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Prevention of Liver Necrosis following Ligation of Hepatic Artery.

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In dogs, ligation of the hepatic artery is followed in approximately 100% of cases by death, as a result of a peculiar necrosis of the liver. In a series of experiments extending over many years we have tried to prevent this mishap by arterializing the blood flow of the portal vein. This year we appeared to be unusually successful, in that the animals survived such ligation. Examination at autopsy, however, always disclosed that the arterioportal anastomosis was thrombosed, although the liver was grossly normal. During this year penicillin has been administered following the operations in one series of animals. Another series did not receive penicillin. The wholly unexpected finding was made, that when dogs with totally ligated hepatic arteries are given massive doses of penicillin, intraperitoneally and intramuscularly for one week, they usually survive, whether or not the gall bladder has been removed. The latter becomes gangrenous, often ruptures, but even this occurrence is well tolerated by the animal unless generalized bile peritonitis develops.

It is suggested that the immediate life-saving function of the hepatic artery is to maintain oxygen tension at a level incompatible with the proliferation of anaerobes constantly present in hepatic tissue.

16908

Relationship of Blood Sugar and Hypoproteinemia to Antibody Response in Diabetics.*

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Evidence has been presented that protein depleted animals as compared with normal controls possess little ability to manufacture antibodies. The poor antibody response in animals can be restored to normal by protein repletion.[1-3] We have reported on similar studies in man, particularly in the hypoproteinemic patient as seen in a large general hospital.[4]

The purpose of this paper is to direct attention to the fact that the diabetic with such complications as gangrene, osteomyelitis, etc., has a diminished antibody production; this low antibody response to antigenic stimulation appears to bear relationship to the blood protein values rather than to the fasting blood sugar levels.

For this study a representative group of 64 diabetic patients attending the metabolic

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[1] Cannon, P. R., *J. Immunol.*, 1942, **44**, 107.

[2] Cannon, P. R., Chase, W. E., and Wissler, R. W., *J. Immunol.*, 1943, **47**, 133.

[3] Wissler, R. T., Woolridge, R. L., Steffee, C. H., Jr., and Cannon, P. R., *J. Immunol.*, 1946, **52**, 267.

[4] Wohl, M. G., Reinhold, J. G., Rose, S. B., Adams, L. A., Harvey, T., Francis, M., and Clough, G., *Arch. Int. Med.*, in press.

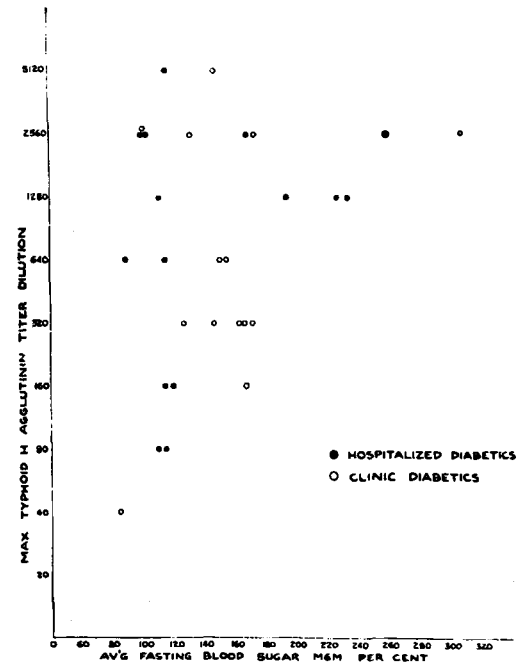

CHART 1.
Relation of the fasting venous blood sugar to antibody response.

clinic and housed in the metabolic wards of the Philadelphia General Hospital were selected. Eleven nondiabetic persons served as controls. Nineteen hypoproteinemic patients received protein supplementation in the form of lactalbumin hydrolysate or casein concentrate. The diet of the patients in the supplemented groups remained isocaloric with that of the nonsupplemented persons by reducing the fat intake by grams equivalent to the calories supplied by the additional protein. The average diet of diabetic men contained 2100 calories, of women 1800 calories.

The patients were studied chemically and immunologically by the methods previously described.[4] In addition, in 14 patients nitrogen balance studies were performed for a period of 36 to 55 days; detailed studies of the latter will be reported elsewhere. The data are plotted in Charts 1 and 2.

In Chart I the ordinates indicate the peak agglutination titre to typhoid H antigen; the abscissas indicate the corresponding average fasting blood sugar levels in mg %. Study of Chart I reveals that there is no relationship between the fasting blood sugar levels and the serum agglutinin content. To illustrate the patients with the highest titres (1:1280 to 1:5120) have fasting venous sugars from 100 to 300 mg %. On the other hand, titre levels of 1:160 or less were found in patients with average fasting venous blood sugars of 170 mg % or less. It would appear then that patients with hyperglycemia do not demonstrate a decreased capacity to produce antibody.

An analysis of Chart 2 shows that the diabetic patients with hypoproteinemia (serum albumin levels below 4 g %, the lower limit of normal for the method used) showed a lower average agglutination titre than the diabetic patients with normal blood protein values. The average serum albumin of the normal controls was 4.87 g %, of the clinic diabetic groups 5.27 and 4.28 g % respectively, of the 2 hospitalized diabetic groups

Typhoid H Agglutinin Titer in Diabetes Mellitus.

