

the intestinal capillaries, the blood from an intestinal vein is not different from that from the jugular vein.

We find therefore that marked damage to the liver and intestine fails to induce acidosis, and that the kidney also is not a necessary factor. We believe at present that the condition essential is an injury to the muscle capillaries.

55 (1637)

The glucose mobilization rate in hyperthyroidism.

By **BERTRAM J. SANGER.**

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The work presented here is a preliminary report of some special investigations we have undertaken during the past twelve months at the Presbyterian Hospital in order to shed more light on the complex problem of hyperthyroidism. The decreased sugar tolerance, so frequently found in this condition, was taken as our point of departure. It occurred to us that the study of the respiratory quotient and the blood sugar at frequent intervals after glucose ingestion might give us a good deal of information as to how cases of Grave's disease utilize carbohydrate.

In brief, our procedure was as follows: the metabolism determinations were made with a 90-liter Tissot apparatus, using a Siebe-Gorman mask and Douglas valves. Samples of gas were taken over mercury in the usual way and were analyzed in duplicate in a Haldane gas analysis apparatus and in triplicate if the two analyses did not check satisfactorily. Previous to the use of the Haldane apparatus each day an analysis of outside air was made as a control. The usual technique was observed as to the preparation of the patient—14 to 16 hours fast and absolute rest for thirty to sixty minutes before the start of the determination.

After obtaining two basal periods each of ten minutes, blood was taken for a fasting blood sugar. The patient was then given a dose of glucose made as palatable as possible with a small amount of fruit juice. For the most part, a standard dose of 1.75 grams

per kilo bodyweight was used. Twenty minutes after the glucose ingestion, the metabolic rate was determined, for a period of ten minutes if possible, and for the next two and a half hours, a determination was made each half hour. Blood was taken for blood sugar estimations 15 minutes, 60 minutes and 120 minutes post glucose. In all six normal controls and eight very definite cases of hyperthyroidism were studied.

The results were analyzed and plotted in the following way: with the fasting blood sugar, the fasting respiratory quotient and the basal metabolic rate taken as zero, the rise after the standard glucose dose was charted from this point, the blood sugar and respiratory quotient directly, and the metabolic rate as the percentage rise above that of the basal period.

In the first place, it was noted that the fasting respiratory quotient of hyperthyroids was somewhat lower on the average than that of the normals. The most striking finding, however, was the very rapid rise of the respiratory quotient in the hyperthyroid to a high level, approaching 1.0—a total carbohydrate respiratory quotient, some even going slightly above unity—and the maintenance of this high level, throughout the two and a half hours, while the normal controls rose more slowly, rarely reaching a figure much above .90 and tending to drop a little before the end of the experiment.

The typical blood sugar curve was found in all but one of the eight cases of Grave's disease studied. This patient was distinctly different from the others however. His metabolic rate was 53 per cent. above the normal, he had all the classical findings—positive eye signs, soft vascular struma, tremor, tachycardia and besides auricular fibrillation—yet in spite of all this, he was not losing weight and had no creatinuria on a creatin free diet. Glycosuria was likewise absent in this patient following the glucose tolerance test, though it was found in six out of seven of the other cases in this series. The respiratory quotient curve also did not fit in with the other curves obtained. Obviously his carbohydrate metabolism was not greatly deranged.

The comparison of the change in the metabolic rate between the normals and the hyperthyroids was very confusing. When plotted alike, the percentage rise above basal was much less in

the cases of Grave's disease than in the controls. This may give an erroneous impression however, as it has been suggested that the abnormal cases should be figured on the basis of what the rise in calories would have amounted to had the patient's metabolic rate been normal. When figured in this way the two curves are very much alike. It seems likely therefore that the specific dynamic action of carbohydrates is much the same in both normal controls and cases of hyperthyroidism.

It seems fairly plausible from an analysis of the blood sugar and respiratory quotient curves that the hyperglycemia and low sugar tolerance so frequently found in Grave's disease are not due to any inability of the tissues to burn carbohydrate, but very probably to a decreased ability of the liver to store it. This is further substantiated by approximate calculations of the grams of carbohydrate burned. If 15 per cent. of the calories are assumed to have been derived from protein and the rest apportioned to carbohydrate and fat according to the respiratory quotient (table of Zunst and Schumburg) and the grams of carbohydrate metabolized, then figured from this, it will be seen that the increase in the amount of carbohydrate burned is very great in the hyperthyroids and very slight in the normals—that is, the normals are apparently storing carbohydrate while the hyperthyroids, stimulated by the carbohydrate plethora, are burning it. This fits in very well with the work of Cramer and his collaborators in England and Kuriyama in this country, who have found that thyroid fed animals (white mice and rabbits) on high carbohydrate diets showed only traces of glycogen in the liver, while control animals showed normal amounts. This would account for the low fasting respiratory quotient in thyroid disease, and would explain a clinical observation that has been noticed by some observers—namely, that it is very easy to produce acidosis in a hyperthyroid. One case in point, on the surgical side of the Presbyterian Hospital (History No. 30699), who was in for the treatment of hyperthyroidism and who had glycosuria on a regular diet, went into severe acidosis on being put on the standard strict diet (10 Carbohydrate — 100 Protein — 120 Fat) in an attempt to clear up the glucosuria.

In all the eight cases of Grave's disease studied, there was an original increase in the total metabolism of 30 per cent. or over;

in all but one case there was an increase in the carbohydrate metabolism as manifest by the high respiratory quotient and the calculated amount of carbohydrate burned. The plethora of carbohydrate in the blood stream might account for this stimulation of carbohydrate metabolism. All the evidence seems to point to the fact that the liver has a decreased ability to demobilize carbohydrate from the blood stream—or perhaps there is a hypermobilization rate.

56 (1638)

**On a volatile sperm-stimulating substance derived from
marine eggs.**

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Sea urchins eggs suspended in sea water secrete a sperm-stimulating substance studied by Jacques Loeb and H. M. Fuchs, as well as the sperm-agglutinating substance investigated by Frank Lillie and O. Glaser. From preliminary experiments carried out last season at Woods Hole, it appears that this sperm-stimulating substance may be derived from the eggs of the sea urchin, star fish and sand dollar; that it is non-specific and is a comparatively simple volatile, organo substance, a product of enzymatic action or fermentation within the cell.

This substance, the exact constitution of which is not yet known, may be distilled from a neutral, acid or alkaline extract, the first distillate exerting an effect almost equal to that of the original extract. It is not destroyed by heating in a sealed tube in an autoclave for several hours, in a neutral or alkaline solution, but is weakened by heating with acid. It is very rapidly destroyed by iodine and other oxidizing agents, a brief exposure to N/5000 or N/10000 iodine solution causing a lowering in its stimulating activity of at least 100 to 1. This substance, when added to quiescent or attenuated sperm, greatly increases the facility with which the eggs are fertilized by the sperm.

A large number of simple volatile organo substances of the type