

In the hind leg, the vascular resistance was either unchanged, or increased, after intraventricular histamine. Figure 4 shows an experiment where histamine produced a moderate increase in resistance. Decrease in resistance was not observed.

In three experiments on blood flow from the forepaw, acute bilateral adrenalectomy was performed prior to the intraventricular administration of histamine. Adrenalectomy did not prevent the pressor response nor the increase in vascular resistance.

Discussion. If the vascular changes in the forepaw are regarded as representative of the skin, the present experiments show that one part of the response to intraventricular histamine is vasoconstriction in the skin. The observations on hind legs indicate that such vasoconstriction is less pronounced, or absent, in skeletal muscle. The role of the adrenals in producing these responses was not investigated in detail, but the responses were not entirely dependent on the presence of the adrenals. This would suggest that there is a nervous pathway, independent of the adrenals, by which intraventricular histamine produces peripheral vasoconstriction. This interpretation is in agreement with the observation by TRENDLENBURG⁹ that spinal section prevented the blood pressure rise after intraventricular histamine. Obviously peripheral vasoconstriction is one factor responsible for the pressor effect of intraventricular histamine. Whether there are others in addition (e.g. increased cardiac output) is not known.

Although it seems clear that histamine in these experiments exerted a direct effect on the brain, this does not necessarily mean that histamine has direct effects on neurons. It could for instance be an action directly on brain blood vessels, as has been claimed for other vasoactive drugs⁷. That the action of intraventricular histamine is a 'true' drug effect is indicated by the observation that the chemically similar substance, methylhistamine (1-methyl-4(β -aminoethyl)-imidazole), is far less active⁸, and also by the inhibition of the pressor response by mepyramine⁸.

The effects of histamine on the brain may be of physiological significance in view of the fact that histamine is normally present in the brain⁶, where it is concentrated in those regions of the brain stem which are most likely to be reached by histamine administered into the ventricular system⁹⁻¹¹.

Zusammenfassung. An narkotisierten Katzen wurden der arterielle Blutdruck und der venöse Ausfluss aus der Vorderpfote oder aus dem Hinterbein registriert. Injektionen von Histamin in die Hirnventrikel bewirkten Erhöhung des Blutdruckes und Vasokonstriktion in der Vorderpfote. Im Hinterbein war die Vasokonstriktion weniger ausgesprochen. Auch nach Entfernung der Nebennieren war der Pressoreffekt vorhanden, woraus folgt, dass die periphere Vasokonstriktion für den durch intraventrikuläres Histamin hervorgerufenen Pressoreffekt verantwortlich ist.

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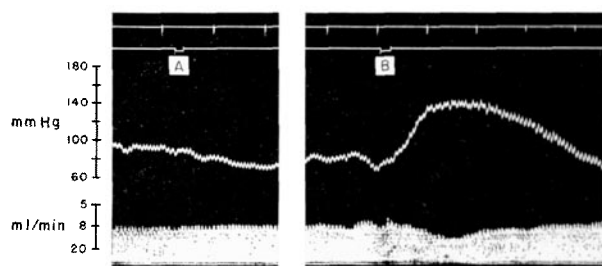


Fig. 4. The effect of intraventricular injection of histamine on arterial blood pressure and venous outflow from a skinned hind leg. Cat, 4.1 kg, chloralose anaesthesia. Records as in Figure 1. A: control injection (Tyrode solution). B: histamine injection (100 μ g).

⁷ Y. KANEKO, J. W. McCUBBIN, and I. H. PAGE, *Circulation Res.* 8, 1228 (1960).

⁸ G. W. HARRIS, D. JACOBSON, and G. KAHLSON, *Ciba Foundation Colloquia on Endocrinology* 4, 186 (1952).

⁹ H. M. ADAM, *Regional Neurochemistry* (Pergamon Press, 1961), p. 293.