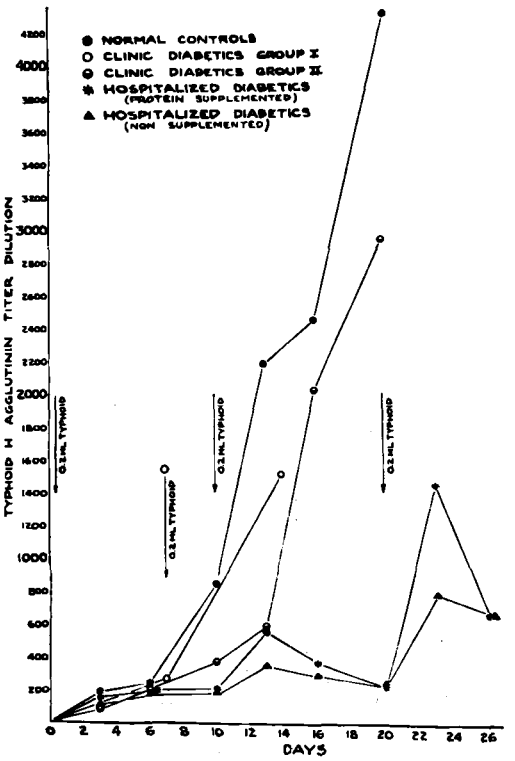

CHART 2.
Comparison of antibody formation in normal controls and diabetic adults with special reference to normoproteinemic and hypoproteinemic diabetics.

TABLE I.
Relation of Protein Repletion (Positive N Balance) to Antibody Titre in Diabetics.

	Balance		Max. titre	Avg alb.	Supplemented
	Days	Avg g N/DA.	1:		
Ha.	20	7.5	40*	3.8	+
Ab.	36	6.6	640	4.7	+
We.	8	5.4	1280*	4.7	+
Cr.	36	4.9	320*	4.4	+
Pe.	74	4.7	5120	3.4	—
Sm.	62	4.4	320	3.1	+
Wat.	42	4.2	640	4.3	+
Cu.	55	2.6	2560	4.4	—
War.	49	—0.3	160	4.0	—

* Two injections typhoid.

TABLE II.
Average Serum Albumin Concentration.

Group	Day 0	17	27
Normal	4.87	4.85	4.80
Clinic diabetics			
I	5.27	5.48	5.37
II	4.28	4.18	4.40
Hospitalized diabetics			
(Supplemented)	3.11	3.77	3.87
(Non-supplemented)	3.31	3.41	3.41

3.11 and 3.31%. (See Table II). These figures remained essentially unchanged during the study except for the protein supplemented group whose albumin rose from a mean of 3.11 g to 3.87 g %.

The average highest titre of 16 diabetic patients with hypoproteinemia but nonsupplemented was 1:800 as compared with the average highest titre of 1:2900 in 9 normoproteinemic uncomplicated diabetics who only received 2 typhoid injections, whereas the hypoproteinemic group received 3 injections. There were 20 normoproteinemic clinic diabetics who also received 2 typhoid injections and whose highest titre was 1:1500 seven days after the second injection.

Nineteen hypoproteinemic patients were provided with oral supplements of protein in the form of lactalbumin hydrolysate or casein concentrate. The diets were carefully calculated and sufficient supplementary protein was added to double the daily protein intake as compared with that of the other hypoproteinemic group.

The results of this study showed an improvement in antibody response. During the first 10 days after initial injection the average titre in both supplemented and unsupplemented groups was approximately the same. Following each subsequent typhoid injection there was a greater rise in titre in the supplemented as compared with the nonsupplemented groups.

It is to be noted, however, that the best antibody response was obtained in the outpatient normoproteinemic diabetics (who were not suffering from an active complication of the disease) even though they received no protein supplementation.

The addition of extra protein to the diet did not appear to result in an increase in the severity of the diabetes during the experimental period of 30 days. There was no appreciable change in blood sugar levels, nor was there any change in plasma CO_2 combining power nor any increase in insulin requirements. It is of interest that there was no apparent relation between the degree of nitrogen storage and the peak of typhoid agglutinin titres (Table I), indicating that the retention of protein (as N) was not immediately reflected in an increase of antibody formation.

Whether the enhanced antibody-producing capacity is due specifically to an increase in the body's protein "pool" for globulin-antibody production or some other factor needs further study.

Summary. Sixty-four diabetic patients were studied immunologically and chemically. Nineteen diabetic patients with hypoproteinemia received nitrogen supplementation in the form of lactalbumin hydrolysate or casein concentrate. The following conclusions appear to be warranted: 1. The decreased capacity to produce antibody in the diabetic is apparently not related to hyperglycemia. 2. Diabetic patients with hypoproteinemia showed a lower average agglutination titre than those with normal blood protein values. 3. Oral supplementation with lactalbumin hydrolysate or casein concentrate enhanced antibody formation.

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