

ticles. Exhaustive washing of these endotoxin-treated particles with non-pyrogenic saline did not remove the fever producing substances.

1. Haskins, W. T., Landy, M., Milner, K. C., Ribb, E., *J. Exp. Med.*, 1961, v114, 665.
2. Braude, A. I., McConnell, J., Douglas, H., *J. Clin. Invest.*, 1960, v39, 1266.
3. Hanna, E. E., Watson, D. W., *Bact. Proc.*, 1963, p56.
4. Sbarra, A. J., Karnovsky, M. L., *J. Biol. Chem.*, 1959, v234, 1355.
5. Strauss, B. S., Stetson, C. A., *J. Exp. Med.*, 1960, v112, 653.

6. Oren, R., Farnham, A. E., Saito, K., Milofsky, E., Karnovsky, M. L., *J. Cell Biol.*, 1963, v17, 487.
7. Sbarra, A. J., Shirley, W., *J. Bact.*, 1963, v86, 259.
8. Dannenberg, A. M., Jr., Walter, P. C., Kapral, F. A., *J. Immunol.*, 1963, v90, 448.
9. Cohn, Z. A., Morse, S. I., *J. Exp. Med.*, 1960, v111, 689.
10. Wallach, D. F. H., Karnovsky, M. L., *Proc. 1st Int. Biophysics Congress, Stockholm*, 1961, p43.
11. Weissman, G., Thomas, L., *Symposium on Bacterial Endotoxins*, 1963, Sept. 4-6, Inst. of Microbiology, Rutgers Univ., New Brunswick, N. J.

Received March 30, 1964. P.S.E.B.M., 1964, v116.

Effect of Cortisone, Amputation, and Food Restriction on Growth of Rat Maxillary Incisors.* (29353)

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We previously observed that cortisone produced an acceleration in the growth (eruption) rate of maxillary incisors in intact, adrenalectomized, and thyro-adrenalectomized rats, concomitant with a reduction in body weight(1,2). The mechanism of this stimulation was not explained and required further investigation. Numerous observations indicate that administration of cortisone in the rat results in a decrease in food consumption(3). Since we had not obtained data on pair fed controls in the previous experiments, it seemed advisable to determine what effect, if any, a decrease in food consumption would have on the eruption rate of the incisor.

It has been reported(4) that factors which increase the attrition rate of rat incisors (lack of sensory innervation, apical amputation, artificial abrasion or hard diet) will increase their growth rate. When the incisor is maintained out of occlusal contact by periodic

cutting, its rate of growth is accelerated thereby expressing its true or potential growth rate(5). Although this unrestricted eruption rate has been studied under a variety of experimental conditions(5), we were unable to discover any reports of the effects of cortisone on this rate. The stimulation of this unimpeded eruption rate following cortisone administration would seem to provide indications of a direct effect on the mechanism controlling eruption.

Procedures. Food consistency and restriction. Sixteen female, Sprague-Dawley rats, age 40 days, were housed in metal cages with sawdust bedding and maintained on Purina dog chow pellets and tap water *ad libitum*, for a control period of 3 weeks. Following this period, 6 animals were moved into separate plastic cages, without sawdust, and fed finely ground chow instead of pellets, in an attempt to restrict the number of environmental objects on which the rats could gnaw. Cages were cleaned daily, food and water provided *ad libitum* and amount of daily food consumption recorded. This regime was followed for 4 weeks. At the end of the fourth week the amount of food daily provided was arbitrarily restricted to

* Supported in part by U.S.P.H.S. grant.

Cortisone (Cortone Acetate) generously supplied by Merck, Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia, Pa.

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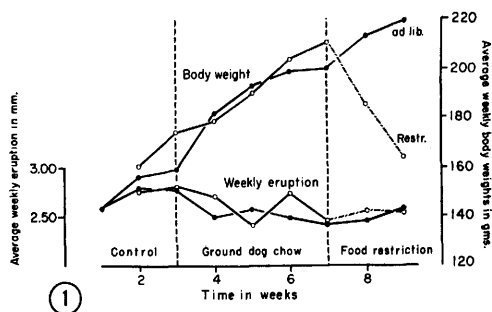


FIG. 1. Effect of food consistency and restriction on incisor eruption rates of female rats. Circles during weeks 3 to 7 represent averages of rats on soft food, *ad libitum* and restricted from objects on which to gnaw.

25% of that previously consumed and observations continued for another 2 weeks. At this time 4 of the animals died during a severe decrease in room temperature, due to a heating system failure thus terminating the experiment. Eruption rates of maxillary incisors were determined weekly by a method previously described(4,6).

Periodic amputation. Twenty-seven male Sprague-Dawley rats, age 250 days (400-450 g), were divided into 3 groups. Ten rats were anesthetized with Nembutal (Abbott) (40 mg/kg) and the left maxillary incisor cut off at the gingival crest (apical amputation) every 3 to 4 days with a dental drill and cutting disk. Group 2 consisted of 9 rats which were similarly treated and in addition received 2.5 mg cortisone daily, beginning on the day of first amputation and daily thereafter for the duration of experiment (10 amputations). Injections were administered subcutaneously. The rats of the first group received daily injections of a comparable volume of saline. The third group of 8 rats was handled and anesthetized in a manner similar to those of the first 2 groups but were not subjected to the apical amputations (normal occlusion). In addition, the growth rates of 11 normal males of the same age, were determined once a week, during the same period for a period of 4 weeks, to evaluate possible effects of the bi-weekly anesthesia and manipulative procedures.

