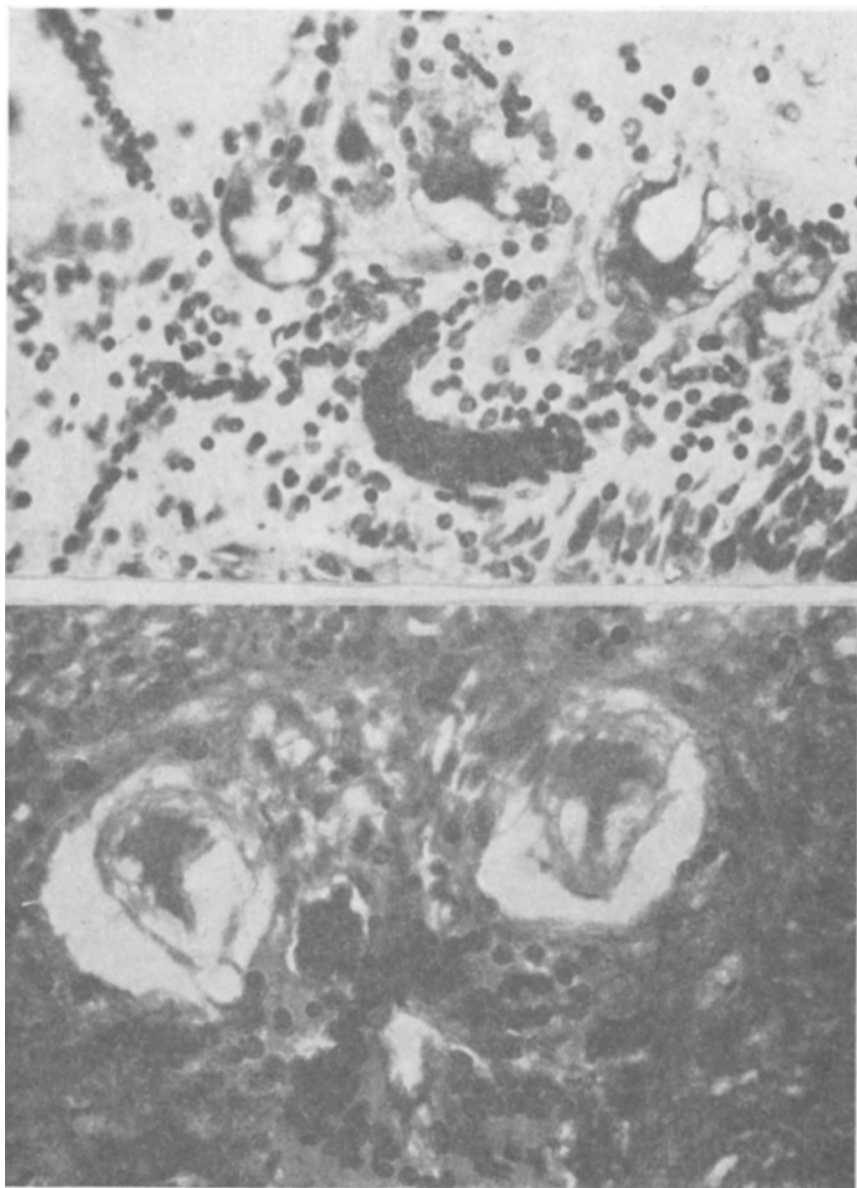


FIG. 2A. (Top).

Medulla oblongata of a fish irradiated with 1500r. Severe cell changes in the area of demyelination: Vacuolization of nerve cells, increase in glia nuclei and congestion of blood vessels.

FIG. 2B (Bottom).

Spinal cord of a fish irradiated with 1500r. Two large vacuolated nerve cells of the anterior horns. Cresyl violet, $\times 480$.

nervous system, occasional minor changes were found in some of the nerve cells. In one area of the archi cortex, there was some slight proliferation of the vessels.

III. *Protocol No. 848.* Goldfish 42A, irradiated with 800 r/air (minimal dose to produce pigmentation⁵). Slight pigmentation appeared on the 21st day and the fish was killed on the 50th day after irradiation.

Microscopic Examination. No abnormalities were noted in sections stained with the cresyl violet method. In the sections stained by the myelin sheath method there was found a slight demyelination of the fiber tracts at the periphery of the medulla oblongata.

Summary and Conclusions. Histological examination of the central nervous system of irradiated goldfish revealed: (1) Pronounced pathological changes in all instances, predominantly in the medulla oblongata and extending into the anterior horns of the spinal cord. (2) Alterations degree depending on the dose of roentgen rays. (3) Changes similar in character to those observed in the central nervous system of mammals. These consisted chiefly in demyelination of fiber tracts, destruction of ganglion cells and a more or less pronounced gliosis.

The fact that these changes are most pronounced in the medulla oblongata, where the chromatomotoric nerve center is located, seems to support the assumption that destruction of this center may be the cause of roentgen pigmentation in the goldfish. In the light of these observations the caudal spread of melanophores can easily be understood as a descending degeneration of the pigmentomotoric nerve fibers. This seems to agree with the experiments of Von Frisch,⁶ who produced in another fish (*Phoxinus laevis* L) pigmentation throughout the entire body after mechanical destruction of the pigmentomotoric center in the medulla oblongata. These observations, besides throwing some more light on the interesting interrelationship between central nervous system and pigmentation in fish, seem to be important as a further evidence for the equality in the effects of rays and mechanical stimuli on living matter.^{7, 8} Furthermore, the similarity of the character of the histological changes in the central nervous system after irradiation in goldfish and mammals seems to emphasize the suitability of the goldfish for purposes of experimental radiation therapy.

⁶ von Frisch, K., *Arch. f. ges. Physiol.*, 1911, **138**, 319.

⁷ Ellinger, F., *The Biologic Fundamentals of Radiation Therapy*, Elsevier Publishing Co., New York, 1941.

⁸ Ellinger, F., *The Problem of Recovery from Radiation Effects*, appears in *Radiology*.