

The question of the reversal by dissociation of the *biologic effects* of immune reactions may be somewhat clarified in view of the variations of K_c for the successive reactions. Thus, other parameters being the same, a system in which the "neutralization" of a molecule of antigen brought about by reaction with considerably less than g molecules of A might appear irreversible, whereas in a system in which neutralization requires many ($\sim g$) molecules of A , reactivation should be readily demonstrable. In practice, success depends on whether the necessary degree of dilution, and the necessary lapse of time, are experimentally feasible.

The free energy data offered are, of course, subject to those errors,¹ of unknown magnitude at present, affecting the measurement of K_v . The values appear to be reasonable. In fact, Boyd *et al.*⁸ recently assumed that $\Delta F^\circ = -10^4$ cal. for a similar reaction "which goes very nearly to completion but may be reversed experimentally."

We are now studying the phage-antiphage equilibrium,⁴ which is in some respects more amenable to measurement, with the expectation of obtaining a more complete thermodynamic description of this typical immune reaction.

A. D. HERSHEY

WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE,
ST. LOUIS

EFFECT OF INSULIN ON PYRUVIC ACID FORMATION IN DEPANCREATIZED DOGS¹

PREVIOUS work on man has revealed an increase in pyruvic acid in the blood following the ingestion of glucose.² In diabetic subjects no increase in blood pyruvic acid occurred under the same conditions. The administration of insulin together with glucose to these patients resulted in an increase in blood pyruvate.³ In order to study the relationship between insulin and pyruvic acid formation 27 experiments have been performed on 14 depancreatized dogs. The animals were maintained with insulin and pancreatin until 72 hours before each observation. The method for estimating pyruvic acid was modified to eliminate interference by the 2, 4 dinitro-phenylhydrazine of acetoacetic acid.^{4,2}

⁸ W. C. Boyd, J. B. Conn, D. C. Gregg, G. B. Kistia-kowsky and R. M. Roberts, *Jour. Biol. Chem.*, 139: 787, 1941

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² E. Bueding, M. H. Stein and H. Wortis, *Jour. Biol. Chem.*, 140: 697, 1941.

³ E. Bueding, H. Wortis and H. Fein: Unpublished observations.

⁴ D. Klein, *Jour. Biol. Chem.*, 137: 311, 1941.

Experiments on normal animals disclosed a significant rise in blood pyruvate over the fasting value after the intravenous injection of 2 gm of glucose per kg body weight. In depancreatized dogs there was no rise in blood pyruvate after a similar injection of glucose. When insulin was administered simultaneously with the glucose a marked rise in pyruvate occurred (see table I representing a typical experi-

TABLE I
BLOOD PYRUVIC ACID AND BLOOD SUGAR AFTER THE INTRA-
VENOUS INJECTION OF GLUCOSE (2 GM PER KG) INTO A
DEPANCREATIZED DOG (BOTH EXPERIMENTS WERE
PERFORMED ON THE SAME ANIMAL)

Time	No insulin		40 units insulin	
	Blood pyruvic acid mg per cent.	Blood sugar mg per cent.	Blood pyruvic acid mg per cent.	Blood sugar mg per cent.
Before injection	1.28	380	1.14	337
10 min. after	1.23	775	1.35	725
20 " "	1.28	662	...	...
30 " "	1.29	572	2.52	445
45 " "	1.28	515	...	...
60 " "	1.19	478	3.46	279
90 " "	1.22	438	...	...
120 " "	...	...	3.12	243

ment) reaching its maximum from one to three hours after the injection. If a second injection of glucose was made four hours after the administration of insulin a second rise in pyruvic acid took place. When the blood sugar level was raised to 750 to 950 mg per cent. for 3 to 5 hours by a continuous infusion of a 5 per cent. glucose solution, (300 ml per hour) after a preliminary injection of 2 gm glucose per kg, an elevation of blood pyruvate occurred despite the absence of insulin. The blood pyruvate under these conditions reached a constant level within one or two hours. The injection of insulin after three hours of glucose infusion produced a further rise in blood pyruvate.

In agreement with previous observations⁵ the rate of removal of intravenously injected pyruvic acid (1 gm per kg as sodium pyruvate) from the blood was the same in normal and depancreatized dogs.

It may be concluded from these experiments that, in the depancreatized dog, insulin increases the formation of pyruvic acid after the administration of glucose.

ERNEST BUEDING

NEW YORK UNIVERSITY
COLLEGE OF MEDICINE

JOSEF F. FAZENKAS
HERMAN HERRLICH
HAROLD E. HIMWICH

ALBANY MEDICAL COLLEGE,
UNION UNIVERSITY

⁵ E. Flock, J. L. Bollman and F. C. Mann, *Jour. Biol. Chem.*, 125: 49, 1938.