sure to normal tissue. Injection of the globulin fraction prevented "takes" of Walker 256 cells in slightly over half of rats inoculated with 10,000 cells. The globulin antibody solution produced a decrease in size by about one quarter when given to rats with tumors 2 to 3 cm in diameter, but the tumor masses did not disappear. The method was tried in 2 patients with decrease in size of the tumor but not disappearance.

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Effect of Thyroidectomy on Pancreatic Amylase.* (24514)

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Hypophysectomy of the rat induced a striking reduction in weight of the pancreas (1,2) and in size and granulation of acinar cells(3). Also, amylolytic(1,4), proteolytic (5) and lipolytic (unpublished) activities were depressed significantly. That some of these changes may have resulted from deficient thyroid secretion was indicated by the occurrence after thyroidectomy of partial pancreatic atrophy(6) and reduced total lipolytic activity. Furthermore, morphological evidence of stimulation appeared following administration of thyroid substance to nonoperated rats(7-11). The purpose of our experiments was to observe the effect of thyroidectomy on pancreatic amylase. If the direction and magnitude of change were similar after both hypophysectomy and thyroidectomy, additional evidence would be provided to support the hypothesis that a significant portion of hypophyseal regulation over enzyme production by the pancreas is mediated by the thyroid gland.

Methods. Young adult female rats of Sprague-Dawley strain were used, with the following treatments given to one-half of the rats in each experiment: Exp. 1, surgical thyroparathyroidectomy; Exp. 2, parathyroidectomy by electrocautery; and Exp. 3, surgical thyroparathyroidectomy in addition to 100 μc of I^{131} subcutaneously 13 days later. Radioactive iodine was given to the third group to insure destruction of thyroid fragments which are often left after surgical thyroidectomy. Completeness of gland removal was verified by microscopic examination of the cervical region in all rats of Exp. 1 and in some of Exp. 3. Those which retained fragments of significant size were eliminated. Exp. 2 acted as a control for Exp. 1 in that an opportunity was provided to observe the effect of parathyroidectomy alone. After operation the controls were pair-fed against the operated rats. The animals in Exp. 1 and 3 were fed "Low Iodine" Test Diet (Nutritional Biochemicals Corp.). To this was added 1 g glucose/100 g of test diet for operated animals, and the same amount of glucose in addition to 3.27 mg of KI for control animals. Animals in Exp. 2 were fed powdered Purina Laboratory Chow. All rats were given water *ad lib.* but no food for 24 hours prior to termination of experiment. After killing the rat by blow on head, the pancreas was excised,

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TABLE I. The Effect of Thyroparathyroidectomy and Parathyroidectomy on the Amylolytic Activity of the Pancreas.

Treatment	No. of rats	Days postop.	Mean body wt (g)		Mean pancr. wt (mg)	Mean amylase activity (mg glucose)	
			Initial	Final		Per unit wt†	Total
Exp. 1							
Control	7		164 ± 4*	187 ± 7	889 ± 37	1.73 ± .15	31,293 ± 3470
Thy.	7	64–72	155 ± 4	167 ± 8	450 ± 20	1.02 ± .12	9,139 ± 1210
					P <.001	P <.01	P = .001
Exp. 2							
Control	9		171 ± 3	207 ± 5	947 ± 36	.85 ± .12	32,584 ± 4939
Parathy.	9	62–69	165 ± 3	216 ± 3	922 ± 21	.88 ± .08	32,697 ± 3252
					P >.5	P >.8	P >.9
Exp. 3							
Control	10		145 ± 1	173 ± 9	846 ± 48	.79 ± .04	26,979 ± 2322
Thy. + I^{131}	10	66–72	145 ± 1	148 ± 8	468 ± 23	.33 ± .02	6,058 ± 308
					P <.001	P <.001	P <.001

Thy. = Thyroparathyroidectomy; Parathy. = Parathyroidectomy.

* Stand. error of mean.

