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Nuclear Changes Following Intravenous Injection of Various Solutions.*

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Opinions differ as to whether intranuclear inclusions are pathognomonic of virus diseases. Thus, Cole and Kuttner[1] expressed the view that when typical intranuclear inclusions are found, the presence of a filterable virus is to be assumed unless its absence can be proved experimentally, while Cowdry[2] stated that the presence of intranuclear inclusions should not be taken at face value as indicating the action of some filterable virus. Cowdry[3] also entertained the possibility that the inclusions may be produced artificially without viruses. Heinbecker and O'Leary[4] described the appearance of bodies simulating intranuclear inclusions in nerve cells after electrical stimulation[5] and Davenport, Ranson and Terwilliger[6] produced similar structures by immersion of ganglia in hypertonic salt solutions.

Cats were injected through the femoral vein, under ether anesthesia, with glucose, sodium chloride, sodium bicarbonate, distilled water, or Salyrgan. At various intervals following the injections, the animals were killed by exsanguination, and material was fixed in Zenker's fluid containing 5% acetic acid, and stained with hematoxylin and eosin, erythrosin and azur I.

(a) *Glucose.* When 60 cc. of 50% glucose per kilo of body weight was injected slowly during 1 hour and the animal killed immediately, marked changes were observed in the nuclei of spinal ganglion, anterior horn and Purkinje cells. The nuclear chromatin, dispersed in reticular fashion in the cells of normal controls, formed

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[1] Cole, R., and Kuttner, A. G., *J. Exp. Med.*, 1926, **44**, 855.

[2] Cowdry, E. V., *Arch. Path.*, 1930, **10**, 23.

[3] Cowdry, E. V., in Rivers' "Filterable Viruses." Baltimore, Williams and Wilkins, 1928, 428.

[4] Heinbecker, P., and O'Leary, J. L., *Anat. Rec.*, 1930, **45**, 219.

[5] In a personal communication Heinbecker and O'Leary express doubt as to the validity of their original interpretation and are inclined to attribute their results to evaporation occurring during *in vitro* stimulation.

[6] Davenport, H. A., Ranson, S. W., and Terwilliger, E. H., *Anat. Rec.*, 1931, **48**, 251.

a compact mass about the nucleolus and was separated from the nuclear membrane by a halo. The nucleolus was noticeably vacuolated and swollen. The only cytoplasmic alteration noted was in the spinal ganglion cells; here a varying degree of central chromatolysis was apparent. When animals of like weight were killed 3 hours after the injection of a similar quantity of glucose, the nuclear change was much less obvious, indicating a return to normal.

(b) *Sodium chloride.* 150 cc. of 30% sodium chloride was injected over a period of 45 minutes and the 3 animals killed immediately. Purkinje, anterior horn and spinal ganglion cells showed changes similar to those seen in glucose injected animals; but the chromatin was more acidophilic and less concentrated about the nucleolus.

(c) *Sodium bicarbonate.* After injection into 3 animals of 50 cc. of a 20% solution of sodium bicarbonate, masses were discovered in the nuclei of spinal ganglion cells very similar to those observed in glucose injected animals.

(d) *Distilled water.* In 4 animals killed following the injection of from 300 to 400 cc. of distilled water in 1 hour and 15 minutes, intranuclear bodies were observed which simulated those described by Covell[7] in the nerve cells of acute experimental poliomyelitis. The nuclei of the water injected animals, in contrast to those containing Covell's inclusions, showed no evidence of margination of basophilic chromatin, or disappearance or conversion of acidophilic chromatin.

(e) *Salyrgan.* This pronounced diuretic was injected intramuscularly into 6 cats in ½ cc. amounts daily for 4 days, and intravenously into 4 cats in 1 cc. doses daily for 5 days. The animals were sacrificed at graded intervals. Nuclear changes were observed in all of the first group, but in none of the second, nor in 35 control cats not subjected to this treatment but employed in the laboratory for other experiments. They occurred in the pancreas of 6, kidneys of 3, testes of 2, and adrenals of 2; were absent in the nervous system and were not noted in these organs after treatment with glucose, sodium chloride, bicarbonate or distilled water. The nuclear alterations were rather localized, but so conspicuous in these 6 cats that they were seen almost immediately. They presented considerable diversity. Some of them were characterized by the margination of basophilic chromatin on the nuclear membrane and the appearance of acidophilic bodies separated from the nuclear mem-

[7] Covell, W. P., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 927.

brane by a halo. The nuclei were hypertrophied to a maximum of twice their normal diameter. There was some accompanying cytoplasmic degeneration, mitotic division and regeneration of acini. The nuclear alterations persisted as long as a month after the last injection.

It is not claimed that any of the changes are identical with those caused by viruses though they resemble them in certain particulars. The experiments do show, however, that nuclear alterations something like those previously reported *in vitro* may be produced *in vivo* by relatively mild procedures which do not kill the animals. They also raise several questions for further study.

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Bronchodilator Activity of Tyramine and its N-Methyl Derivatives.*

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There are few reported quantitative comparisons of the relative pressor and bronchodilator effects of chemicals in the epinephrine series, and it is an open question whether certain structural changes in such compounds may result in a relative increase of bronchodilator activity without a corresponding increase in pressor activity.

Tyramine, an extensively studied compound of this type, is a comparatively good pressor agent, but Jackson[1] reports that it does not exert any bronchodilator activity. He found, however, that hordenine, the N-dimethyl derivative of tyramine, dilates the bronchi, although it exerts considerably less pressor activity. Thus, with these compounds there seems to be a differentiation between pressor and bronchodilator effects which is compatible with the evidence of Cannon and Rosenblueth[2] that the chemical mediators involved in the transmission of sympathetic stimulation to the bronchi and the blood vessels are not the same.

In the present work, a comparative study of the pressor and bronchodilator activities of the following compounds was made upon a series of 6 dogs and 4 cats, following technique already described.[3]

* Supported in part by the Christine Breon Fund for Medical Research.

[1] Jackson, D. E., *J. Pharm. and Exp. Therap.*, 1913, **5**, 479.

[2] Cannon, W. B., and Rosenblueth, A., *Am. J. Physiol.*, 1933, **104**, 557.

[3] Alles, G. A., and Prinzmetal, M., *J. Pharm. and Exp. Ther.*, 1933, **48**, 161.