influence like glutathione, which in large doses has been found by Lazarow(30,31) to completely protect rats against the development of alloxan diabetes.

Summary. 1. The repeated daily injection of sodium acetoacetate in progressively increasing doses (beginning at 50 mg/kg body weight) caused a progressive hyperglycemia in rabbits after an initial hypoglycemic stage. 2. The glucose tolerance of these animals was decreased after 30 days of injection and the tolerance curve taken at 30, 50, 70, 90, 110 and 130 days became progressively more diabetic. 3. The shape of the tolerance curves changed considerably on prolonged treatment with acetoacetate and in most cases the blood sugar levels at 3½ hours were far greater than the pre-injection level. 4. The glycogen content of liver and muscle is gradually depleted, so that after 130 days of injection it was decreased 64.9% and 73.4% respectively. 5. When Amellin was injected daily for 40 days in doses of 10-12 mg/kg into these hyperglycemia animals it reduced the blood sugar to 105 mg/100 cc (normal value). Insulin, although it relieved the fasting hyperglycemia initially, had little effect on the fasting hyperglycemia in later stages. Increasing the insulin dose leads to death. 6. The glucose tolerance of the animals treated with sodium acetoacetate became absolutely normal after Amellin had been administered for 40 days, whereas the tolerance of similar animals treated with insulin was not normal at 40 days.

Addendum. After this paper was presented for publication Griffiths(32) reported that uric acid produced diabetes in rabbits only when their blood glutathione was lowered to about half the normal value. Acetoacetate injection has recently been found in this laboratory to lower blood glutathione considerably(33). These observations may help to explain how acetoacetate favors the development of hyperglycemia and how Amellin acts as a protective substance.

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Alpha Tocopherol in Treatment of Alloxan Diabetes in Dogs.* (18188)

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Reports have appeared in the literature on the use of alpha tocopherol, in treatment of diabetes(1,2). Recent publications reviewing therapy of diabetes mellitus have invariably made a plea for fundamental controlled work to be done on the use of alpha tocopherol in the treatment of diabetes mellitus(3). Therefore, it was considered worth while to study the effect of alpha tocopherol on alloxan diabetes in the dog.

Method of study. Ten dogs were rendered diabetic by a freshly prepared 5% solution of alloxan administered in intravenous doses of 65 to 75 mg per kilo body weight. The dogs were then divided into 2 groups, 7 comprising the experimental group, 3 the control group. The experimental dogs were treated with diet, insulin and alpha tocopherol. The control

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3. Joslin, E. P., *J.A.M.A.*, 1949, v140, 581.

TABLE I. Influence of Alpha Tocopherol on Insulin Requirements of Alloxanized Dogs.

Dog No.	Wt, kg	Fasting blood sugar, mg %	Alloxan dosage, mg/kg	Blood sugar after alloxan, mg %	Prot. zinc insulin daily units before α-tocoph.	α-tocoph. oral daily I.U.	α-tocoph. intramusc. 2 day intervals, mg	No. of days	Prot. zinc insulin concluding daily units
1	11.4	55	75	252	10	300	0	40	10
6	15.5	64	100	319	25	300-600	0	40	25
9	13.6	68	65	92	8	300-600	0	40	8
12	6.4	64	75	210	5	300-600	0	35	5
24	20.5	55	65	216	10	300	0	27	10
15	21.0	68	75	207	25	0	50-200	28	25
18	15.9	53	65	136	10	0	50-200	26	10
16	17.7	57	65	104	5	0	0	36	8
Control									
17	11.8	49	65	118	6	0	0	35	8
Control									
23	14.5	55	65	74	5	0	0	33	5
Control									

dogs were treated with diet and insulin. In all instances protamine zinc insulin was used to control the diabetes. Blood sugar determinations were done before alloxan and approximately 48 hours after alloxan. Thereafter, blood sugars were determined at various intervals in order to follow the hyperglycemic state. Insulin dosage was established by daily morning urinalysis. After control of the glycosuria was definitely established, alpha tocopherol was administered to the experimental dogs an average of 4½ weeks. Five of the experimental dogs received oral alpha tocopherol daily, 2 of the experimental dogs received injectable alpha tocopherol every other day.

Results. Table I presents data on each dog. In all cases regulation of the diabetes was readily attained. The general nutritional status of all dogs was well maintained throughout the experiment. In no instance was the insulin requirement reduced in the experimental animals.

Summary and conclusions. 1. Alpha tocopherol does not alter the insulin requirements of alloxan diabetes in the dog.

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Hyperpigmentation in Acute Leukemia Treated with Folic Acid Antagonists.* (18189)

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The treatment of acute leukemia with folic acid antagonists has resulted in encouraging clinical responses. While it is recognized that such antagonists as Aminopterin and A-methopterin (Lederle) do not cure acute leukemia they nevertheless depress abnormal bone marrow response by correcting the dysplastic process and thereby prolong life in many instances. Folic acid antagonists can therefore be useful tools in studies designed to elucidate the abnormal cellular metabolism of the leukemic marrow. During our observations on 10 children who received the antagonists over long periods we were impressed by the development of

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