viously described proteolytic enzymes of the pancreas for 3 reasons: 1. The degree of digestion is at least 3 times as great as that obtained from trypsin. 2. Heating trypsin to destroy its collagen digesting ability, but not its proteolytic properties, reduces the amount of collagen digested to zero. 3. Pancreatic juice from a dog fistula which has not been activated by intestinal juice has no tryptic activity, nevertheless, it has marked collagenase activity. The inability of trypsin to digest any significant amount of collagen has also been reported by Neuman and Tytell(6).

These findings suggest that collagenase must be considered in the pathogenesis of pancreatitis and other pancreatic diseases.

Summary. Evidence has been presented to show that pancreatic juice of the dog has the ability to digest collagen. This ability is not due to the proteolytic enzymes of the pancreas, trypsin, chymotrypsin, or carboxypeptidase.

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Effects of Thyroid Hormone and Propylthiouracil on Eruption Rate of Upper Incisor Teeth in Rats. (22125)

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Though the rat's incisor teeth continue to erupt throughout life, they are kept to a fairly constant length by the process of attrition. The rate of eruption, that is, the linear quantity by which the incisor teeth extrude into the oral cavity in a unit of time, is subject to alteration by hormonal action. Hoskins(1) found that thyroid hormone caused the incisors of newborn rats to erupt earlier than those in untreated control rats. This observation was confirmed by Karnofsky and Cronkite(2). Herzberg(3) noted that thyroid hormone caused an increase in the incisor eruption rate (I.E.R.) in adult rats; however, he offered no data to substantiate his claim. Baume, Becks and Evans(4) reported that ablation of the thyroid in adult rats produced a decrease in the I.E.R. In conformity with this view it seemed of interest therefore to extend these data by 1) quantitating the effect of thyroid hormone on the I.E.R. of adult rats and 2) testing the effect of a thyroid blocking agent, propylthiouracil (PTU) on I.E.R. The latter procedure has the advantage that it leaves the parathyroid glands in a functional state. In many of the earlier studies the parathyroids were removed indiscriminately at the time of surgical thyroidectomy.

Procedures. Twenty-three male white rats (Holtzman strain), 80 days of age, were treated as follows: 8 animals were fed ground rat chow containing 0.5% desiccated thyroid; 8 rats were fed processed chow containing 0.15% PTU and 7 animals, which served as untreated controls, were fed only ground rat chow. Four rats on PTU-feeding were shifted at the end of the fifth week to a diet of ground rat chow containing instead 0.5% desiccated thyroid for an additional 2 weeks. The I.E.R. of all animals was measured according to the method of Schour(5) once each week during the course of the experimental period. Dental roentgenograms of upper incisors of rats fed thyroid were taken after 2 weeks on the diet, and those of the animals receiving PTU were taken after 5

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TABLE I. Effect of Desiccated Thyroid and Propylthiouracil on Incisor Eruption Rate of the Rat.

Group	Wk I			Wk II			Wk III			Wk IV			Wk V		
	No. rats	I.E.R., mm/wk	Wt, g	No. rats	I.E.R., mm/wk	Wt, g	No. rats	I.E.R., mm/wk	Wt, g	No. rats	I.E.R., mm/wk	Wt, g	No. rats	I.E.R., mm/wk	Wt, g
Control	7	2.6 ± .15*	256	7	2.7 ± .33	268	7	2.6 ± .20	260	7	2.3 ± .24	273	7	2.3 ± .22	270
Thyroid, .5%	8	3.1 ± .24†	232	8	3.5 ± .24†	220	7	3.0 ± .37	193	6	3.1 ± .40	197	5	2.6 ± .36	190
PTU, .15%	8	2.4 ± .14	233	8	1.95 ± .35	237	8	1.5 ± .20	240	8	1.2 ± .39	225	8	1.2 ± .28	219

* Stand. dev.
† T test performed for difference of I.E.R. of thyroid group from control group for Weeks I and II; $P = <0.01$—highly significant.

weeks of treatment. These were compared with corresponding films of the controls at the respective times.

