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THE EFFECT OF PHLORIDZIN ON THE MORTALITY FROM INSULIN HYPOGLYCAEMIA IN MICE

by

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(Submitted for publication 22nd December, 1923.)

Previous experiments (3) in which Insulin was administered to phloridzinized mice appeared to indicate that Phloridzin increases their tolerance for the hypoglycaemia produced by Insulin. The following investigations were undertaken to ascertain whether Phloridzin has any definite effect upon the mortality from over-doses of Insulin.

Phloridzin was administered to a number of healthy young mice, averaging 21 grams in weight, and the animals were thereafter starved for 24 hours. A similar number of normal mice were starved for 24 hours and employed as controls.

Insulin was then administered subcutaneously to both the phloridzinized and the normal mice. Three different dosages of Insulin (see table which follows) were administered.

All the animals went into deep coma, with convulsions at intervals, and in some cases displayed the deep convulsive inspirations symptomatic of "air-hunger." Death resulted much sooner in the normal than in the phloridzinized animals, in which it was often greatly delayed, more than half the animals recovering.

As will be seen from the table of experimental results, only one out of fourteen normal animals survived, while eight out of fourteen phloridzinized animals recovered. Of the five phloridzinized mice which received the smallest dose of Insulin, all survived, while only one of the corresponding controls recovered. Food was not given to the animals until 20 hours after the administration of Insulin.

The "antagonization" of the toxicity of Insulin by Phloridzin might be explained by the hypothesis that the Phloridzin breaks up, to some extent, a glucose-complex in the blood, the synthesis of which is accomplished or accelerated by Insulin, and that it is this glucose-complex which is oxidized, or removed in some manner, causing the hypoglycaemia which normally succeeds the administration of over-doses of Insulin.

That Phloridzin produces some impairment of the sugar-burning mechanism

has been suggested by Nash and Benedict (2). Loewi (1) has put forward the theory that the action of Phloridzin in normal animals is to split a combined form of glucose, the free glucose being eliminated by the kidney. However, no very definite explanation of the phenomenon can as yet be offered, in view of our present very imperfect knowledge of the nature of the normal blood-sugar.

EXPERIMENTAL RESULTS.

INFLUENCE OF PHLORIDZIN UPON THE MORTALITY DUE TO OVERDOSAGE OF INSULIN.

Normal, starved 24 hours.				Phloridzin 16 mg., starved 24 hours.			
Mouse No.	Wt. gm.	Insulin Kg. Rabbit Units.	Results.	Mouse No.	Wt. gm.	Insulin Kg. Rabbit Units.	Results.
1	21	0.20	died in 4 hrs.	2	20	0.20	died next day.
3	22	0.20	died in 4 hrs.	4	19.5	0.20	died next day.
5	20.5	0.20	died in 4 hrs.	6	21.5	0.20	Convulsions, but recovered.
7	18.5	0.20	died in 2 hrs.	8	19	0.20	died in 2 hrs.
9	20.5	0.166	died in 2 hrs.	10	22	0.166	died in 5 hrs.
11	21	0.166	died in 2 hrs.	12	24.5	0.166	Convulsions and coma, but recovered.
13	20.5	0.166	died in 3½ hrs.	14	21	0.166	died in 3½ hrs.
15	21	0.166	died in 2 hrs.	16	21	0.166	died in 7 hrs.
17	18	0.166	died in 2 hrs.	18	21.5	0.166	Coma and convulsions, but recovered.
19	22	0.10	died in 3 hrs.	20	21.5	0.10	Coma and convulsions, but recovered.
21	19.5	0.10	died in 2 hrs.	22	22.5	0.10	Coma and convulsions, but recovered.
23	20.5	0.10	Coma and convulsions, but recovered.	24	21	0.10	Coma and convulsions, but recovered.
25	19.5	0.10	died in 3 hrs.	26	21	0.10	Coma and convulsions, but recovered.
27	19	0.10	died in 5 hrs.	28	19.5	0.10	Coma and convulsions, but recovered.

CONCLUSION.

Phloridzin, in some manner which is yet to be explained, decreases the mortality from Insulin hypoglycaemia, but has no effect on the convulsions and other physical symptoms which accompany this hypoglycaemia.

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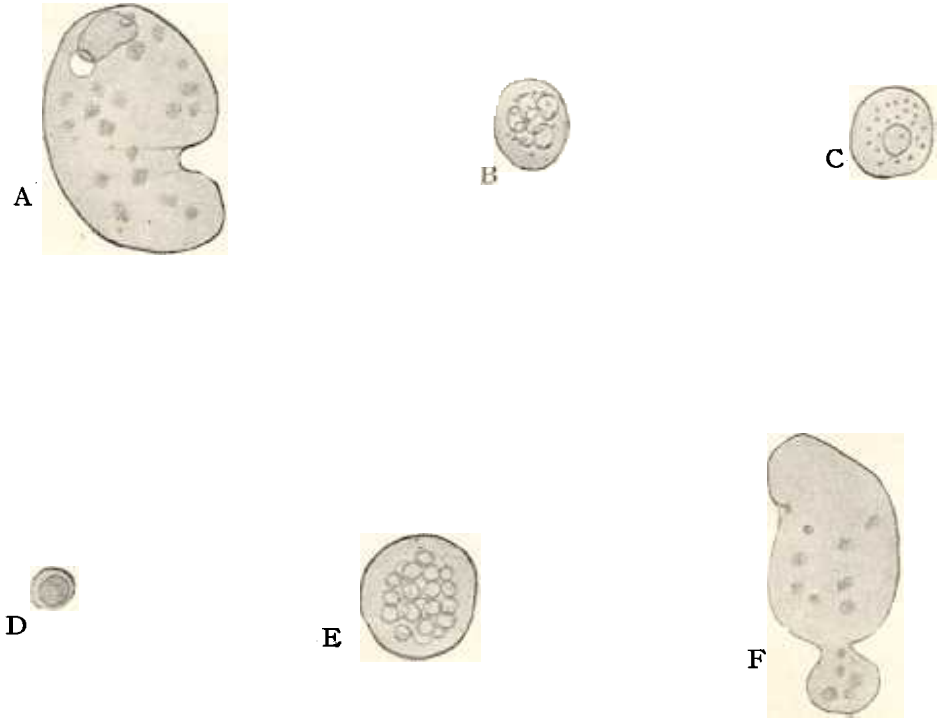


Fig. 5.

A, a normal individual of *Colpidium* Sp. B, C, D, E, and F, abnormal forms found in cultures arising from repeatedly washed individuals. B and C, no mouth, cilia shorter than usual, rotating movement. D, motionless. E, ciliated and undergoing slow rotation. F, swimming rapidly and producing one of the small forms illustrated in B, C, and E by undergoing fission at the posterior extremity. Cilia are not indicated.

(Drawings by Dr. O. W. Tiegs from Culture B.65 on the fifth day. This culture arose from two individuals, each of which had undergone two washings after isolation from the parent culture.)