¹⁰ M. DRASKOCI, W. FELDBERG, K. FLEISCHHAUER, and P. S. R. K. HARANATH, *J. Physiol.* 150, 50 (1960).

¹¹ This work was supported by the Swedish Medical Research Council (Project No. W 349). Rheomacrodex was kindly supplied by Pharmacia, Uppsala (Sweden).

Effect of Internal Radiophosphorus Irradiation on the Ovary of *Puntius sophore* Hamilton

Histological, histochemical and cytochemical studies on the fish gametes have been carried out extensively by various workers, but literature dealing with the effect of radiation on fish gametes is rather scanty. Effect of X-ray irradiation on fish gametes and developing embryo has been studied by some workers¹⁻³. Availability of radioisotopes from atomic piles has made it possible to study the effect of internal β - and γ -rays on various tissues. Internal exposure is usually more significant since radioactive substances may enter into the metabolism of the

organism and become preferentially deposited in particular organs rather than being uniformly distributed throughout the body. In the present study, an attempt has been made to study the effect of internal P^{32} radiation on the ovary of *Puntius sophore* Hamilton.

By the courtesy of the Fisheries Department of the Government of Rajasthan, *Puntius sophore* were collected from the local tanks and they were acclimatized to the

¹ R. RUGH and H. CLUGSTON, *Biol. Bull.* 108, 318 (1955).

² A. N. SOLBERG, *J. exp. Zool.* 78, 417 (1938).

³ A. N. SOLBERG, *J. exp. Zool.* 78, 441 (1938).

laboratory conditions for a week. Fifty fish, weighing 13.0 ± 2.0 g, were intraperitoneally injected with $20 \mu\text{C}$ of radiophosphorus. Controls were injected with physiological saline. To avoid loss due to leakage, the hypodermic needle was inserted under a lateral line scale of the caudal peduncle about half an inch posterior to the peritoneal cavity and passed through the hypaxial muscle into the peritoneal cavity; the muscle mass sealed the opening into the cavity when the needle was withdrawn. The fish were not fed during the tenure of the experiment. Carrier-free P^{32} was received from the Atomic Energy Establishment, Trombay, Bombay (India) in the form of H_3PO_4 in dilute HCl. Fish were sacrificed after 2, 5, 7, 15 days of irradiation. Ovaries were fixed in various fixatives and after routine paraffin embedding, sections were cut at 6μ and were stained with various techniques.

Puntius sophore is an annual breeding fish. In January, when the experiments were carried out, the ovaries were immature. According to the cytological appearance, all the ova were in the first two stages of development, i.e. (i) chromatin-nucleolus stage and (ii) early peri-nucleolus stage⁴. In the first stage, ova were very small in size, having a large nucleus and a thin layer of cytoplasm. In the next stage, the ova had a comparatively thick layer of cytoplasm and the nucleoli were generally peripheral in arrangement. The number of nucleoli varied from egg to egg, but normally one big and several small nucleoli were found.

The effect of irradiation was maximum on the seventh day; from then onwards there was a recovery and by the fifteenth day of irradiation eggs were restored to their normal condition. Irradiation resulted in the change of the shape of the ova. The margin became wavy, cytoplasm showed shrinkage, vacuolation became quite distinct and the follicular epithelium became hypertrophied. In a number of ova the nucleus was pushed to one side. In some oocytes the nucleus became very much enlarged and can be referred to as a giant nucleus. This could happen because of the cessation of mitotic division while growth is in progress. Since β -rays of radiophosphorus can penetrate a maximum of only a few millimetres of tissue,

