Editorial

Glucagon—A New Hormone

Glucagon, also known as the hyperglycemic-glycogenolytic factor of the pancreas, is a protein or polypeptide which has just been crystallized by Staub and co-workers at the Lilly Research Laboratories.[1] But that there was a "contaminant" in insulin, which had the effect of transiently elevating the blood sugar, had been known for thirty years. A great deal of interest has centered about this substance recently, but the difficulty in separating glucagon from insulin proved to be a stubborn hurdle. However, the information available to date clearly suggests that this substance will be of clinical significance to physicians in the future.

It appears almost certain that glucagon is a hormone secreted by the alpha cells of the islets of Langerhans in the pancreas. One, if not the major, action of glucagon is to increase the amount of active phosphorylase in the liver. This has the effect of increasing the breakdown of liver glycogen—glycogenolysis—resulting in a rise in blood sugar. There is a possibility that glucagon is controlled by the growth hormone (or the "diabetogenic hormone") of the anterior pituitary. There is also some experimental evidence suggesting that glucagon inhibits glycogen formation under certain conditions and that it has an anti-insulin action.[2] Foa[3] has indicated, by cross-circulation experiments, that glucagon bears a reciprocal relationship to insulin, the secretion of both perhaps being dependent on the blood sugar level. Finally, the actions of glucagon may eventually explain the differences between alloxan and pancreatectomy diabetes—the differences presumably being due to the presence of glucagon in the former, and its absence in the latter.

Clinical studies with relatively purified materials have been limited. By catheterizing the hepatic vein, Myers *et al.*[4] have shown that glucagon promptly produces a rise in the sugar in the blood leaving the liver.

Likewise, glucagon may be part of the explanation of the significant differences between "stable" and "unstable" human diabetes. Kirtley, Waife, and Peck[5] studied the response of blood sugar and serum inorganic phosphorus in various types of diabetic subjects compared to normal persons. The unstable diabetic had almost a normal blood sugar curve and had a normal fall in inorganic phosphorus. That is, in these subjects the presence of glucagon modified the blood sugar and phosphorus reactions resulting in curves which were different from those following simple exogenous glucose as in a tolerance test. The stable diabetic, on the other hand, showed the typical reaction expected in this disorder—a "diabetic type" glucose curve and poor phosphorylation.

It is clear that many questions remain to be answered, and problems solved, before the significance of the "alpha-cell hormone" is fully appreciated. The role of glucagon in the pathogenesis of human diabetes, in insulin-resistance, in spontaneous hypoglycemia, glycogen-storage disease, Kimmelstiel-Wilson syndrome, and other clinical states remains to be discovered.

An ingenious theory, attributed to Bürger,[2] states that normally "alimentary hyperglycemia evokes early discharge of glucagon and

insulin, causing the hepatic reserves of glycogen to be mobilized and stored in the periphery, thus preparing the liver for the uptake of the newly absorbed glucose." Here, then, is the possibility that our knowledge of man's utilization of carbohydrate will be enhanced when we learn more about the "newest" of the hormones—glucagon.

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Life in a Test Tube?

From time to time there appear articles in scientific journals that stir the imagination, not alone by their scientific ingenuity but by their deeper and more profound philosophical implications. One such brief report (Miller, S. L.: A production of amino acids under possible primitive earth conditions, *Science* 117: 528, May 15, 1953) has the touch of simplicity often found in significant contributions.

It has been suggested previously that the organic compounds "that serve as the basis of life" were formed when the earth had an atmosphere of water, hydrogen, ammonia, and methane—instead of carbon dioxide, nitrogen, oxygen, and water, as it has at present. Since electrical discharge may have also played a significant role in the formation of compounds in the primitive atmosphere, Miller (at the University of Chicago) prepared a simple apparatus which circulated methane, ammonia, hydrogen gases in the presence of water and water vapor past electrodes, which, it was hoped, would form free radicals. Water was boiled, mixed with the gases, circulated past the electrodes, and condensed, to empty back into the boiling flask. It was noted by the end of the week of slow circulation by this method that the aqueous solution became red and turbid. The turbidity was due to colloidal silica from the glass and the red color due to organic compounds absorbed on the silica.

By paper chromatography it was shown that a number of amino acids were now present in the solution. On this basis, glycine alpha-alanine, and beta-alanine were identified. The amino acids were not due to living organisms because growth was prevented by the boiling water during the run and by the presence of certain chemicals such as mercuric chloride, barium hydroxide, and sulfuric acid used during the analysis. It was also noted that it was possible that aspartic acid and various other amino acids, which have not as yet been identified, may have been present in smaller concentration.

As the author mentions, this apparatus was an attempt to duplicate the primitive atmosphere of the earth and not to obtain optimum conditions for the formation of amino acids. Nevertheless, it is conceivable that by modification of this system a higher and different yield of amino acids may be accomplished.

If this finding can be substantiated it will not only open up new fields for research but may present a hint as to those momentous events when the earth was cooling many cons ago, events which led to the development of the greatest enigma of all—life.