Results. Feeding of desiccated thyroid (0.5%) admixed in ground chow caused a significant increase ($P = <.01$) in the I.E.R. after one week, and this rose to a maximum at 2 weeks when the I.E.R. was 30% above that manifested by the control animals (Table I). Thereafter the I.E.R. declined gradually despite continued thyroid feeding and by the fifth week had returned almost to the level of that of the controls. These thyroid-fed animals manifested a severe weight loss, most of which occurred during the period of the second through the third week of treatment. From the second through the fifth weeks of the experiment 3 rats of this group died. There were no deaths in the other experimental groups during this period.

The inclusion of 0.15% PTU in the diet produced a slowing of the I.E.R. which was significant by the second week and which continued to decrease until the fourth week when it reached a minimum of 48% of that observed in the control group. The I.E.R. did not decrease further even though PTU feeding was continued through the fifth week (Table I).

When desiccated thyroid 0.5% was substituted in the diet of 4 of the above animals which had received PTU for the previous 5 weeks, the I.E.R. increased within one week to 260% over that which these same animals had registered the previous week (Table II). Thyroid feeding was continued for an additional week and the increase in I.E.R. was maintained.

The upper incisors of the animals treated with PTU for 5 weeks possessed an increased amount of dentine per unit area of incisor. (Fig. 1). This had occurred at the expense of

TABLE II. Effect of Thyroid Hormone on I.E.R. of 4 Rats Previously Treated with PTU.

Treatment	I.E.R.	
PTU, 0.15% in diet, wk I-V	mm during wk V,	1.0±.24
Thyroid, 0.5% in diet, wk VI & VII	VI,	3.6±.18
	VII,	3.5±.20

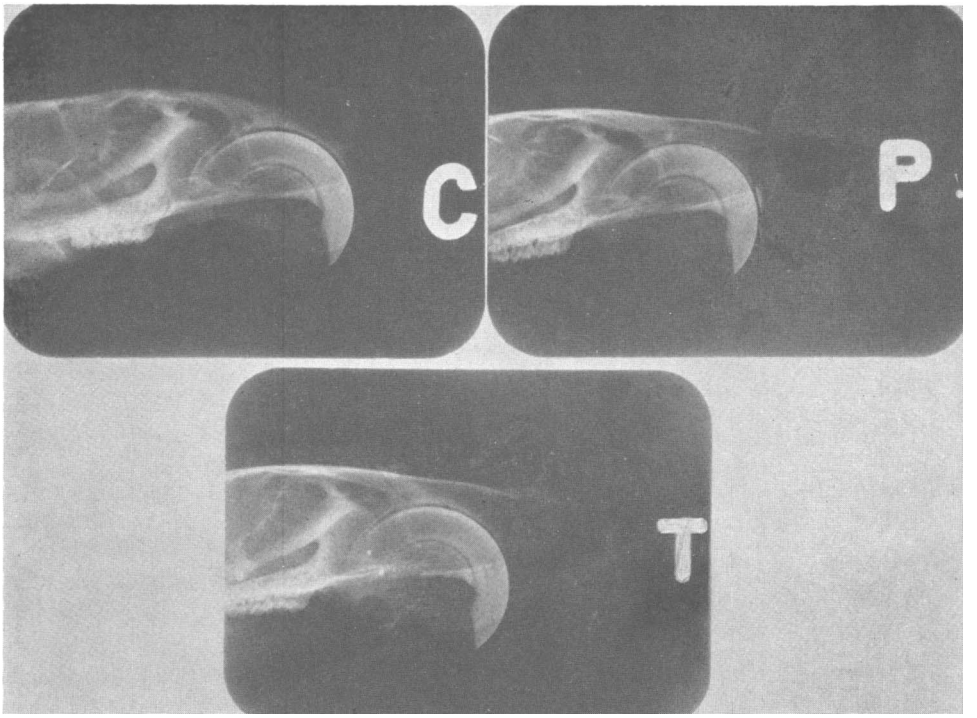

FIG. 1. Roentgenographs of incisors: C—Control animal. P—After 5 wk propylthiouracil feeding showing an increased amount of dentine which partially obliterates pulp chamber. T—Two wk of thyroid feeding showing enlarged pulp chamber associated with decreased amount of dentine per unit area of tooth.

the pulp chamber which was partially obliterated. Conversely the incisors of the thyroid-treated rats had large pulp chambers with a decreased amount of dentine by comparison with the films of control animals. It is to be noted that the roentgenograms were taken at the time when the maximum effects of the experimental treatment on the I.E.R. were demonstrated, *i.e.*, the second week of desiccated thyroid- and the fifth week of PTU-feedings.