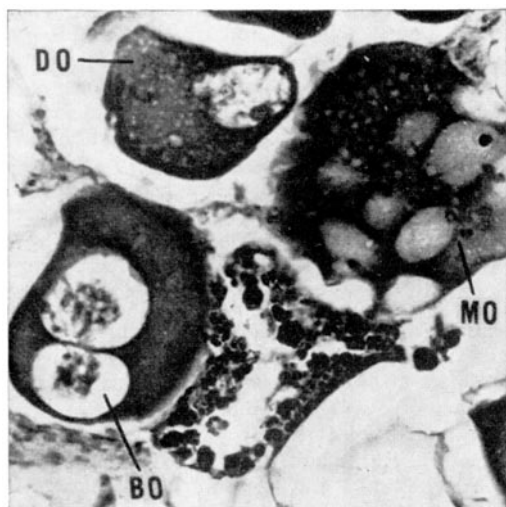
the peripheral and central oocytes show a difference in their reaction to radiation.

The most important observations after irradiation were the appearance of giant nuclei, binucleate oocytes and aggregation of ova which appeared as multinucleate oocyte. The appearance of binucleate oocyte may be due to many reasons. An ovum may complete an apparently normal division up to the complete telophase separation. At this time a cytoplasmic bridge between the two daughter cells remains and after a short while this widens. The two daughter cells thus combine across the bridge to form a binucleate cell. It could also happen that one ovum divides and gives rise to a binucleate oocyte without any attempt at telophase separation. The karyokinesis is as usual but plasmokinesis is suppressed, as a result of which cytoplasm may not get divided into two portions along with two daughter nuclei of the parent nucleus. The appearance of multinucleated aggregation of ova is due to the cytoplasmic fusion which takes place at the point of contact between cytoplasmic membranes of the adjacent ova. At the point of contact the membranes appear to merge into one, thereby creating a multinucleated aggregation of oocytes (Figure). Mononucleated, binucleated, and multinucleated giant cells have also been reported recently by MONTGOMERY et al.⁵ after Chang liver cells in tissue culture were irradiated with 600 R X-ray and 0.6 mc/cm^3 radiophosphorus, and by POMERAT et al.⁶ in tissue culture cells following γ -irradiation at 2000 R and 4000 R. These observations have, however, been made in tissue culture cells. As far as the authors are aware, such an aggregation of cells due to cytoplasmic fusion has not been reported in any animal tissue after irradiation. Such an appearance of binucleate and multinucleate oocytes has also not been observed in *Oryzias latipes* after irradiation with 32,000 R X-rays⁷. A detailed report of the observations will be published elsewhere⁸.

Zusammenfassung. Die innere Bestrahlung von *Puntius sophore* Hamilton mit P^{32} bewirkt Veränderung der Eiform. Die Eihülle wird gewellt, das Cytoplasma schrumpft, die Vakuolenbildung wird besonders deutlich, und in gewissen Fällen hypertrophiert das Follikularepithel. Es wurden Riesenkerne doppelkerniger Oocyten und Oocytenanhäufungen beobachtet.

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T.S. of the ovary of *Puntius sophore* Hamilton seven days after irradiation. Note the deformed oocyte (DO), binucleate oocyte (BO), and aggregation of oocytes which appears as multinucleate oocyte (MO). Bouin: Hematoxylin-eosin, $\times 450$.

⁴ K. YAMAMOTO, J. Fac. Sci. Hokkaido Univ. 12, 362 (1956).

⁵ P. O. B. MONTGOMERY, D. KARNEY, R. C. REYNOLDS, and D. MCCLENDON, Am. J. Path. 14, 724 (1964).

⁶ C. M. POMERAT, S. P. KENT, and L. C. LOGIE, Z. Zellforsch. 47, 175 (1957).

⁷ P. N. SRIVASTAVA, Acta anat., in press.

⁸ The authors are indebted to the Rockefeller Foundation (USA) and the University Grants Commission of India for funds for the establishment of the Radiation Biology Laboratory in this University. Thanks are also due to the Ford Foundation (USA) for generous grants for the project *Endocrinological and Radiation-Biological Studies on the Physiology of Reproduction*, and to Professor L. S. RAMASWAMI for various suggestions and facilities in the Department.