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Blood Sugar Response to Intravenous Insulin in Normals and in Diabetics.

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Studies in the literature lead one to conclude that the blood of diabetics contains a substance that has an inactivating influence upon insulin. Some observers have been led to believe that this phenomenon plays a rôle in the pathogenesis of diabetes mellitus. Karelitz[1] studied the effect of insulin after its incubation with normal and diabetic serum and found that diabetic serum has a definite retarding influence upon the activity of insulin. He concluded that diabetic serum contained an anti-insulin substance. Loewi[2, 3] has recently withdrawn his previous hypothesis that the liver elaborates a substance that is capable of inactivating insulin. He called this substance glykamin. Epstein[4] believed that the presence of trypsin in the blood inactivates insulin and thought that this is the cause of diabetes.

On the basis of such conclusions, one may reasonably suspect that equivalent intravenous doses of insulin would show a less marked depression in blood sugar in the diabetic than in the normal individual. We, therefore, undertook a study of the comparative response of the blood sugar of the normal and diabetic subjects to the intravenous administration of insulin.

Method. The intravenous route was used in order to eliminate the factor of absorption from the subcutaneous tissue. Twelve diabetic patients, encompassing a wide variation in severity and age incidence, were selected for these studies. Two normal human beings and a normal dog were used as controls. The blood sugar content was studied by the Folin-Wu method. Lilly insulin of U 20 strength was employed. 0.2 of a unit of insulin per kgm. body weight was given in all the cases. This dose was selected on the basis of preliminary trials, as the desirable optimal dose for these experiments. The fasting blood sugar was obtained after a 14-hour fast and blood was taken at the following intervals after the intra-

[1] Karelitz, S., Cohen, P., and Leader, S. D., PROC. SOC. EXP. BIOL. AND MED., 1928, **26**, 11.

[2] Loewi, O., *Wien. Klin. Woch.*, 1926, **39**, 1074.

[3] Loewi, O., *Wien. Klin. Woch.*, 1928, **8**, 391.

[4] Epstein, A. A., *J. Am. Med. Assn.*, 1925, **85**, 29.

TABLE I.

Name	Age Yrs.	Fasting Blood Sugar	Insulin 0.2 U per Kgm.	Blood Sugar After Insulin in Hours mgm. per 100 cc. blood										Total Drop mgm. %	Time of Max. Drop
				¼	½	¾	1	1½	2	2½	3	4	5		
		Normal													hr.
H. G.	30	117	13.0	119	74	89	95	110	111	108	106			43	½
W. C.	32	114	14.0	107	67	82	89	87	109					47	½
Dog		93	3.4	96	46		50	63	90	95	98			47	½
		Diabetic													
S. C.	8	363	5.0	342	236	204	187	141	113		88			275	3
Y. K.	9	151	4.3	149	120	82	83	81	91		85			70	1½
M. G.	12	193	9.0	126	100	80	99	103	104	130				113	¾
A. E.	13	365	5.0	312	262	229	198	131	119	102				253	2½
J. L.	24	303	13.0	295	248	219	197	153	129	104	111			199	2½
B. L.	14	269	7.8	228	147	92	78	85	97	102	106			191	1
M. S.	44	203	12.0	158	136	114	97	100	96	111	107			106	1
M. G.	51	195	15.0	110	65	72	80	90	106	111				130	½
T. K.	25	220	11.0	191	162	116	100	75	70	78	77			152	1½
S. C.	8	398	6.0				195		86		62	66	86	336	2½
M. W.	11	133	9.0	111	102		67	61	65	62	63			72	1½
K. M.	19	278	11.0	263	244	189	166	123	111	78	64			214	3

venous administration of insulin: ¼, ½, ¾, 1, 1½, 2, 2½, 3, 4, and 5 hours.

Results. It will be observed from the accompanying table that

in the three control experiments there was a uniform response to the injection of intravenous insulin. It is noted that there is a 15-minute refractory period, during which time the blood sugar level remained essentially the same as it was before the insulin was administered. At the end of ½ hour, the blood sugar dropped precipitously to its lowest level. Within 45 minutes after the injection, the blood showed evidence of rapid recovery of its sugar content. The total drop in these 3 control experiments was between 43 and 47 mgm. %. In both humans there occurred mild symptoms of hyper-insulinism, which lasted about 5 minutes, from which there was a spontaneous recovery.

It is seen from the table that in most of the diabetic patients there existed no refractory period, that the blood sugar showed evidence of rapid drop 15 minutes after injection. The depression continued for a much longer period than in the normals. In the milder diabetics, the maximum drop occurred from 45 minutes to 1 hour after injection, and in the severest diabetics the blood sugar was still dropping at the end of 3 hours. The total drop in blood sugar ranged between 70 and 336 mgm. % in the various cases, and the higher the initial fasting blood sugar the greater the total drop.

This enormous drop in blood sugar in diabetics of 70 to 336 mgm. %, is far different from the disappearance of an average of 43 to 47 mgm. % in controls, with the same dose of insulin. It seems difficult to reconcile the conclusions drawn from such results, with the possibility of the presence of an inactivating substance in the blood of diabetics. The presence of such a substance should prevent such phenomenal depressions. The nature of this response resembles the results obtained by Thaysen,[5] and Norgaard and Thaysen.[6]

It is interesting to mention that the symptoms of hyper-insulinism occurred with blood sugars of 74 and 67 mgm. % in the normal, and of 75, 78, 65, 61, and 62 mgm. % in the diabetic patients. The blood sugar of one diabetic reached 64 mgm. % without any symptoms. The symptoms existed at the lowest level of the curve and all these cases recovered spontaneously.

Conclusions. Equivalent doses of insulin on the basis of body weight when administered intravenously, produce a much greater depression in the blood sugar level in diabetics than in normals. This seems to indicate the absence of any substance in the blood of diabetics which might inhibit insulin action.

[5] Thaysen, T. E., Hess, *Hospitalstidende,* 1930, **73**, 357.

[6] Norgaard, A., Thaysen, T. E., Hess, *Hospitalstidende,* 1929, **72**, 881.