Microscopic sections through different levels of the myocardium of a normal rabbit showed the muscle bundles sharply outlined and the nuclei well stained. No evidence of degeneration or inflammation was present. Sections through the myocardium of rabbit No. 7 showed (Plates 1 and 2) areas of necrosis everywhere, chiefly affecting the muscle and largely involving the right ventricle and interventricular septum. In the left ventricle the areas of necrosis were chiefly beneath the endocardium. The papillary muscles were prominently affected. Slight periarterial infiltration was present and areas of necrosis were seen in both the auricular walls. The anterolateral ventricular epicardium showed a hyaline fat necrosis. The pathological diagnosis was degeneration and necrosis of the myocardium.

Summary. The incidence of non-induced cardiopathic disease among laboratory animals may greatly alter the prognosis, course and reaction to given control or experimental conditions. Disease of the myocardium as confirmed by pathologic studies may greatly alter the electrocardiogram in the rabbit. The changes found suggesting a localized lesion of the ventricle by the electrocardiogram were not supported by pathologic studies. Since bacteriologic studies were not done, no conclusive evidence as to the etiology of the myocarditis was suggested.

11483

Variability of Action on Heart Rate Compared with Metabolic Effect of Various Thyroid Preparations.

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In our previous publication[1] we have shown that certain thyroid preparations fed to thyroidectomized rats exert a stimulating action on the heart rate which varied from one product to the other in its relation to the corresponding metabolic increase obtained. While in 2 U.S.P. thyroid preparations the cardiac effect prevailed, thyroxine and thyroid globulin proved to be of low action on the heart if given at a dose to produce an equal metabolic response. It was shown furthermore, that alkaline hydrolysis of thyroid globulin

[1] Meyer, A. E., and Yost, M., *Endocrinology*, 1939, **24**, 806.

caused the formation of 2 split products, representing essentially the thyroxine and diiodotyrosine fractions, which differed widely in the degree of their metabolic potency, but which both showed a quite conspicuous action on the heart. It was concluded that hydrolysis produced a heart stimulator from either the thyroid hormone itself or from some unspecific substance contained in the material subjected to hydrolyzing agents. The question whether or not the heart stimulation obtainable with U.S.P. thyroid was caused by a substance contained originally in the gland, or to some split product formed by post-mortem changes could not be decided upon.

In continuation of this work we compared a number of other thyroid preparations, either dried gland powders of different commercial provenience or extracts prepared from thyroid, with respect to metabolic effect and action on heart rate, using the same technic as described before,[2] which consisted in feeding the medication (calculated in gamma per 10 g body weight) for 3 days and determining the metabolic and heart effect on the fifth day.

Samples of dried whole thyroid (U.S.P.) used in our previous work gave the standard metabolic response of 30% increase at a dosage of 310 to 320 γ, corresponding to 0.62 to 0.64 γ of iodine. In the following experiments the dosage producing 30% metabolic

TABLE I.

Product tested	Actual iodine content of undiluted product, %	Quantity of material after dilution to 0.2% I content, producing 27-32% metabolic stimulation, γ	Quantity of thyroxine contained in quantity given in column 3 γ	Avg heart stimulation obtained at about 30% inc. of metabolism, Before	After	Incr.
d,l-thyroxine as Na salt	65.0	244	.75	190	220	30
Thyroid Globulin						
No. 123	.565	260	.23	180	210	30
134	.78	293	.25	190	226	36
136	.72	310	.22	188	236	48
141	.44	275	.27	190	227	37
143	.76	289	.26	190	212	22
U.S.P. A.	.2	320	.30	185	340	155
W-1	.465	309	.25	190	365	175
U.S.P. W-2	.2	240	.19	192	310	118
W-3	.63	236	.20	195	284	89
U.S.P. C.	.23	320	.26	192	275	83
U.S.P. L.	.2	320	—	190	273	83
Thyroid Ext. P.	.3	300	—	190	275	85
Commercial Thyroid Protein	.94	446	.3	195	260	65

[2] Meyer, A. E., and Wertz, A., *Endocrinology*, 1939, **24**, 683.

response was determined in every instance and the effect on the heart rate obtained simultaneously was noted.

