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.

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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.

obtained through the courtesy of Dr. R. C. Eley,[2] instead of trypsin. The addition of 0.3 cc., whether boiled or unboiled, to 5 cc. of blood reduced the clotting time from 72 minutes to 5 minutes.

Oxalate was then added to normal and to hemophilic blood in sufficient concentration to prevent clotting over night. The addition of 0.3 cc. of a 5% solution of oxalated commercial trypsin (Fairchild and Foster) to the oxalated bloods was followed by clotting in 10 minutes.

When 5 mg. of heparin per 5 cc. of blood was substituted for oxalate, the addition of commercial trypsin did not cause clotting in either normal or hemophilic blood. Fresh normal human serum acted in a similar manner to trypsin. When 0.2 cc. of serum was added to 5 cc. of oxalated normal and oxalated hemophilic blood both clotted within 4 minutes; whereas, when the same amount of serum was added to 5 cc. samples of heparinized normal and heparinized hemophilic blood, no clotting occurred.

TABLE I.

Hemophilic blood	Crystalline trypsin in 0.7% NaCl. 0.1 cc. = 0.3 mg.	Clotting time
cc.	mg.	min.
5	0	85
5	0.3	30
5	0.6	10
5	1.2	3
5	1.2 (boiled)	90

The addition of 0.1 cc. of fresh normal human serum to 5 cc. of hemophilic blood reduced the clotting time from 70 to 4 minutes, while the addition of the hemophiliac's own fresh serum was without effect in doses of 0.2 cc. but reduced the clotting time from 80 to 25 minutes when 0.4 cc. was used. This effect was wholly destroyed by boiling the sera. This is in accord with the findings of Patek.[3]

The oral administration of the placental extract, chilled and fed with calcium carbonate on an empty stomach, was without effect on the clotting time in 2 cases of hemophilia (aged 26 and 14 years), as was the oral administration of 30 gm. of commercial trypsin daily under similar conditions, and of 12 gm. daily in enteric coated capsules.

The intravenous injection of commercial trypsin solution in a rabbit caused instant death with thrombus formation on the right auricle.

[2] Eley, R. C., Green, A. A., and McKhann, C. F., *J. Pediat.*, 1936, **8**, 135.

[3] Patek, A. J., Jr., and Taylor, F. H. L., *J. Clin. Invest.*, 1937, **16**, 113.

Summary. Trypsin accelerates the coagulation of hemophilic blood *in vitro*. Its action is similar to that of thrombin.

9284

Relation of Urinary Excretion of Estrone to Menstrual Cycle of Normal Woman.

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Although earlier work[1, 2] had failed to demonstrate a greater efficacy of the intravaginal method of assaying estrone, Berger[3] reported that 1/12th of the parenteral unit of estrone could be detected by intravaginal administration. Lyons and Templeton[4] reported that by their intravaginal method 1/200th of a rat unit of estrone could be detected. The latter workers reported estimates of the amount of urinary estrogenic substance excreted daily, at 4 periods in the normal menstrual cycles of 4 nulliparous women.

It seemed desirable to follow the daily excretion of estrogenic substance throughout the cycle, and for this purpose the cooperation of 2 normal nulliparous women was secured. For more than a full cycle these women collected 24-hour samples of urine preserving them with hexylresorcinol (1 part to 20 of urine) and storing them at 0°C. Crude extracts were made of a fraction of each sample according to the method formerly given,[4] and these extracts were administered vaginally to rats by means of a Breed and Brew 0.01 cc. micro-pipette to which was attached a short rubber tube such as is used on a blood-diluting pipette. Care was taken to remove any of the extract adhering to the outside of the pipette before inserting in the vagina.

Of a group of 40 ovariectomized adult rats, 24 were found sufficiently uniform and consistent in their reaction to 1/200th of a rat unit of Progynon B* administered intravaginally, to permit their

[1] Pratt, J. P., and Schmeltzer, M., *Endocrinology*, 1929, **13**, 320.

[2] Powers, H. H., Varley, J. R., and Morrell, J. A., *Endocrinology*, 1929, **13**, 395.

[3] Berger, M., *Klin. Wochnschr.*, 1935, **14**, 1601.

[4] Lyons, W. R., and Templeton, H. J., PROC. SOC. EXP. BIOL. AND MED., 1936, **33**, 587.

* The Progynon B (in oil) was supplied to Dr. H. M. Evans by the Schering Corporation of New Jersey. Dilutions were made with sesame oil. It is probable that differences encountered in standardizing estrone in oil and in water by the