be responsible for the increased non-protein nitrogen and urea which he found in the blood of fasting rabbits. A similar condition seems to obtain in fasting rats leading to a relative concentration of the blood as contrasted with its dilution in the fasting pigeon. In this connection the results of Arima[1] on human blood are of interest in showing that the non-protein nitrogen in various forms of beri-beri is 32 to 67 mg. per 100 c.c.

AVERAGE ANALYSES OF RATS' BLOOD

| Condition | Number of animals | Per cent. loss in weight | Total solids per cent. | Total non-protein nitrogen | Urea nitrogen | Preformed Creatinine | Total Creatinine | Creatine |
|---|---|---|---|---|---|---|---|---|
| | | | | milligrams per 100 c.c. | | | | |
| Normal ..... | 11 | | 21.1 | 41 | 21 | 1.1 | 2.3 | 1.2 |
| Without B . | 17 | 20-44 | 21.5 | 39 | 19 | 1.3 | 3.0 | 1.7 |
| Fasting ..... | 10 | 22-37 | 23.2 | 67 | 40 | 1.3 | 2.8 | 1.5 |
| Fasting with forced water intake ..... | 5 | 28-37 | 21.2 | 39 | 18 | | | |

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### Antagonistic effects of insulin and thyroxin.

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Continued subcutaneous administration of thyroxin is known to produce hyperglycemia. In normal sheep the blood-sugar is raised from about 70 mg. to over 80 mg.

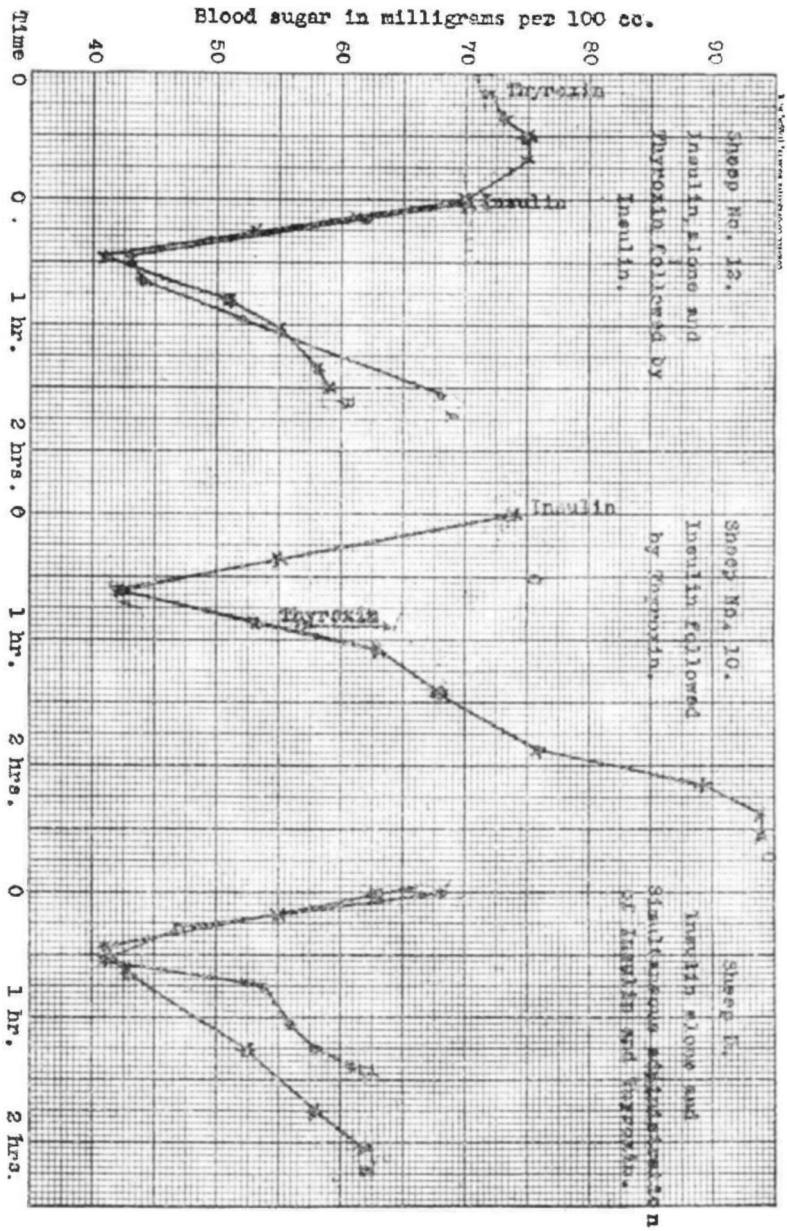
A single subcutaneous administration of thyroxin has only a slight effect on the blood sugar.

A single *subcutaneous* administration of insulin (10 units) produced no demonstrable effect within two hours after injection.

*Intravenous* administration of varying amounts of insulin (5

[1] Arima, E., 1916, abstracted in *Chem. Abstr.*, 1918, xii, 64.

to 15 units) produced prompt hypoglycemia in normal sheep, the sugar decreasing from about 70 to about 40 mgs. per 100 c.c. of blood within about 30 minutes. (No unfavorable symptoms were observed). The drop is regular, and when plotted is repre-



sented by a practically straight line. The slope of this portion of the curve is constant for the same sheep upon administration of varying amounts of insulin.

The portion of the curve representing recovery from hypoglycemia shows characteristic differences: When 5 units of insulin were administered, the recovery to normal sugar values began immediately after the low values had been reached. With 10 to 15 units the minimum sugar values obtained were only slightly lower than for the smaller doses, although analyses were taken at sufficiently close intervals (10 to 20 minutes) to enable a fair approximation to the minimum. The larger doses, however, showed an extensive flat portion in the curves before recovery began. The results with five units were reproducible with the same sheep and similar in different sheep.

Five units were therefore selected as the standard dose of insulin to be tested against varying amounts of thyroxin under different conditions. Administered alone, the effects produced are represented by curves A and D. Curve B shows the effect of a preliminary administration of thyroxin (1 mg. intravenously). Curve C shows the effect of a similar injection of thyroxin after the recovery from insulin had begun. The simultaneous administration of thyroxin (1.5 mg.) and insulin produced a typical divergence of the ascending arm of curve E from that of curve D (insulin alone). With a smaller dose of thyroxin (0.75 mg.) in another sheep a similar effect was obtained, though not quite as pronounced as in Sheep H.

These results may be explained tentatively on the following assumptions: Insulin causes an accumulation of glycogen in the liver, simulating the condition in a well fed animal; subsequent administration of thyroxin produces the marked hyperglycemia due to increased glycogenolysis, shown in Curve C. A preliminary administration of thyroxin increases sugar metabolism, depletes the glycogen store, thus simulating the condition in a poorly nourished animal, when recovery from a subsequent administration of insulin occurs, the normal blood-sugar levels are not reached therefore within the usual time.

This work was carried out under a grant from the Heckscher Research Foundation to Professor Sutherland Simpson. Further work is in progress on the relations of thyroxin and insulin, and their possible application to the assay of insulin.