Group Discussion

GEORGE E. ANDERSON, M.D., (*Brooklyn*): We observed a dog for seventy-two days on 250 mg. per kg. per day. There were no observable changes whatsoever in the islet cells, certainly none in the alpha cells. This corresponds with Dr. Goldner's findings.

A. E. RENOLD, M.D., (*Boston*): I was interested in Dr. Izzo's observations on prolonged glucagon administration. It was not quite clear when the last dose of glucagon was administered before the fasting blood sugar was done. I also wanted to ask whether or not you have given glucagon over prolonged periods of time as in studies on normal subjects. It seems to me perhaps a little questionable whether one can interpret rises in blood sugar as meaning exacerbation of the diabetic state when the glucosuria did not increase. Perhaps the glucosuria is a better indication of over-all diabetic control than just one blood sugar value after giving an agent which affects blood sugar per se.

JOSEPH L. IZZO, M.D., (*Rochester, New York*): The glucagon was given at 7 o'clock, and the blood sugar was taken at 8:30. The administration of 6 mg. of glucagon daily caused a change in blood sugar from 100-150 mg. to about 300 mg. The most interesting feature is that this person then instead of having little or no glucose output increased it to 60 or 80 gm. per day. In addition there was a change in nitrogen balance and a fall in plasma inorganic phosphorus. But the most significant finding is this consistent effect on nitrogen balance. Whether this is due to glucagon itself or to some impurities in the glucagon, I can't say at the present time.

As for your other question about experiments on normals—we plan to use normals as controls. One of the difficulties in interpreting experiments on glucagon in normal individuals is that glucagon stimulates the pancreas to secrete insulin because of the increase of the blood sugar. We wanted to study the effect of the drug where the central secretion did not compensate for rises in blood sugar. We were surprised that glucagon could have a marked effect on blood and urine sugar if there is presumably no compensatory secretion of insulin.

LAURANCE W. KINSELL, M.D., (*Oakland, California*): As an assumption, those patients who respond to sulfonamide also make insulin. Also by assumption they don't do quite a normal job of it; otherwise they wouldn't be diabetic. The fact that they do respond and are not in the proteinuric-ketonemic group means that unquestionably they make perhaps quite appreciable amounts of insulin. Second, as I recall your figures, your increases, with perhaps one exception, were in urinary sugar predominantly in those patients who initially had high levels of blood sugar.

FRANCIS D. W. LUKENS, M.D., (*Philadelphia*): Dr. Izzo, what diet did you put those patients on?

DR. IZZO: Diets of approximately 2,000 calories with 90 gm. of protein, 200 gm. of carbohydrate, and about 100 gm. of fat.

Effects of Sulfonylurea Drugs in Hospitalized Diabetic Patients

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The published literature available to us now (September, 1956) contains reports of at least 1,035 patients treated with the sulfonylurea compounds, and doubtless many times this number have actually received the drugs. As nearly as can be ascertained, all but thirty of these patients have been studied and evaluated by methods which are either incompletely described or, in our opinion, inadequate to permit valid conclusions as to the efficacy of the treatment. Unpublished reports presented at this symposium are not included in this survey.

Methods that are satisfactory for such studies include the use of patients with well-established diabetes of relatively remote onset, hospitalization (preferably on a metabolic ward), a sufficiently long fore-period to ensure a stabilized diabetic state, provision of a diet that maintains body weight, administration of the test substance when blood and urine sugars are fairly constant or rising, and the employment of changes in well-marked hyperglycemia and glycosuria rather than changes in the so-

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