TABLE I.
Effect of Trypsin-Inhibitor on B Hemolytic Streptococci.

Incubation period before plating, hr	Colony count*	
	Trypsin-inhibitor $MgSO_4$ compound 5%	$MgSO_4$ 5%
2	†	†
4	656	†
6	23	†
8	0	†

* 0.1 cc of 1:1000 dilution of 18-hour culture removed at stated intervals after incubation with test substance and transferred to blood agar pour plates and incubated at 37°C for 24 hours.
† Too many to count.

in that inhibition of growth ensued on incubation with pancreatic trypsin-inhibitor.

In an excellent study of the effect of trypsin inhibitor on bacterial growth, Grob[4] demonstrated that growth was "somewhat retarded" in the presence of the inhibitor. He concluded that the trypsin-inhibitor had no bacteriostatic action but affected growth through the prevention of proteolysis in the medium. However, he could not demonstrate any action on *Staphylococcus aureus*. Our studies suggest that the inhibitor can be bacteriostatic when employed in adequate concentration (Table I).

It is obvious that the trypsin-inhibitor compound is not nearly as potent an antibiotic agent as is penicillin and other antibiotics. However, the relative ineffectiveness of penicillin on *E. coli* and the fact that trypsin-inhibitor affects *E. coli* to the same degree as hemolytic streptococci suggests a greater non-specificity of the antibiotic action of the protease inhibitor.

Unpublished data reveal that penicillin has a weak but definite antiproteolytic action as do Actinomycin A and Tyrothricin.[5] It is probable that the efficacy of penicillin as an antibiotic agent lies in its ability to inhibit enzymes other than the proteases. On the other hand, the effect of trypsin-inhibitor can be attributed solely to its inhibition of the bacterial proteases since it has been observed that this protease inhibitor is not specific but can inhibit a number of proteolytic enzymes. Further, the fact that synthetic detergents which are antiproteolytic are also germicidal lends support to this hypothesis.

The significance of the above observations and those of Grob lies not so much in the demonstration that the protease inhibitor has an antibiotic action as in the suggestion that the rise of the antiprotease titer of blood which occurs in a variety of pathologic states in man may play an important role in "resistance" to infection. In this respect the role of numerous other anti-enzymes known to be present *in vivo* merits intensive investigation.

Summary. Trypsin-inhibitor has antibiotic properties.

We wish to express our appreciation of the courtesies and facilities extended by Dr. T. Duckett Jones and the staff of the House of the Good Samaritan, and of our indebtedness to Col. W. Paul Holbrook for his interest and cooperation.

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14970

Alloxan Administration to the Duck.

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One of the perplexing problems in carbohydrate metabolism is the fact that pancreatectomy does not result in the development of diabetes mellitus in the duck or chicken. Further, the administration of crude saline extracts of the anterior pituitary gland to such

TABLE I.
Alloxan Administration to the Duck.

Alloxan, mg/kg intravenously	Blood sugar, mg %				Survival, hr
	Avg initial	Max. first 24 hr	Max. second 24 hr	Max. after 48 hr	
715	104	263	—	—	20
575	97	—	—	—	2
360	115	252	—	—	20
300	118	127	—	—	24 to 36
250	130	168	107	—	36 to 48
200	133	125	134	112	
150	108	126	123	118	
100	105	116	102	122	
50	114	100	107	110	

depancreatized birds does not result in the hyperglycemia observed in other species.[1] Estrogens, which cause a marked lipemia in fowl, are likewise without effect in producing hyperglycemia.[1]

It has been demonstrated that islet tissue is present in the fowl's pancreas and that appreciable amounts of insulin can be extracted from that organ.[2] Nevertheless, it is possible that aberrant islet tissue may be present in other parts of the body, and for that reason removal of the pancreas might not produce diabetes. Consequently, we deemed it of interest to examine the effect of alloxan in this species, since the administration of this compound produces necrosis of the β cells of the Islets of Langerhans and diabetes in all species that have been studied hitherto, including the pigeon.[3]

A variety of ducks (white, mallard, canvasback) were employed in this study. The dosage of alloxan administered as a 5% solution in a single intravenous injection varied from 50 mg to 750 mg per kilogram. Blood samples were drawn at frequent intervals from the wing veins and the sugar concentration determined by Nelson's modification of the Somogyi-Shaffer-Hartman method.[4]

The intravenous administration of more than 200 mg alloxan per kilogram resulted in death of the birds in from 3 to 48 hours. No constant blood sugar response was observed when such toxic doses were employed. Thus, some animals developed an immediate hyperglycemia which culminated with the death of the fowl in about 12 hours while others developed no hyperglycemia and died at variable periods up to 48 hours. In no instance was hypoglycemia noted.

The administration of smaller doses of alloxan did not produce any significant change in the blood sugar concentration (Table I).

