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The Effect of Acetyl Thyroxin on the Teeth of Newborn Rats.

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In the acetyl derivatives of thyroxin certain parts of the thyroxin molecule have been replaced by the acetyl group giving a compound which does not affect the metabolic rate of mammals.[1] It retains, however, its effect on the development of young organisms. Tadpoles, to which acetyl thyroxin is given by injections or feeding, develop rapidly into frogs. Newborn rats are similarly affected, going through changes of form normal for the first 25 days of life in a period of 15 days. These general changes are shown in the proportions of the skull, the development of the hair, eyes, auricles and feet. These effects, and the method of the experiments have been described elsewhere.[2] During the course of the work it was noted that the injections hastened the eruption of the incisors, but this point was not studied in detail. A brief sketch of the changes occurring in incisors and molars is presented below.

Animals were injected as in the above experiments, with the same general results. On the third, fifth, and eighth days of life, specimens were killed. In each case a normal litter mate was killed also and studied for comparison. The heads of the animals were fixed in Bouin's fixing fluid. The upper and posterior part of each head was then cut away, leaving the jaws, tongue and surrounding tissues to be sectioned. This piece was decalcified in weak nitric acid, embedded and sectioned.

In material prepared in this way, the following conditions were observed. In a normal rat at 3 days of age, the incisors began to penetrate the oral epithelium, the tips being about a third of the way from the base to the surface. In the injected animal, after only 0.1 mg. of acetyl thyroxin had been given, the tooth had grown considerably farther into the epithelium, its tip being half to three-quarters of the way through. The labial groove is also noticeably more advanced in its development in the injected than in the normal rat. By the fifth day the incisors of injected animals are fully erupted. The surface of the epithelial layer is intact over the tip of the incisors of normal rats at this time. Eruption does not normally occur until the eighth, ninth, or tenth day.

In contrast to the conditions just described in incisors, the molars of newborn rats are not affected by injections of acetyl thyroxin.

In the same specimens which show erupted incisors at 5 days of age, the stage of development of the molars is not to be distinguished from that of the controls; and in older specimens the same lack of effect is to be observed.

It has been thought by some that enamel formation is particularly subject to thyroid influence, and on that account a special study has been made of that process. It is found that enamel formation is undoubtedly accelerated by the treatment. A well defined band of enamel is present in injected rats at 3 days of age, while in the controls the process of its formation has barely begun. If, however, one compares the incisor of a 5-day rat, just at the time of eruption, with that of a normal specimen at 8 days, the same amount of enamel will be found in each. It is evident that although enamel formation is stimulated by acetyl thyroxin, it does not show any greater degree of response than any other process of tooth formation.

It should be noted that animals injected with acetyl thyroxin are not truly hyperthyroid individuals. The over-functioning thyroid accelerates metabolism as well as differentiation, while acetyl thyroxin stimulates the latter process only. Therefore our conclusions concern the rate of development, but not abnormalities of the fully formed tooth due to changes in the metabolic rate of the adult. It is clear that the rate of development of the incisors of rats is influenced by the thyroid. In this respect the teeth are like various other structures of the body; for instance the nasal bone, which grows with abnormal rapidity in these same animals. The development is normal in character, but abnormal in rate.

It should also be remembered that the incisors of rats are different from human teeth and from the molars of rats, in that they grow actively throughout the life of the animal. Attempts have been made to correlate overgrowth of certain teeth in human beings with particular endocrine abnormalities; for instance, enlarged canines have been considered by some to be a sign of excessive adrenal activity. Although it has been shown in the above study that the growth of the incisors of rats is more accelerated than that of the molars, the facts do not warrant the conclusion that human incisors are more influenced by the thyroid than other teeth. It is more probable that the difference observed is due to the peculiarly active growth tendency in rat incisors.

The experiments give no explanation for enamel deficiencies in hypothyroid patients. Amelification is stimulated by the injections, but not more than any other process of tooth development. One

must conclude that the fragile enamel seen in hypothyroid patients is a result of disturbed metabolism, not a developmental anomaly.

[1] Swingle, W. W., *Am. J. Physiol.*, 1924, lxx, 70.
[2] Hoskins, M. M., *J. Exp. Zool.*, 1927, iv, 48.

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Pressor Effect of Guanidine Salts on the Non-anesthetized Rabbit.

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A possible relationship between guanidine intoxication and essential hypertension has been suggested.[1] It was of interest to study the question in non-anesthetized animals. This report contains the results of daily examinations for blood pressure and pulse rate in 12 experiments performed on 5 rabbits provided with a good carotid loop (Van Leersum). The salts used (Eastman Kodak Co.) were methylguanidine nitrate (9 experiments), methylguanidine sulphate (2 experiments), and guanidine nitrate (1 experiment). All the rabbits received 0.1 gm. per kilo of body weight but in different concentrations, 1:10 and 1:20 in distilled water, and 1:20, 1:30 and 1:50 in salt solution (4 and 8 per 1000). The total volume of fluid injected was from 3.7 to 8.2 cc. of distilled water and from 6 to 18 cc. of saline. The weights of the rabbits varied from 2.945 to

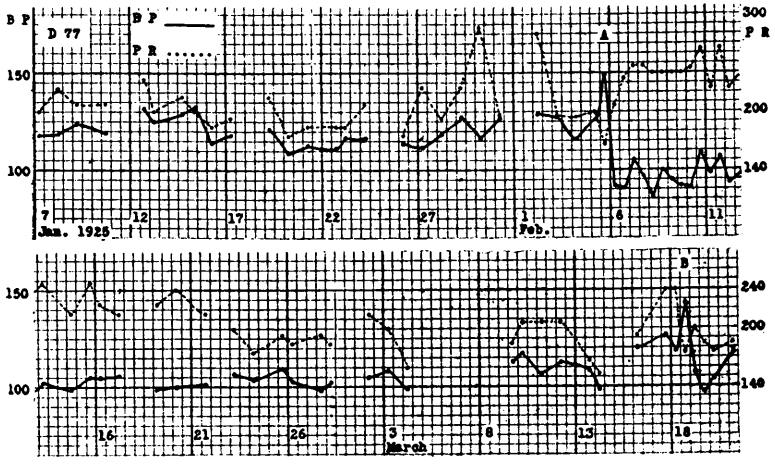

Figure 1.