shown[3] that sulfapyridine administered to normal mice, as in the above experiments, was completely eliminated from blood and urine within 72 hours after the last dose of the drug. Yet mice were immune to reinfection as long as 8 days after the last dose of sulfapyridine.

The second possibility was eliminated by the following experiment. Twenty-five normal mice received 20 mg doses of sulfapyridine as described previously; 24 hours after the last dose of the drug, they were infected with 100 lethal doses of Type I pneumococcus. The administration of sulfapyridine did not increase the resistance of these animals for they were all dead within 36 hours, as were 12 untreated controls infected similarly.

These data justify the conclusion that mice that have recovered from infection with Type I pneumococcus, through treatment with sulfapyridine, are immune to reinfection for a limited time. Our experiments have confirmed Whitby's observation. Since Long has not presented his experimental data, it is impossible to explain the apparent discrepancy between his conclusion and that warranted by Whitby's results and our own. The discrepancy could be explained if one assumed that Long reinfected his mice later than 14 days after the initial infection. In this event our data would support his conclusion.

Summary. Mice recovering from a Type I pneumococcal infection, as a result of sulfapyridine therapy, are generally immune to reinfection for at least 14 days after the initial infection. This immunity is lost within 28 days.

10588 P

Effect of Artificially Induced Hyperpyrexia on Tooth Structure of the Rabbit.

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The increasing therapeutic importance of artificially induced fever raises the question of its effect on developing tooth structure. Damage to the enamel by infections accompanied by high fever during the

[3] Schmidt, L. H., and Hughes, H. B., results to be published.

period of tooth formation has been recognized clinically for many years. It is evidenced as a hypoplastic condition with superficial pits and grooves, often markedly disfiguring the anterior teeth. Detrimental effects in the dentin would be an internal dystrophy and would escape clinical notice but might well be expected under conditions which would affect the enamel.

Normal dentin is a homogeneously calcified tissue produced by the dental pulp. It is laid down around the periphery of the pulp in periodic increments as an organic matrix which is subsequently calcified to a bone-like consistency. Unlike bone, dentin once formed is not subject to further physiologic change to any marked degree, and hence it affords a permanent record of any variations in the calcification process. The dentin of the continuously growing teeth of the rabbit, therefore, affords a suitable medium for the recording of any effect which might be caused by artificially induced hyperpyrexia.

In the same series of rabbits used for observations on other tissues by the Departments of Medicine and Pathology and reported elsewhere,[1, 2, 3] histologic studies were made on thin ground sections cut longitudinally through the incisor teeth. Schour and Hoffman,[4] reporting on dentin deposition in growing mammalian teeth, state that it is laid down at the approximate rate of 16 micra in 24 hours. Their work included, among other animals, a series of rabbits. Thus, any periodic interference with calcification would be characterized by the presence in the dentin of alternate layers of normal and abnormal tissue, the latter coinciding with the periods of disturbance.

Sections of the incisor dentin of the rabbits, previously intermittently fevered at 106.5° to 108.5°F by both radiotherm and Kettering hypertherm and allowed definite intervening recovery periods, demonstrated linear striations characterized by the presence of numerous uncalcified spaces resulting from a lack of fusion of the individual calcification globules. These areas alternated with more homogeneously calcified tissue and corresponded in number with the number of fevering periods of the animal in question. The degree of interference with calcification, as judged by the size and frequency of the uncalcified spaces, was directly related to the intensity of the induced fever during the early periods of fevering. Subsequently the disturbance became less marked.

Poorly calcified tooth tissue, both enamel and dentin, offers less

1 v. Haam, E., and Frost, T. T., PROC. SOC. EXP. BIOL. AND MED., 1939,

2 Weaver, H. M., in press.

3 Hargraves, M. M., Doan, C. A., and Kester, L., in press.

4 Schour, I., and Hoffman, M. M., *J. D. Res.*, 1935, **15**, 161.

resistance to the progress of dental caries than does a well calcified structure. In addition, the presence of interglobular spaces in the dentin increases the pain incident to the preparation of cavities for dental restorations. Thus the importance of efforts to reduce or eliminate this undesirable effect of artificially induced fever on tooth structure becomes quite apparent.

While the use of sodium fluoride injections and vital staining with alizarine have already provided means of inquiring into some of the biological processes associated with dental calcifications, controlled artificial fever would seem to offer another and somewhat different approach to the study of such physiological phenomena.

Further work, using the albino rat as the subject of artificially induced hyperpyrexia, is being carried on in order to observe the effects over a wider range and duration of temperatures, and in an attempt to lessen the undesirable effects by a preliminary increase of the available supply of materials concerned in the calcification process.

10589 P

Pathogenesis of Hemorrhage in Artificially Induced Fever.

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Every therapeutic agent of value has its potential dangers and hyperpyrexia is no exception to this general rule. Two of the most constant pathologic findings following induced fever in experimental animals and in human subjects are hemorrhage and acute parenchymatous degeneration of the liver. Hartman[1] has pointed out the similarity of these pathologic changes to those encountered following prolonged mild asphyxia, and has demonstrated that anoxia is a common accompaniment of artificially induced fever.

The mechanism underlying the hemorrhage following artificially induced fever has never been entirely satisfactorily explained. In the present study selected cellular and humoral factors important in the complex phenomenon of blood coagulation have been determined under experimental conditions in rabbits and during fever therapy in human patients. Total platelet counts have been correlated with

[1] Hartman, F. W., *J. Am. Med. Assn.*, 1937, **109**, 2116.