Sections of the pancreas taken from animals sacrificed at various intervals after the injection of alloxan revealed that those animals which lived more than 12 hours developed islet lesions irrespective of the dose employed. Thus, the pancreas from one duck which was sacrificed 9 days after receiving 50 mg alloxan per kilogram, and which at no time developed hyperglycemia showed extensive necrosis of the islets. On the other hand, the pancreas of another duck which died within 2 hours after the injection of 750 mg alloxan per kilogram showed no significant deviation from the normal.

From the preceding it may be concluded that the duck, like other species is susceptible to the action of alloxan on the Islets of Langerhans. The fact that a permanent hyperglycemia did not result suggests that the duck has no extrapancreatic Islets of Langerhans. This is supported by the fact that the injection of 200 mg alloxan per kilogram to a depancreatized duck did not produce any change in the blood sugar level. Consequently, it can now be reiterated more definitely that the duck

[1] Mirsky, I. A., Nelson, N., Grayman, I., and Korenberg, M., *Am. J. Physiol.*, 1941, **135**, 223.

[2] Redenbaugh, H. E., Ivy, A. C., and Koppanyi, T., PROC. SOC. EXP. BIOL. AND MED., 1926, **23**, 756.

[3] Goldner, M. G., and Gomori, G., *Proc. Am. Diab. Assn.*, 1944, 4.

[4] Nelson, N., *J. Biol. Chem.*, 1944, **153**, 375.

does not need insulin to maintain its carbohydrate metabolism, implying thereby the existence of regulatory mechanisms which differ markedly from those of other species. That a similar situation may exist in the chicken is indicated by our experience with two chickens which, after alloxan administration, showed no abnormality of the blood sugar level.

Summary. Alloxan does not produce diabetes mellitus in the duck in spite of the fact that the drug does produce necrosis of the Islets of Langerhans.

We wish to acknowledge our appreciation of the cooperation and facilities extended by Dr. Kenneth G. Kohlstaedt, Director, and the staff of the Lilly Laboratory for Clinical Research, and our indebtedness to Dr. A. Nettleship for the histologic examination of the pancreases.

14971

Influence of Pantothenic Acid Deficiency on Resistance of Mice and Rats to Experimental Pneumococcal Infection.*

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Several recent reports are concerned with the effects of pantothenic acid deficiency in animals on their resistance to various infectious agents. Becker, Manresa, and Johnson found that pantothenic acid increases the production of oöcysts by rats infected by *Eimeria nieschulzi*[1] and reduces the efficiency of ablastic action of pantothenic acid-deficient rats infected with *Trypanosoma lewisii*.[2] According to Trager[3] the survival of *Plasmodium lophuræ in vitro* is favored by the presence of pantothenic acid. Lichstein, Waisman, Elvehjem, and Clark[4] reported that young, pantothenic acid-deficient, Swiss mice show increased resistance to Theiler's encephalomyelitis virus, but little or no change in resistance to the Lansing strain of poliomyelitis. West, Bent, Rivera, and Tisdale,[5] using 15 animals, claimed that pantothenic acid deficiency greatly increased the resistance of the rat, infected by nasal insufflation, to a strain of Type I pneumococcus. Since these organisms require pantothenic acid for growth, West *et al.* postulated that the apparent increase in resistance was due to inability of the pathogenic organisms to secure sufficient pantothenic acid from the host rats to permit maximal growth. Robinson and Siegel[6] did not find a change in resistance to experimental pneumococcal pneumonia in 20 young adult rats restricted to a pantothenic acid-deficient diet as compared to the resistance of control animals which were fed the vitamin.

Wooley and Sebrell[7] reported that young mice deficient in riboflavin or thiamine are more susceptible to Type I pneumococcus by nasal insufflation than controls which received these vitamins. Robinson and Siegel,[6] using 20 young adult rats, appeared to confirm these findings for thiamine.

An important problem in investigations of

* Supported by a grant from the Graduate Research Fund of Indiana University. The authors are indebted to Miss Ruth Toabe and Mr. David K. Barnes for technical assistance.

1 Becker, E. R., Manresa, M., Jr., and Smith, L., *Iowa State Coll. J. Sci.*, 1943, **17**, 257; *Chem. Abstr.*, 1943, **37**, 1478.

2 Becker, E. R., Manresa, M., Jr., and Johnson, E., *Iowa State Coll. J. Sci.*, 1943, **17**, 431; *Chem. Abstr.*, 1943, **37**, 3801.

3 Trager, Wm., *J. Exp. Med.*, 1943, **77**, 411.

4 Lichstein, H. C., Waisman, H. A., Elvehjem, C. A., and Clark, P. F., PROC. SOC. EXP. BIOL. AND MED., 1944, **56**, 3.

5 West, H. D., Bent, M. J., Rivera, R. E., and Tisdale, R. E., *Arch. Biochem.*, 1944, **3**, 321.

6 Robinson, H. J., and Siegel, H., *J. Infect. Dis.*, 1944, **75**, 127.

7 Wooley, J. G., and Sebrell, W. H., *U. S. Pub. Health Rep.*, 1942, **57**, 149.