

million parts of blood. The method is applicable to codein, heroin, and quinin, and almost certainly to nearly all the common vegetable alkaloids. Morphin is extracted less readily than most of the alkaloids.

About 20 per cent of an intravenous dose of codein was recovered from blood drawn immediately after the injection. Quinin was recovered from blood drawn at once after the intravenous injection in the cat, but very small amounts were present in the defibrinated blood.

Urine and bile may be extracted in the same way with slight modifications.

The defibrinated blood of the cat yields less than a milligramme (as a rule) of chloroform-soluble matter.

74 (2597)

The relation of adrenalin to the action of insulin upon the blood sugar content.

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During the course of experimental work on the effect of insulin upon the blood sugar content in rabbits, the question arose as to whether insulin and adrenalin were antagonists.

It is well known that insulin acts by diminishing the blood sugar, while adrenalin increases it. It was, therefore, thought highly probable that the administration of both drugs would result in a neutralization of these effects so that the blood sugar would remain practically normal.

A study of the literature gave support to the assumption. Magenti and Biagotti conclude that adrenalin, when given simultaneously with insulin, acts by strongly disturbing the usual insulin effect. These tests were repeated only for the reason that in the first papers on insulin by Banting and Best, and especially in a recent article by McLeod and Orr, special attention was called to the individual differences in rabbits, for sugar test, after the administration of insulin.

A series of rabbits was tested primarily for the separate effects of insulin and adrenalin.

Insulin was injected in quantities of 0.5 units per 1 kg. body weight. This amount was chosen because our former work, on the differing effects of insulin in different body tissues, was done with like quantities. These quantities seemed sufficient to lower the blood sugar content of normal rabbits markedly, without the danger of an overdosage. Thus convulsions and other by-effects, possibly without determinable manifestation, could be avoided. This seemed necessary because other tests, published recently, have shown that every struggle of the animals is followed by an increase in the blood sugar content, thus disturbing the reading of the exact results of the final findings.

The results of these tests are given in a table, the columns of which represent the values of the blood sugar content in intervals of two hours after the administration of insulin. For an easy comparison the numbers are given in percentage, assuming the original value of the blood sugar in every animal as 0.0.

TABLE I.

Rabbit	Insulin alone subcutaneously		
	2	4	6
58	—63.5	—18.7	4.9
76	—42.5	— 5.5	7.8
78	—62.6	—13.7	— 5.8
79	—40.8	—37.7	—23.8
80	—65.7	— 0.0	0.8
82	—22.8	0.8	5.5
84	— 1.6	— 0.8	1.6
85	—43.0	—15.6	— 8.2
86	—31.6	— 6.7	— 9.6

In the second table the same animals were injected with adrenalin. 0.1 cc. of a solution of adrenalin, 1:1000 was used in each animal, because previous tests developed that this amount of adrenalin would increase the blood sugar, while as much as 0.5 units of insulin would diminish it. Thus, by using the indicated amount of adrenalin combined with 0.5 units of insulin in the first series, a neutralizing result could be expected.

The results of adrenalin in the same rabbits are tabulated as follows:

TABLE II.

Rabbit	Adrenalin alone subcutaneously		
	2	4	6
58	62.3	4.9	— 4.1
76	64.0	26.0	14.0
78	48.8	16.8	0.8
79	30.2	12.2	— 0.6
80	20.2	— 5.6	— 6.5
82	123.0	16.1	—11.5

The columns of Table II demonstrate the blood sugar findings after adrenalin, using the same two-hour intervals as in the insulin tests.

In a third table the results will be found to indicate the changes in the blood sugar content when both adrenalin and insulin were administered:

TABLE III.

Rabbit	Insulin and adrenalin, subcutaneously and simultaneously at different sites		
	2	4	6
58	—33.1	—24.8	5.0
78	—26.8	—41.3	42.3
79	—42.6	—32.5	—25.0
84	13.8	—41.3	28.3
85	26.5	6.0	2.6
76	—45.6	11.9	16.5

The results are not absolutely uniform; but four of the animals unexpectedly showed a decrease in the blood sugar content. In some the four-hour test was surprisingly lower than in the same animal when injected with insulin only.

