flow of the virus from the perivascular spaces of the central nervous system, into the blood and thence to the organs.

## 8212 P

## "Mottling of Enamel" Effected by a Single Fluorine Dose.

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In a study of the minimal effective dosage of fluorine, as determined by various biological criteria, one of the authors[1] observed "fluorine-rickets" as a significant response to very small amounts of fluorine. The biological effectiveness of even smaller amounts of this element has been established by the discovery of the "mottling of enamel."[2] Until now, mottling of enamel has been studied only on frequently repeated fluorine administration. The question arose whether it can also be produced by a short "fluorine shock."

The following is a report on a preliminary series of experiments on 20 young rats. In the first experiment (Table I) doses from 9 to

TABLE I.
Effect of Fluorine Administration on Incisors of Recently Weaned Rats.

| No. | Wt at start gm. | Wt on 11th day gm. | Administered mg. F per kg. b. w. | Enamel Spot Day of Appearance | Disappearance |
|---|---|---|---|---|---|
| 1 | 31 | 25 | $CaF_2$ 37 | — | — |
| 2 | 29 | 30 | NaF 30 | — | — |
| 3 | 23 | 32 | $CaF_2$ 19 | — | — |
| 4 | 23 | 34 | $CaF_2$ 19 | — | — |
| 5 | 35 | 38 | NaF 17 | 12 | 24 |
| 6 | 30 | 38 | NaF 15 | — | — |
| 7 | 36 | 39 | $CaF_2$ 10 | — | — |
| 8 | 28 | 29 | $CaF_2$ 9 | 9 | 21 |
| 9 | 35 | 36 | $CaF_2$ 9 | 9 | 24 |
| 10 | 31 | 37 | NaF 7 | — | — |

37 mg. fluorine per kilo of b.w. were administered through a stomach tube to just weaned albino rats weighing from 21 to 35 gm. (solutions of 0.625% or less NaF and a finely dispersed sol of 0.375% or less $CaF_2$[3]). Such a single dose was able to produce a definite alteration on the enamel. In 3 out of 10 animals, a sharply

[1] Loewe, S., *Schweizer med. Ws.*, 1934, **64**, 1177.

[2] Smith, M. C., and Leverton, R. M., *Ind. Eng. Chem.*, 1934, **26**, 792; De Eds, F., *Medicine*, 1933, **12**, 1.

[3] Bachmann, W., D. R. P., 485,052.

limited milky white spot of about 1-2 mm. in diameter, round or oval, appeared on the frontal surface of one lower incisor between the 12th and 14th day following fluorine ingestion. First, the spot was seen only at the base of the incisor after slight retraction of the gum. Later, it moved slowly along the tooth and finally between the 21st and 24th day it disappeared at the cutting surface. The incidence of positive results is not increased by increasing the fluorine dosage, nor does it depend on the degree of general effects of fluorine shown by the growth curve (*cf.*, animal No. 1 vs. animal No. 6). Nor is there an obvious difference between the 2 compounds used. Thus, fluorine is but one of several factors capable of impairing enamel development. In the range of the dosage studied the behavior of these other coefficients (*e. g.*, vitamin D, food calcium, food fluorine, natural irradiation) must be decisive for the issue.

In another group, single doses of 20 or 30 mg. F per kg. as NaF and 10 or 30 mg. F per kg. as $CaF_2$ were administered to 10 albino rats of 40 to 116 gm. No lesions were detectable; thus, age is a further factor controlling fluorine action on enamel formation.

None of the coefficients mentioned above deviated sufficiently from its physiological range as to produce mottling of enamel by itself without fluorine administration. A careful observation of 40 control animals from the age of weaning showed no spontaneous mottling.

In spite of the irregularity of the results, the experiments demonstrate that a short "fluorine shock" is sufficient to evoke irreversible changes in enamel, presumably by inhibiting a phosphatase action necessary for the process of calcification. The effects of intermittent subcutaneous injections of fluorine on rats, recently reported by M. C. Smith,[4] point in the same direction: Stripes of defective calcification alternating with normal enamel areas are produced by this interrupted chronic treatment. This fluorine shock permits one to mark by an indelible stamp on the tooth surface the date of fluorine administration.

Acute and chronic fluorine action differ only in the extensiveness of the effect and in the effectiveness of the dosage. Single administration causes a single lesion, repeated administration produces mottling. The minimal single dose that may possibly produce an effect is yet to be determined, the very low daily dose invariably effective in chronic experiments fails to produce macroscopically detectable in-

[4] Smith, M. C., *A. J. P. H.*, 1935, **25**, 698.

juries, if administered only once. The larger single dose necessary to produce enamel injury, also causes general effects. The high selectivity (*i. e.,* the absence of other detectable symptoms) of the enamel mottling action in chronic fluorine administration is not encountered in acute experiments.

## 8213 P

### Histological Changes Observed in the Intestinal Wall Following Simple Mechanical Obstruction in Rabbits.

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Due to the almost miraculous recovery of the intestinal wall in cases of ileus after surgical relief of mechanical obstruction as well as the recovery of the intestinal wall in certain forms of mesenteric thrombosis after simple enterostomy, this investigation was undertaken to demonstrate what changes, if any, may occur following simple mechanical obstruction in the various tissues of the intestinal wall.

Simple mechanical ileus of the terminal ileum was produced in 11 rabbits. At varying postoperative intervals (12, 24, 36, 48, and 72 hours), the rabbits were sacrificed, and sections from 3 different levels of the ileum were removed—1 cm., 10 cm., and 20 cm. proximal to the obstructing ligature. Sufficient intestine was removed from each level to obtain 10 specimens for immediate fixation, making a total of 30 gross sections from each animal. For controls, sections were removed also from a normal rabbit corresponding to the different levels mentioned above.

Gross lesions observed postoperatively were: After 12 hours, ileum proximal to the obstruction was reddish in color and on section some blood was seen in the lumen. 24 hours: Slight distention of the terminal ileum; lumen filled with liquid intestinal contents; very few gross changes were evident. 36 hours: Distention of the terminal ileum; few ecchymotic spots in the mucous membrane; intestines filled with liquid feces. 48 hours: Marked distention of ileum with considerable congestion; contents yellow watery fluid; ecchymotic areas in mucosa near the obstruction. 72 hours: Marked distention, especially just above the obstruction, and containing much yellowish-red fluid, with marked congestion of the