Since not all these preparations were U.S.P. and some had a higher iodine content, the products were diluted with milk-sugar to contain 0.2% iodine in order to obtain comparable figures.

The table giving the averages, obtained on 6-12 rats in each case, shows that the metabolic effect in a large percentage of preparations is proportionate to the iodine content, the standard dose being about 300 γ, but that deviations even in U.S.P. thyroid do occur, as shown in sample W-2 and W-3. The effect on the heart was not in proportion with the metabolic efficiency, confirming our previous findings that both effects are to some extent independent.

The commercial thyroid protein, claimed to be "detoxified," gave a relatively low heart stimulation but a 50% higher dosage was required for the standard metabolic effect. The thyroxine content of the products was determined by the Leland-Foster method.[3] From the data presented in the table the ratio between thyroxine and metabolic effect seems to be slightly more variable than that between iodine and that action, the quantity in the dosage varying from 0.19 to 0.3 γ.

Incidentally, iodized protein and peptone supplied by Dr. W. T. Salter, Thorndike Memorial Laboratory, Boston, gave proportionate metabolic responses in agreement with clinical tests but induced practically no heart acceleration.[4, 5]

The observation mentioned above that hydrolysis of the thyroid globulin produces split products of strong action on the heart was met with the criticism that this effect might be due to some unspecific product of decomposition obtainable by hydrolysis from any animal tissue and perhaps present in the commercial product of high effect on the heart as a consequence of autolytic changes in the structural elements of the gland tissue occurring before the drying process was completed.

To answer the question beef muscle was minced and subjected to hydrolysis. The water-insoluble part was extracted with alcohol and both aqueous and alcoholic extract combined and evaporated. The extract did not show any sign of metabolic effect when tested on rats nor did it affect the heart rate. It was admixed to a standardized thyroid globulin that at 85 γ dosage per 10 g given for 3 days produced a metabolic increment of 30% and heart rate increase of about 25 beats per minute. The figures obtained by the

3 Leland, J. P., and Foster, G. L., *J. Biol. Chem.*, 1932, **95**, 165.

4 Lerman, J., and Salter, W. T., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 94.

5 Salter, W. T., and Lerman, J., *Trans. Assn. Am. Phys.*, 1938, **53**, 202.

use of the mixture were absolutely identical. The conclusion, therefore, is justified that the heart stimulator is not a split product obtainable by hydrolysis from this type of animal tissue.

Conclusions. The iodine content in thyroid preparations seems to be an approximate guide for the estimation of metabolic effect; however relatively large deviations do occur in some products. The effect on the heart is not related to the metabolic action. The thyroxine content has still less demonstrable proportionality to either physiologic effect. While hydrolysis of thyroid globulin increases its heart action hydrolysate from muscle tissue is inert in that respect.

11484 P

Growth-Stimulating Effect of Testosterone Propionate.*

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For this purpose 24 male albino rats of Wistar Institute strain were used. Of these 12 animals were treated (test group) and 12 served as untreated controls. All animals were kept under similar conditions, Purina Dog Chow used as food, and water were constantly present. In addition, green vegetables were given twice weekly. The treated animals received daily (except Sunday) intraperitoneal injections of 0.05 mg testosterone propionate (Perandren) for 53 days beginning at 26 days of age. Control animals remained uninjected.

Weights were taken at 26 days of age and weekly thereafter. Twenty-four hours after the last injection, *i.e.* at 80 days of age, all animals were anesthetized with ether, their carotid vessels were cut and exitus was allowed to result from bleeding. Body lengths measured from the tip of the snout to the anus were then determined.

All data were treated statistically[1] and observed differences between test and control groups were considered as being probably significant only if the "significance ratio" was 3 or more.

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1 Pearl, R., *Medical Biometry and Statistics*, second edition, Saunders, Philadelphia, 1930.