These findings were more marked when both agents were not given simultaneously, but the insulin injection postponed until 20 minutes after a subcutaneous administration of adrenalin. The results of these findings, tabulated in Table IV, demonstrate unusually low figures in some animals, even in the first and in the second tests.

TABLE IV.

Rabbit	Adrenalin 20 minutes before insulin, at different sites, subcutaneously		
	2	4	6
78	—68.5	—50.0	13.9
80	—40.8	—48.0	— 7.2
82	—19.1	— 6.7	— 0.0
86	—17.1	0.8	— 8.9

An explanation of these facts has hitherto not been furnished. It must be assumed from our experimental experience that the final effect of the injection of insulin and of adrenalin, separately administered, namely the change in the blood sugar content, is not produced by a like mechanism.

If, for instance, insulin would have a direct influence on the liver or on another organ that on its part would cause the blood sugar decrease, adrenalin probably does not act in the same way, merely producing a contrary effect on the organ's function. If so, the action of insulin and adrenalin must eliminate each other like the neutralization of a positive and a corresponding negative power.

In accordance with the findings described, it may perhaps be concluded that adrenalin effects the action of the insulin by blocking its way from the site of administration to the organ which in turn acts upon the blood sugar changes. This assumption would explain the fact, for instance, that in some tests the effect of insulin is postponed and becomes effective after four hours, while usually the principal effect upon the blood sugar takes place two hours after administration.

Neither can the findings shown in Table IV be explained, especially those in which the insulin action is markedly enlarged. Perhaps the stimulation of the sympathetic part of the involuntary nervous system plays a part also in these findings. As there is no definite proof of it, it must be conceded that the reasons are unknown.

Lack of knowledge or of a satisfactory explanation do not affect the importance of a fact. In these interesting biologic processes, represented by the action of insulin and adrenalin in the healthy body, we have had results which must be accepted as positive findings, the cause and significance of which still remain to be established.

The observations have been discussed because they do not agree with the expected results. They show the following conclusions:

1. Adrenalin and insulin, administered to the same animal, do not eliminate their mutual actions.
2. In some instances, adrenalin injections, made simultaneously with the administration of insulin, increase the action of insulin by lowering the blood sugar content more than usual.
3. In some instances, the action of insulin is only slightly

diminished in the first tests (2 hours after administration), while the findings after four hours manifest an increase in the insulin action, usually observed at that period.

4. It has been demonstrated that (in more than 70 percent of the cases examined) the insulin effect is generally not eliminated by adrenalin, but is sometimes enlarged.

5. The reasons for these findings have hitherto not been discovered. They may be based upon an action of the involuntary nervous system.

75 (2598)

Diluting lipid antigen with a constant dropping syphon.

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In order slowly and uniformly to dilute an alcoholic solution of tissue lipoids as required in such serologic methods as that of Meinicke,¹ an apparatus was desired that could easily and quickly be set to deliver water dropwise at a definite rate. Numerous trials by Kohler² indicated that the lipid extract should be diluted in such fashion that seven volumes of distilled water are dropped into one volume of lipid extract in twenty-eight minutes. A stable suspension of fine lipid particles is formed, which obviously should be prepared as often as desired under identical conditions. The syphon herein described is simpler than the floating syphon used by Dreyer and Ward.³

It delivers 49 cc. in exactly 28 minutes, but it can easily be set to deliver other amounts. From the figure the construction is almost self explanatory. The syphon itself is made by bending a piece of heavy wall soft glass tubing twice at right angles in the same plane. For convenience it is held in a rubber stopper perforated horizontally. Two capillary buret tips were attached to

¹ Meinicke, E., *Berliner klinische Wochenschr.*, 1918, Jahrg. lv, pp. 83-96.

² Kohler, E., *Ztschr. f. Infektionskrankheiten d. Haustiere*, 1921, xxi, 288-314.

³ Dreyer, G., and Ward, H. K., *Lancet*, 1921, cc, 956-961.