Discussion. These data confirm the statement of Hertzberg that thyroid hormone increases the I.E.R. in normal rats. The response was most marked during the first two weeks of treatment and thereafter subsiding toward normal. An explanation of this phenomenon may be that in the first 2 weeks the effects on eruption are those of increased thyroid hormone action in healthy animals, whereas with continued thyroid treatment the toxic effects of the increased dosage, manifested by severe weight loss as well as the death of some of the treated animals, are noted. That the effects of thyroid hormone administration are accumulative is well known. Although the eruption rate decreases from the peak reached in the first two weeks of treatment it does not return to the rate measured in the control animals.

The increased size of the pulp chambers of the incisors of the thyroid-fed group is probably due to the increase in the I.E.R. with no apparent change in the rate of dentinogenesis. There is therefore less time for dentine to be deposited per unit area of tooth with the result that there is less encroachment upon the pulp chamber. Conversely the roentgenograms of the upper incisors of animals given PTU demonstrate an obliteration of a large portion of the pulp chamber by dentine. A likely explanation here is that while the I.E.R. is decreased the rate of dentinogenesis is apparently not affected, hence the period during which dentine can be layed down per unit area of tooth is extended. This is also in agreement with the histological evidence

from the thyroidectomized animals of Baume *et al.*(4).

The increased sensitivity of the eruptive mechanism to thyroid hormone manifested by the PTU rats is probably due to the hypothyroid state of these animals and thus the end organs which are normally affected by this hormone become more reactive.

PTU causes a chemical thyroidectomy and produces a retardation of the I.E.R. which confirms the work of Baume *et al.*(4) in demonstrating a decreased eruption rate in the thyroidectomized adult rat. Since PTU does not affect the parathyroid gland, it is evident that the reduced I.E.R. can only be due to the lack of thyroid hormone.

Conclusions. Thyroid hormone is essential for a normal rate of incisor eruption. An excess of this hormone will cause an increased eruption rate. The use of the incisor eruption rate as a tool for demonstrating hormonal activity should be considered.

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Relative Pathogenicity of Newly Isolated Strains of Poliomyelitis for Monkey Kidney Cells and Mice. (22126)

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Adaptation of poliomyelitis viruses to passage in mice has been accomplished only with difficulty or after laboratory manipulation of newly isolated strains(1-7). Quantitative comparisons of the pathogenicity of poliomyelitis viruses in tissue culture and in animals have usually been carried out with well adapted laboratory strains(8-11) or have been limited because of the necessary use of large numbers of monkeys(12).

The purpose of this study is to compare the quantitative relationships of the ability of freshly isolated polio virus strains to cause cytopathogenic effect in monkey kidney epithelium in tissue culture and paralysis in mice. For this purpose a number of strains of each of the three types of polio virus isolated in tissue culture from stools of patients during a national survey in 1952 was available for this study(13).

Materials and methods. Ten percent suspensions of stools were prepared in a mortar with phosphate buffered saline containing 2500 units of penicillin and 1250 μg of streptomycin per ml, clarified by centrifugation at 8,000 r.p.m. for one-half hour, and the supernates used as inocula. Primary isolations were made in cultures of monkey kidney, either in flasks of suspended tissue fragments, according to the method of Weller, Enders, Robbins and Stoddard(14), with subsequent passage in roller tubes, or directly in monocellular layer roller tubes, prepared by the method of Youngner(15). Isolates were typed in roller tubes by neutralization with specific monkey antisera. All inoculations of mice and titrations in both mice and kidney roller tubes were carried out on virus strains in the first or second tissue culture passage from the original stool. Groups of ten 4-5-week-old CFW mice were inoculated intraspinally (I.S.) with 0.02 ml, and observed for 21 days. Type 2 isolates were also inoculated intracerebrally (I.C.), in a dose of 0.03 ml, into 10 mice each, which were observed for 28 days. Wherever indi-

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