The unimpeded eruption rates were determined each time the amputations were performed by a method similar to that pre-

viously described(5). Measurements were averaged for the experimental period and analyzed using the t-test.

Results. Food consistency and restriction. The eruption rates of the incisors of the 2 groups (Fig. 1) were essentially identical during the control period. During the period when food pellets were replaced by ground meal, eruption rates showed some variation. However, average rates for the 4 week period were the same for both groups (2.57 mm vs 2.50 mm/week for controls). A restriction of food intake to 25% of that previously consumed had no effect on eruption rate, despite a severe loss in body weight (55 g or a 25% reduction below that of *ad libitum* controls). It is unfortunate that the experiment terminated somewhat prematurely; however, the 50 g loss in body weight corresponds to a similar reduction, for corresponding period, in cortisone-treated, thyro-adrenalectomized rats(2), which was accompanied by an acceleration in the incisor eruption rate.

Cortisone and periodic amputation. Removal of the left maxillary incisor from occlusal contact, by periodic cutting, resulted in a marked increase in the eruption rate to almost double ($0.76 \pm 0.08 \pm$ mm/day) the rate of incisors in normal occlusion (0.40 mm/day) (Fig. 2), whereas the eruption rate of the right incisor decreased slightly (0.34 mm/day) during this period. Cortisone administration produced an additional increase in this accelerated rate (0.92 ± 0.13 mm/day) and a slight increase in the rate of the right incisor in occlusal contact (0.40 mm/day), restoring this rate to normal. The difference between the unimpeded eruption rates for the two groups was highly significant ($P=0.1\%$). The average daily eruption rate of 11 normal males, measured weekly during the same period, was 0.41 mm/day. This average closely approximates the average for the controls subjected to the twice weekly anesthesia, marking, and handling but not the apical incisor amputations.

Discussion. The lack of an effect of the soft consistency diet on the eruption rate of

‡ Standard deviation.

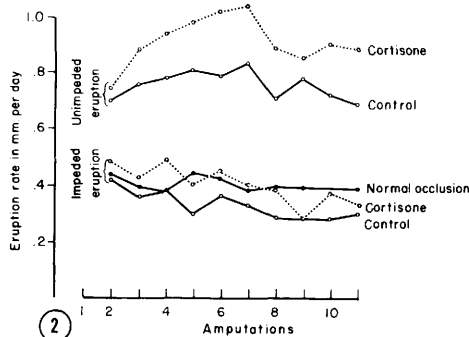


FIG. 2. Effect of cortisone on unimpeded eruption rates of male rats. Unimpeded eruption indicates average eruption rates of left incisors, following release from occlusal contact by amputation, in cortisone-treated and non-treated control rats. Impeded eruption indicates average eruption rates of right incisors in occlusal contact for both groups. Normal occlusion indicates averages of rats in group 3, subjected to the same manipulative procedures but not to incisor apical amputation.

maxillary incisors appears to contradict previous reports(4) of similar observations on mandibular incisors. However, if one examines rat incisors, differences between the maxillary and mandibular incisors become apparent. Particularly evident is the fact that those in the mandible have a smaller diameter and are more mobile. These differences could produce a higher rate of attrition in the normal back and forward masticatory movements of the mandible and explain the higher eruption rate reported(6) for the mandibular incisors.

The effects of occlusal stresses in modify-

ing the eruption rate of incisors have been demonstrated(4). When these stresses are removed by maintaining the incisor free of occlusal contact the rate is accelerated, revealing the true growth potential of the incisor(5). That this growth can be further accelerated by cortisone treatment probably indicates a direct effect on the tissues of the incisor, or the mechanism controlling eruption, in a manner not yet understood.

Summary. Observations on rats maintained on a soft consistency diet or restricted food intake, revealed little if any effect on the eruption rate of the maxillary incisors. However, when these incisors were kept out of occlusal contact by periodic apical cutting, rate of eruption was accelerated. Cortisone treatment brought about a further increase in this accelerated rate indicating a direct effect on the mechanism or mechanisms responsible for incisor eruption or growth.

1. Domm, L. V., Wellband, W. A., *Proc. Soc. Exp. Biol. and Med.*, 1960, v104, 582.
2. ———, *ibid.*, 1961, v107, 268.
3. Greenberg, S. M., Aterman, K., *Metab. Clin. and Exper.*, 1955, v4, 264.
4. Taylor, A. C., Butcher, E. O., *J. Exp. Zool.*, 1951, v117, 165.
5. Bryer, L. W., *Intern. Dent. J.*, 1957, v7, 432.
6. Schour, I., Massler, M., *The Rat in Laboratory Investigation*, Lippincott, Philadelphia, 1949, Chap. 6.

Received March 30, 1964. P.S.E.B.M., 1964, v116.

Lipolytic Activity in the Blood After Lipase Ingestion.* (29354)

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The studies of Frazer(1), Becker *et al*(2) Tietz and coworkers(3) suggested the possible importance of a lipolytic enzyme appearing in the blood after lipase ingestion.

* This study was supported in part by grants from Robert A. Welch Foundation, Division of Research and Development, Office of Surgeon General, and A. H. Robins Company.

Blood lipid levels were found to be lowered by ingestion of the pancreatic lipase as a supplement to a fat test meal as measured by either chylomicron or esterified fatty acid levels. Possible explanations advanced for these findings were that an increased fat hydrolysis caused a loss of the fatty acids from the systemic to the portal blood(1,2)