† Unit wt of pancreas in Exp. 2 and 3 = 0.025 mg; in Exp. 1, 0.05 mg.

weighed and homogenized in chilled physiological saline. The homogenate was diluted with physiological saline to a concentration of 0.1 g of pancreas/4 l of saline in Exp. 2 and 3 and to 0.1 g/2.0 l in Exp. 1, and filtered thru glass wool. To 1 ml of this homogenate was added 2 ml of 0.2 M KH_2PO_4-Na_2HPO_4 buffer (pH 7.0) and 5 ml of 0.5% Lintner soluble starch made up in 1% NaCl, the latter warmed previously to 37°C. A similar preparation was used as a blank except that it contained 1 ml of water instead of the homogenate. Both tubes were incubated at 37°C with constant agitation. After 10 minutes incubation, the tubes were placed in boiling water bath for 5 minutes to stop enzyme activity in tube containing the homogenate. The tubes were cooled in running tap water and protein was precipitated by addition of 1 ml of 5% $ZnSO_4$ and 1 ml of 4.5% $Ba(OH)_2$ followed by centrifugation at 2000 rpm for 3 minutes. The Nelson-Somogyi method was employed for determination of amount of reducing substance released by amylase. Amylase activity was expressed as mg of glucose released from starch in 10 minutes at 37°C by 1 ml of homogenate (0.025 mg of pancreas in Exp. 2 and 3 and by 0.05 mg of pancreas in Exp. 1) by reference to a standard curve. The significance of the difference between mean values for control and experimental groups was determined by the Student-Fisher t formula.

Results. Surgical thyroparathyroidectomy significantly reduced the weight of pancreas from 889 ± standard error 37 mg for controls to 450 ± 20 mg. The amylolytic activity after thyroparathyroidectomy was reduced from 1.735 ± 0.147 mg to 1.018 ± 0.125 mg/unit weight of pancreas and from 31,293 ± 3470 mg to 9139 ± 1210 mg for the whole gland (Table I). After surgical thyroparathyroidectomy, amylase/unit weight of pancreas was reduced 41% while after thyroparathyroidectomy followed with I^{131} there was a 58% reduction (Exp. 3). Reduction in total amylase and amylase/unit weight of pancreas was significant at the 1% level or better in Exp. 1 and 3. Surgical parathyroidectomy had no effect on pancreatic weight or amylolytic activity.

Discussion. Hashimoto(11) studied the effect of thyroidectomy on pancreatic amylase in rats. Unfortunately, because of the small number of animals and failure to remove all of the thyroid gland, his conclusions carry little weight. He observed that secretion of amylase was depressed only during the brief period of 2 weeks after thyroidectomy and that between 15 and 17 days there was no evidence of an influence of thyroid deficiency on pancreatic secretion. Hashimoto concluded

that after 2 weeks some mechanism (which in his case appeared to be regeneration of thyroid tissue) had compensated for glandular deficiency. Our results show clearly that 9 to 10 weeks after thyroidectomy an approximately 50% reduction in pancreatic amylase is evident.

Since the effects of hypophysectomy and thyroidectomy on pancreatic weight and amylase are of comparable magnitude it may be inferred that a large proportion of pituitary control over pancreatic acini is exerted through the thyroid gland. However, no aspect of altered pancreatic function in the hypophysectomized rat has yet been fully restored by therapy with thyroid hormones.

Summary. After surgical thyroparathyroidectomy, with or without additional treatment with I^{131}, the pancreatic weight and amylolytic activity/unit weight and /total weight of the pancreas were reduced significantly, the fall in concentration of enzyme being greater with the latter experimental procedure.

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Toxic Protein Degradation Products. (24515)

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Vaughan(1) first noted that toxic polypeptides may be prepared from a variety of bacterial, plant and animal proteins by relatively simple chemical procedures. As more recent investigations(2-10) suggest that a number of products of endogenous proteolysis may possess substantial physiological activity it was decided to reinvestigate several of Vaughan's easily accessible and toxic "protein split products" with the aid of more modern procedures than those used previously(1) with the expectation that the results of such a study would be useful for detection and examination of similar products of *in vivo* origin. Before presenting our own observations it is necessary to refer to some results obtained by Vaughan and his associates(1). When bacterial and other proteins were treated with boiling 2% ethanolic sodium hydroxide these workers obtained, after neutralization of the reaction mixture with hydrochloric acid, ethanol-soluble fractions containing "protein split products" which, when injected into guinea pigs, progressively elicited all symptoms associated with anaphylactic shock, i.e., peripheral irritation, muscular incoordination, severe cyanosis, convulsions and death by respiratory failure. Such fractions invariably gave positive protein tests but a negative Molisch test. The preparations were hydroscopic golden-yellow powders which were readily soluble in water. Because of the slightly acid reaction of aqueous solutions of the preparations, Vaughan(1) concluded that the products were acidic in nature and that their physiological action was associated with blocking of some vital basic groups of tissue and serum proteins. Fractionation of the above materials failed to give crystalline products but did lead to preparations with con-

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