in its proximal tubules, especially at their brush borders, whereas the distal convolutions are negative. The glomeruli show a moderate alkaline reaction, categorizing the frog in a class with the cat (the only other animal thus far investigated that gives this reaction). With regards to the neoplastic kidney, the tumor cells themselves are alkaline phosphatase negative with an accompanying depletion of the enzyme in adjacent non-tumorous portions of the renal tissue.

Both normal and tumorous kidneys are essentially negative for acid glycerophosphatase. The significance of these results is discussed.

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Depressing Effect of Inositol on Serum Cholesterol and Lipid Phosphorus in Diabetics.* (17437)

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The problem of the relation of serum cholesterol levels to human atherosclerosis is much debated. An agent capable of depressing serum cholesterol levels in hypercholesteremic individuals would offer a new approach to its study. There is some evidence to show that inositol is such an agent.

McHenry and Patterson[1] suggested that inositol has a specific effect on cholesterol metabolism; they pointed out that it is an effective lipotropic agent particularly when large amounts of cholesterol are present in the liver. Herrmann[2] found that inositol depressed blood levels of cholesterol and choles-

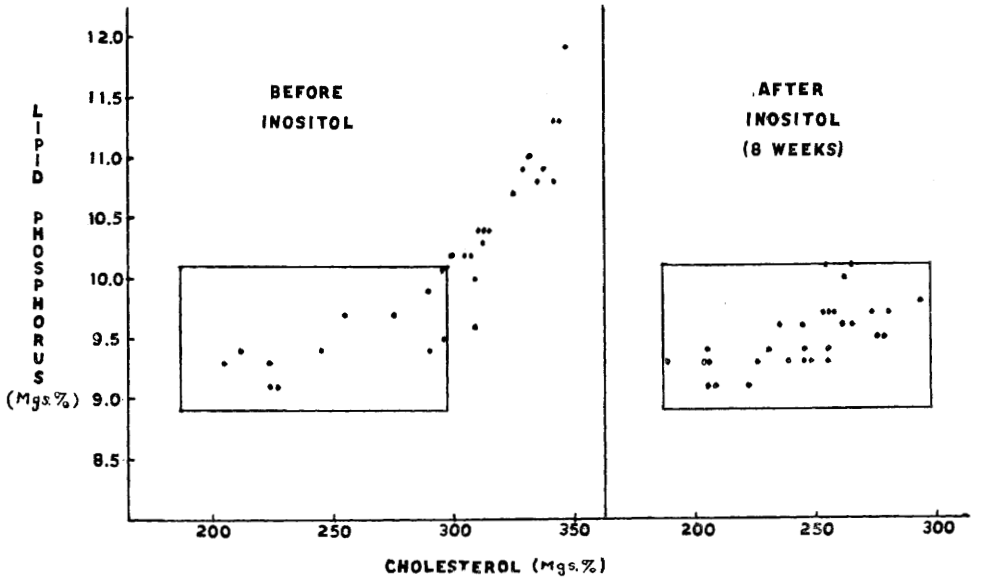

FIG. 1.

Values of serum total cholesterol and lipid phosphorus for 30 diabetic patients before and 8 weeks after inositol. Enclosed areas represent range of normal.

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1 McHenry, E. W., and Patterson, J. M., *Physiol. Rev.*, 1944, **24**, 129.

2 Herrmann, G. R., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 436.

terol esters in old hens. Gephardt[3] found that in one case of xanthomatous biliary cirrhosis doses of 3 g of inositol per day for 3 months produced a marked drop in total lipids and some drop in cholesterol and cholesterol esters; the patient, however, received a low-fat diet concurrently. On the other hand, Shay[4] states that doses of 1.2 g a day for 3 weeks had no effect on blood cholesterol in human diabetics. Herrmann[5] found that 20 hypercholesteremic patients given 2 g of inositol a day for 25-30 days had an average drop of 19% and 17% of cholesterol and cholesterol esters respectively; one showed no change; he found also that there was a tendency for phospholipids to rise.

The action of inositol on serum lipids and on the atherosclerotic process is being studied in this hospital. The present paper reports its effect on certain serum lipids in a group of diabetic patients.†

Procedure. Total cholesterol and cholesterol esters[6] and lipid phosphorus[7] were determined on the blood serum of all experimental subjects. Similar determinations were made on 100 control subjects, consisting of staff physicians, nurses and hospital patients not known to have any disease affecting cholesterol metabolism.

Of the 30 diabetic patients used, 13 were selected because of high blood cholesterol levels previously established in this clinic; the remainder were picked at random from the diabetic clinic provided they fulfilled the criteria of fixed diet, fixed insulin dosage and adequate diabetic control for 6 months prior to beginning the experiment. Repeated de-

TABLE I.
The Mean, Range, Standard Deviation, and Standard Error of the Mean of Total Cholesterol, Cholesterol Esters and Lipid Phosphorus in Normals and in Diabetics Before and After Taking Inositol.

