It seems that when the quantity of the catalyst, iron, falls below the normal, the biologic system attempts to compensate for the dangers of lessened oxidative activity by an increase in the content of the more vigorous and the more highly efficient catalyst, copper. The body needs little copper under normal conditions and the rise under abnormal conditions need not be very high, since a small quantity of this element goes a long way in the mechanism of catalysis.

In the event of hypoferronemia the observed rise in the copper content of the blood leads to the conclusion that the biologic organism mobilizes copper, which is poured into the blood from the storehouses. The copper thus mobilized not only acts in the capacity of a stimulator of hematopoietic activity, but also in the capacity of an emergency oxidative catalyst.

8835 P

Visualization of Preparalytic Lesions of Poliomyelitis by Intravital Staining.*

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The gradual descent of poliomyelitic infection, after intranasal inoculation, through the olfactory tract, the basal ganglia, midbrain, pons and medulla to the spinal cord was demonstrated in experimental animals (monkeys) by Faber and Gebhardt,[1] using the method of recovering virus from bits of nervous tissue excised on successive days of the preparalytic period. Evidence was presented by Faber[2] that the infection in man may follow a similar pathway. Since this method of recovering virus permits only a rough localization, other means were sought to obtain a more precise definition. Evans and MacCurdy[3] reported successful vital staining of poliomyelitic lesions in monkeys, but failed to state the dye used or the period of infection when the animals were examined. McClellan and Goodpasture[4] were able, by means of intravital staining with

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1 Faber, H. K., and Gebhardt, L. P., *J. Exp. Med.*, 1933, **57**, 933.

2 Faber, H. K., *Medicine*, 1933, **12**, 83.

3 Evans, H. M., and MacCurdy, J. T., *Berl. klin. Wchnschr.*, 1912, **49**, 1695.

4 McClellan, R. H., and Goodpasture, E. W., *J. Med. Res.*, 1924, **44**, 201.

trypan blue and subsequent clearing of the tissues, to visualize the lesions of another axon-conducted viral disease, herpetic encephalitis. Their method has been used in the present study of the sites and character of the lesions in the preparalytic stage of experimental poliomyelitis after intranasal inoculation carried out by the technic of Schultz and Gebhardt.[5]†

Results in 3 rhesus monkeys are here reported: 1. a control; 2. an animal killed 3 days after inoculation; 3. an animal killed 6 days after inoculation, before paralysis or weakness occurred.

In the control, which was given no inoculation with virus but received trypan blue in the same manner as the inoculated animals, there is no visible staining of the nervous tissues proper. The dura, velum interpositum and choroid plexuses are deeply stained, while the leptomeninges are faintly stained. The smaller arteries and veins are inconspicuous and there is no evidence of capillary dilatation.

In the 3-day animal, the appearance of the tissues is similar except in the diencephalon, where the smaller blood vessels appear dilated, giving this area a streaked and dotted appearance; and just ventral to the main body of the thalamus and dorsal to the corpus mammillare, somewhat lateral to the midline, there is an oval area about 3 by 5 mm. in diameter which is stained blue. On inspection with a hand lens, minute bluish specks can be seen in the thalamus itself.

In the 6-day animal, in which no poliomyelitic signs or symptoms had been noted, the appearance of the nervous tissues presents a striking contrast with that of the control and of the 3-day animal. Within the brainstem are many large rounded and banded areas of deep blue, in which the corpora mammillaria, the nuclei of the thalamus, the midbrain (red nucleus), the ventral portion of the pons and several portions of the medulla are conspicuous. Much of the striate body escapes staining but some is found in the head of the caudate nucleus and in the putamen. The olfactory bulbs are completely unstained, as is the cerebellum. In the cortex scattered small areas of fairly intense staining are found in the precentral region, in the hippocampal gyrus and in the parolfactory area. The gray matter of the spinal cord also shows good blue staining, particularly the anterior horns and the posteromedial portion.

[5] Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1010.

† The monkeys were inoculated for us by Mr. L. P. Gebhardt at the laboratories of the Department of Bacteriology of Stanford University through the kindness of the Head of the Department, Professor E. W. Schultz.

Under the microscope the localizations of the stain are found to be of two sorts. In the brain stem, the macroscopically visible blue color is due to an accumulation of dye in the walls (especially the endothelial nuclei), and to some small extent in the plasma, of the capillaries. The number of these which are open is enormously greater than in the control. No perivascular, pericellular or meningeal invasion with wandering cells has occurred, except in the medulla where some small pericellular infiltrates are visible. The same phenomenon is found in the spinal cord. In addition, some, but not more than half, of the anterior and posterior horn cells are found to be stained blue, usually with the dye collected in granules at or near the periphery and in some cases within the nucleus. The distribution of the stained cells is curiously uneven: it is neither symmetrical nor uniform at different levels; moreover stained and unstained cells are to be found side by side in the same section. Although no nerve-cell staining is seen outside the spinal cord, the microscopic appearance of some of the cells in the brainstem, particularly the medulla, is not entirely normal. The experiments indicate that the earliest secondary reaction in the central nervous system to invasion by virus is simple hyperemia, beginning about the third day and reaching a high degree by the sixth day of the incubationary period. This reaction precedes general invasion of the pericellular, perivascular and meningeal spaces by wandering cells of the microglial, leucocytic and lymphocytic series. It may, moreover, be completely absent, as in the olfactory bulbs, where virus first appears and is known to be continuously present in high concentration throughout the period of invasion.

8836 C

Effect of Low Levels of Fluorine Intake on Bones and Teeth.

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A large number of investigations with different species are in agreement that the toxicity of fluorine, as measured by growth and certain physical and chemical changes in the bones, varies with the form of fluorine fed. A recent study by Smith and Leverton[1] with rats, while substantiating this conclusion as regards levels necessary

[1] Smith, M. C., and Leverton, R. M., *Ind. Eng. Chem.*, 1934, **26**, 791.