

lowing hypophysectomy of the rabbit, they are apparently normally dependent to a degree upon the anterior pituitary. In the young animal they may form in response to gonad-stimulating substances before the follicle granulosa is capable of responding, and alternately, may fail to appear when the granulosa shows prompt and widespread luteinization during treatment. The possible effects upon them of continued gonadotropic treatment, such as can be seen in the theca of the rat, may be obscured by the rapid development of refractory states in the rabbit. Other features of their reactions indicate that they are not strictly comparable with the luteinized theca cells of the rat and guinea pig. In very young rabbits gonadotropic extracts may produce corpora lutea without eliciting a progestational uterine reaction.

8489 P

Blood Pressure Responses to Insulin.

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Kugelmann¹ reported 7 cases of angina pectoris who developed an elevation in blood pressure and substernal pain during hypoglycemia induced by the intravenous administration of insulin. The attacks of substernal pain and symptoms brought about by this procedure were similar to those which occurred spontaneously in these patients under ordinary circumstances. The studies of Kugelmann suggested to us using insulin hypoglycemia as a method of determining blood pressure responses. We have studied the blood pressure and blood sugar changes in normal individuals, in patients with essential hypertension, and in cases of Addison's disease following the intravenous administration of insulin. In each case a blood sugar determination (Folin Micro-method using venous blood) was made following a 12-hour fast; 15 units of insulin (Mulford) were then given intravenously, and subsequent blood sugar determinations made every 10 minutes for 90 minutes. To circumvent the effects due to emotional disturbances from repeated vena punctures only one puncture was made and the lumen of the needle kept

¹ Kugelmann, B., *Klin. Wochenschr.*, 1933, **12**, 1488.

unobstructed by a flow of 1 cc. normal saline per minute. Blood pressure readings with the patient supine and resting were made every 10 minutes for one-half hour preceding the test and every 2 minutes following the administration of insulin.

In 25 normal individuals following insulin and at a variable time interval, but usually within the first 40 minutes, there was a drop in blood sugar to an average level of 30 mg. % without any appreciable changes in blood pressure. There then occurred a sharp rise in blood pressure averaging 40 mm. Hg., systolic, and 7 mm. Hg., diastolic, over the previous readings. With this event the blood sugar rose from 30 mg. % to 46 mg. % with a gradual return to the fasting level. In the study of 20 cases of essential hypertension, the same phenomena occurred in a more striking fashion. The initial fall in blood sugar following insulin was to an average of 40 mg. % without changes in blood pressure. The blood pressure then rose sharply above the previous readings 70 mm. Hg. systolic, and 20 mm. Hg. diastolic. In most cases there was a fall in blood pressure to below the original reading during the so-called crisis of hypertension. However, this fall lasted in most instances for not longer than a period of 2 or 3 minutes and the blood pressure would return to levels much higher than the original readings. This phenomenon was of a variable character. The blood pressures would then be sustained at higher levels for a duration which varied from 30 minutes to 2 hours. The rise of blood sugar at the point of the maximum initial increase of blood pressure was from 40 mg. % to 60 mg. %. Four patients with Addison's disease had an initial drop in blood sugar following insulin to 20 mg. %. This level of hypoglycemia lasted for 2 hours with a subsequent slow and gradual elevation in blood sugar in the next 3 hours. The blood pressures showed no changes whatsoever during this experiment. Controlled studies were carried out in diabetics who after having attained a hypoglycemic state with insulin responded in the same fashion as normal individuals. Insulin in varying amounts given intravenously and covered with dextrose failed to produce any reaction.

To test further the mechanism responsible for these phenomena controlled experiments were carried out with the cooperation of Dr. C. W. Walter in 2 normal dogs, which were subsequently adrenalectomized. In their normal state following intravenous insulin (1 unit per kilo) they showed a drop in blood sugar from 90 mg. % to 25 mg. % without changes in blood pressure. At this level there was a sharp rise in both systolic and diastolic tensions (from 125 mm. Hg. to 200 mm. Hg. systolic and from 80 mm. Hg. systolic

to 120 mm. Hg. diastolic). With this episode the blood sugars rose from 25 mg. % to 45 mg. % with a subsequent slow rise to normal. There were no changes in blood pressures in the adrenalectomized dogs. From these investigations we concluded that insulin hypoglycemia is an adequate method for studying changes in blood pressure, and that this hypoglycemic condition calls forth a secretion of adrenalin which is responsible for the sudden elevation in blood pressure and the initial rise in blood sugar. As far as adrenalin is concerned, the response of the hypertensive person is excessive, whereas the response in the patients with Addison's disease is negative.

8490 C

Diazotization of Proteins.

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Proteins treated with nitrous acid are said to be "diazotized" insofar as, like true diazonium compounds, they couple in alkaline reaction with substances containing an aromatic OH or NH_2 group, often forming a colored compound resembling the azo dyes. This reactivity of proteins is puzzling, since there is no known primary aromatic amine in protein which would react with HNO_2 to form a diazonium compound. Flick¹ contended that the reactivity of wool treated with HNO_2 was due to the formation of a nitroso rather than a diazonium compound. More recently, Morel and Sisley,² confirming previous work by Landsteiner³ with salicylic acid, have reported that tyrosine treated with nitrous acid forms a diazonium compound which couples with naphthol to form azo dyes. They therefore ascribed the reactivity of diazotized protein to its tyrosine content. Their contention remains plausible even if tyrosine forms a nitrosophenol instead of a diazonium compound on treatment with HNO_2 , as found in the case of phenol by Baeyer and

¹ Flick, *Bull. Soc. Chem.*, 1899, **69**, 221. Quoted from Morel and Sisley.

² Morel, A., and Sisley, P., *Bull. Soc. Chem. de France*, 1927, **41**, 1217; 1928, **43**, 881.

³ Landsteiner, K., *Centralbl. Physiol.*, 1895, **14**, Oct. 5.