with that when benzoate is given during starvation. Under like conditions the administration of meat protein results in a small increase in hippuric acid formation, while administration of gelatin, with its content of 25 per cent of glycine, causes a marked increase in the output of the substance.

When the pig was under the influence of benzoic acid certain reducing substances were eliminated in the urine, which were determined quantitatively, using Benedict's method for sugar. It was found that the quantity is largest when casein is the food given and smallest when gelatin is given, pointing to an inverse relation to the preformed glycine content of the protein ingested. The separation and identification of these glycuronates is being attempted. There is undoubtedly an increased N elimination when benzoic acid is administered, which supports the conclusion of those investigators who claim that an elevated protein metabolism follows its ingestion.

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Some cardio-vascular changes accompanying insulin hypoglycemia.

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It is evident from perfusion experiments on an isolated mammalian heart that this organ can functionate for several hours on its own stores of energy. Locke and Rosenheim[1] showed that the addition of glucose to the perfusion fluid produces a beneficial and sustaining effect upon the heart and that in turn this substance appeared to be actually utilized. More recently Hepburn and Latchford[2] have observed an increase in the sugar utilization of the isolated heart of over threefold when the pancreatic hormone was added to the perfusion fluid. These consid-

1 Locke and Rosenheim, *J. Physiol.*, 1904, xiv, 31.

2 Hepburn and Latchford, *Am. J. Physiol*, 1922, lxii, 177.

erations indicate, therefore, that not only is the isolated heart capable of taking up carbohydrate for its activity but that its utilization of this substance is greatly augmented by insulin.

The energy requirements of the heart beating outside of the body are obviously much less than they are when *in situ*. Can the heart continue functional activity without impairment very long under the conditions of high pressure and rate prevailing in the body, when its supply of carbohydrate is practically cut off from the circulating blood and its own capacity for using up this substance is increased?

In the present experiments hypoglycemia was produced by giving large doses (20-30 units per kg.) of insulin. The activity of the heart was studied by means of intraventricular pressure and ventricular volume curves, and the electrocardiogram. The vascular system was studied by means of optically recorded central arterial pulse tracings.

All of the experiments were performed on dogs. It was necessary to have an anesthetic that did not influence the blood sugar and for this we have obtained very satisfactory results with a new hypnotic iso-amyl-ethyl-barbituric acid.*

The mean blood pressure taken over periods of three to four hours shows a decline of not more than 20 to 30 mm. Hg. The intra-arterial pulse tracings, recorded from the carotid artery, exhibit only slight changes in form even in those instances where the blood sugar was maintained for two hours at a figure not exceeding 0.05 per cent. The change in pulse form consists of a more rapid primary rise followed immediately by the prediastolic fall. These characteristics of the pulse form become very marked in extreme relaxation of peripheral tone. Since these changes appear in a very moderate degree in these experiments we interpret it to mean that there is little primary change in the peripheral vessels accompanying the hypoglycemia.

The experimental results on the activity of the heart under low blood sugar seem to indicate a lessening of the dynamic function of this organ. The conduction function of the heart as shown by the electrocardiogram presents insignificant changes both in the auricular-ventricular conduction (P-R interval) and in the conduction through the ventricle (Q. R. S group). On the other

* Kindly supplied by Eli Lilly & Co.

hand there is shown in many instances a change in the form or an actual inversion of the T-wave during the progress of the experiment. The significance of this wave is still a matter of some doubt but there is much evidence in support of the view that it is an expression of the potential differences following muscular activity and as such undergoes modifications through influences that alter the muscular process.

In the records of intraventricular pressure we have an index of the dynamic capacity of the heart. The curves obtained in these experiments from hearts acting under a low blood sugar show a lengthening of the isometric period, or the phase of developing tension and a marked decrease in the maximum pressure developed during systole. We have also noted that the hearts in the animals with low blood sugar do not withstand the experimental procedures as well as those of normal animals. In some experiments where the heart was exhibiting a much weakened condition we have tried intravenous injections of glucose and have been able in this way to restore greatly its action as shown by the higher intraventricular pressure developed.

In two experiments we have recorded the volume changes of the heart by the cardiometer method as this technique seems less likely to interfere with the heart action. The results of these experiments confirm the changes already noted from the ventricular pressure records.

SUMMARY

In the hypoglycemia following the administration of large doses of insulin to dogs the experimental results show:

1. A small decline in mean blood pressure.
2. Slight alterations in the intra-arterial pulse curve.
3. No conduction time changes in the heart as signified by the electrocardiogram. The T-wave in some instances changed in form and in some instances inverted.
4. A lengthening of the period of developing tension of the ventricle and a decrease in the maximum pressure developed. Some restoration of ventricular activity by injecting glucose.