	Total cholesterol, mg %				Cholesterol esters, mg %				Lipid phosphorus, mg %		
	Mean	S.D.	S.E.	Range	Mean	S.D.	S.E.	Range	Mean	S.D.	S.E.
Normals (100)	236.3	±24.0	±2.4	(188-297)	167	±16.8	±1.7	(137-204)	9.29	±0.20	±0.02
Diabetics (30)											
Control	294	±43.5	±8.0	(205-346)	208	±29.6	±5.4	(144-246)	10.2	±0.71	±0.13
Inositol: 1 week	268	±33.9	±6.2	(198-321)	189	±24.0	±4.4	(138-225)	10.0	±0.61	±0.11
2 ,,	254	±31.3	±5.7	(188-303)	178	±22.6	±4.1	(136-213)	9.7	±0.42	±0.08
4 ,,	247	±27.7	±5.1	(186-292)	173	±19.3	±3.5	(129-207)	9.5	±0.31	±0.06
8 ,,	244	±26.8	±4.9	(189-293)	171	±18.7	±3.4	(131-208)	9.5	±0.27	±0.05

[3] Gephardt, M. C., *Ann. Int. Med.*, 1947, **26**, 764.

[4] Shay, H., in discussion of Vorhaus, M. G., Gompertz, M. L., and Feder, A., *Am. J. Dig. Dis.*, 1943, **10**, 48.

[5] Herrmann, G. R., *Exp. Med. and Surg.*, 1947, **5**, 149.

† The authors are indebted to Dr. John H. Keating for his helpful advice and to Miss Stephanie Ilka for technical assistance in this investigation.

[6] Sperry, W., and Brand, F. C., *J. Biol. Chem.*, 1943, **150**, 315.

[7] Youngburg, G. E., and Youngburg, M. V., *J. Lab. and Clin. Med.*, 1930, **16**, 158.

terminations on these 2 diabetic groups were practically identical as far as mean, range and standard deviation of cholesterol fractions and lipid phosphorus were concerned; they are therefore considered as one unit.

At least 2 baseline total cholesterol, cholesterol esters and lipid phosphorus determinations were made on all diabetic patients before they were given inositol. They then began taking 3 g of inositol daily (two 0.5 g capsules after each meal); bloods were taken at intervals of 1, 2, 4, and 8 weeks thereafter.

Results. The range of normals is indicated by the enclosed area in Fig. 1. The mean, range and standard deviations are shown in Table I. No apparent variation was found with regard to age or sex and repeated determinations on the same subject showed little or no variation over a period of several months.

Before taking the inositol, the diabetic patients tended to show elevated serum total cholesterol, 18 (60%) being outside the range of normals as shown in Fig. 1, only 4 below the normal average, the rest high normal. Cholesterol esters were proportional to total cholesterol, the ratio of esters to total being relatively constant (68-73%). Lipid phosphorus tended to be high when the total cholesterol was high, but the correlation was not as consistent as with the cholesterol esters. No correlation between the level of cholesterol fractions or lipid phosphorus and the severity of diabetes or the accuracy of its control could be made.

In all of the diabetic patients fed the inositol a fall occurred in the serum cholesterol and lipid phosphorus. After 8 weeks (Fig. 1) all determinations were within the normal range. As shown in Table I, the total cholesterol tended to fall abruptly over the first 2 weeks, then to fall more slowly or become stationary. The higher initial total cholesterol showed the greater tendency to fall; thus, 17 diabetics with an initial total cholesterol above 300 mg% had an average drop of 69.2 mg% in 8 weeks, while the 13 diabetics below 300 mg% had an average drop of only 29.0 mg%. The proportion of esters to the total remained constant after inositol, and lipid phosphorus tended to fall in conjunction with fall in total cholesterol, contrary to Herrmann's findings. When the patients were taken off inositol, a gradual rise occurred in the determined serum lipids, but after 6 weeks none had returned to the baseline levels.

The only possible untoward effect of inositol observed occurred in one woman who complained of gastric distress; many of the patients reported a feeling of increased vigor and well-being. No consistent change in the diabetic status of any of the patients was noted.

Conclusions. Inositol is an effective agent in lowering serum cholesterol and lipid phosphorus in hypercholesteremic diabetics. Further study of its action and applications is warranted.

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Metabolism of Some 9-Aminoacridine Derivatives. (17438)

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Many compounds in the 9-aminoacridine series have been synthesized for the purpose of studying their action against a variety of parasitic infections, and as disinfectants. The recent antimalarial survey[1] included a large number of these compounds. One of them was Acranil (SN-186), which was found to be only slightly active against avian malaria.[2] Previously[3-6] it had been used successfully for

1 Wiselogle, F. Y., A Survey of Antimalarial Drugs, J. W. Edwards, Ann Arbor, 1946, pp. 1321-1377.

2 Gingrich, W. D., and Fillmore, R. S., *Am. J. Hyg.*, 1942, **36**, 276.