testosterone propionate for 14 days, with marked effect. The thymus decreased from an average of 327 mg. to 160 mg.

We conclude that thymus involution occurs in adrenalectomized rats following the administration of substances other than oestrone. Both oestradiol and testosterone were effective. None of the sexually inert substances caused any thymus change. This suggests a relationship between the sex stimulating property of the sterols and the thymus effect, but the amount necessary to cause thymus involution is many times that required for the physiological effect. The toxicity of the sterols in adrenalectomized rats also appears to run parallel with their physiological activity.

9282

Serum Sodium in Relation to Liver Damage and Hyperthyroidism.*

SVEND PEDERSEN, WALTER G. MADDOCK AND FREDERICK A. COLLER. (Introduced by L. H. Newburgh.)

From the Department of Surgery, University of Michigan.

The liver of patients with severe hyperthyroidism has shown impairment of function and marked pathological changes.[1] In a search for the cause of thyroid crisis, we were unable to find any definite relation between impairment of liver function, as measured by blood bilirubin and bromsulphalein dye retention, and the degree of postoperative reaction, the latter being of the same nature and in its severe form, true thyroid crisis.[2]

Our attention was then drawn to a publication by Schneider[3] concerning a marked disturbance of serum sodium in relation to liver damage and hyperthyroidism. This investigator has shown experimentally in guinea pigs that daily injections of the thyrotropic hormone from the anterior lobe of the pituitary gland or injections of thyroxine reduce serum and liver sodium below one-half of its normal value, while potassium and chlorides are not significantly

* This investigation was assisted by a grant from the Horace H. Rackham School of Graduate Studies.

1 Weller, C. V., *Ann. Int. Med.*, 1933, **7**, 543.

2 Maddock, W. G., Coller, F. A., and Pedersen, S., *West. J. Surg.*, 1936, **44**, 513.

3 Schneider, E., *Internat. Clin.*, 1934, **2**, 87. Schneider, E., Widmann, E., *Deutsche Z. f. Chir.*, 1933, **241**, 15, 778; *Z. f. d. ges. exp. Med.*, 1933, **90**, 45. Schneider, E., *Klin. Wchnschr.*, 1933, **12**, 1708.

changed. The reduction of serum sodium paralleled the depletion of glycogen in the liver and he stated that thyrogenic liver damage could be followed indirectly by determining sodium in the serum. In a transfer of his study to humans, Schneider found in 6 cases of hyperthyroidism the following values for serum sodium in mg. %: 53.0, 74.0, 134.0, 138.5, 162.0, and 195.0.

When one realizes that sodium, according to McCance,[4] comprises about 94.0% of the total base of the extracellular fluids, except gastric juice and semen, then it is evident that a tremendous decrease in the alkali reserve and great changes of the osmotic pressure of the blood must have taken place in these patients, since there was no compensation of the alkali reserve by a decrease in chlorides. Serum sodium as low as 53.0 mg. % has never been reported, as far as we are aware, in hyperthyroidism or any other disease and is in our opinion incompatible with life.

The purpose of this investigation was to verify Schneider's work on humans, and serum sodium in a group of 10 patients with hyperthyroidism, 9 of whom had evidence of impaired liver function by other tests, is herewith reported.

In this work, serum sodium was determined according to the method of Butler and Tuthill[5] except for minor modifications. Plasma bilirubin was determined by the standard method and figures from 1.0 to 3.0 mg. per liter were considered to be normal. For the bromsulphalein excretion test 5.0 mg. of the dye per kilo of body weight was administered. A retention of 10% or more after 30 minutes was considered to be abnormal.[6]

The data from the 10 cases of hyperthyroidism are presented in Table I. Eight of the 10 had evidence of marked hyperthyroidism, two (9 and 10) dying on the Medical service, two (2 and 3) developing severe thyroid crisis postoperatively during which time one of them died, and one (4) had jaundice preoperatively for which no other cause except toxic hepatitis associated with severe hyperthyroidism could be found.

Concerning the evidence of liver damage from the plasma bilirubin or bromsulphalein dye retention data, 9 of the 10 patients (except No. 10) showed impaired function. The serum sodium, however, during the height of the hyperthyroid reaction, was normal in 7 of the 10 cases and only a little below 300 mg. % in the remain-

[4] McCance, R. A., The Goulstonian Lectures on Medical Problems in Mineral Metabolism. Reprinted from *The Lancet*, March 21, 1936, p. 643, March 28, p. 704, April 4, p. 765, and April 11, p. 823.

[5] Butler, A. M., and Tuthill, E., *J. Biol. Chem.*, 1931, **93**, 171.

[6] Soffer, L. J., *Medicine*, 1935, **14**, 185.

TABLE I.
Serum Sodium in Relation to Liver Damage and Hyperthyroidism.

Patient	Age	Diagnosis	BMR %	Serum Sodium Mg. %	Evidence of Liver Damage: Blood Bilirubin	Evidence of Liver Damage: Bsp.* dye retention	Severity of disease
					mg.	%	
1	39	Exophthalmic goiter	+77	308.5	4	20	General evidence of marked toxicity.
2	36	" "	+70	310.8	2	60	Considerable toxicity. Died postoperatively in thyroid crisis.
3	17	" "	+75	308.7	2	30	Considerable toxicity. Developed severe postoperative thyroid crisis.
4	65	Toxic adenoma	+39	291.0	60	100	Jaundice from liver damage associated with hyperthyroidism.
5	39	Exophthalmic goiter	+63	279.0	4	15	Considerable toxicity.
6	23	" "	+26	304.0	3	15	Moderate toxicity.
7	44	Toxic adenoma	+30	311.6	16	100	" "
8	28	Exophthalmic goiter	+65	354.6	2	35	Considerable toxicity.
9	59	Toxic adenoma	+31	316.5	8	—	Irrational. Died before operation
10	39	" "	+58	281.9	3	10	Depressed thyroid type. Died before operation.

* Bromsulphalein.

ing 3. The 2 patients with typical thyroid crisis were among the 7 cases having normal serum sodium.

In this study, determinations of serum sodium did not show impaired liver function in a group of patients known to have impaired function by other tests. The work of Schneider in this regard was, therefore, not confirmed. In addition, Schneider stated that operative treatment could be safely employed in patients with hyperthyroidism in whom the risk from clinical indications alone appeared to be excessive, if the serum sodium was above 100 mg. % and reaching 200 mg. %. This was not used as the indication for operation in this series of cases, and fortunately so, since 3 of these patients (2, 9, and 10) died, 2 failing on conservative treatment to be improved to the point that operation could even be considered.

From this study it is apparent that serum sodium determinations have no value in relation to hyperthyroidism found in a typical North American goiter district. Essentially the same findings have been obtained by Feldmaus[7] from a similar investigation in Poland, the publication of which appeared in the literature after our work had been completed.

9283 P

Effect of Trypsin on the Clotting of the Blood in Hemophilia.

T. LLOYD TYSON AND R. WEST.

From the Department of Medicine, Presbyterian Hospital, Columbia University, New York City.

It is known that trypsin will coagulate blood. Its effect on the blood in hemophilia has been studied using crystalline trypsin obtained through the courtesy of Dr. John Northrop.[1] Blood was drawn from the antecubital vein of patients with hemophilia into an oiled glass syringe, great care being taken to avoid unnecessary trauma, and cautiously run into clean glass test tubes. These were let stand at room temperature and carefully tilted every 5 minutes until clotting occurred. Duplicate observations were averaged. The clots retracted and liquefied more rapidly when large amounts of trypsin were used.

A similar experiment was carried out using placental extract,

[7] Feldmaus, B., *Acta. Med. Scandinav.*, 1936, **88**, 39.

[1] Northrop, J. H., The Harvey Lectures, 1934-5, **30**, 229.