In four White Leghorns (Table 1), the decrease in shell thickness varied between 19 and 25 per cent. In Fig. 1, it is seen that a single dose of sulfapyridine affected the shell thickness for at least four days. The feeding of the same substance at 0.3 per cent. level in the dry mash for a period of six days gave thinner shells and upon withdrawal of the drug, the effect was observed for three to four days (Fig. 1). These findings are analogous to those of Benesch *et al.*[7] who note that sulfanilamide and sulfapyridine both inhibit to the same extent the calcification of the femurs in rat foetuses.

It is believed that this effect of sulfapyridine on shell formation, though not in agreement with the observations of Benesch *et al.*,[3] does not exclude carbonic anhydrase as a factor in shell formation. One is led to suggest, however, that certain sulfonamides such as sulfapyridine may interfere with normal shell formation by inhibiting enzymes other than carbonic anhydrase. A temporary vitamin deficiency always remains a possibility when dealing with sulfa drugs.

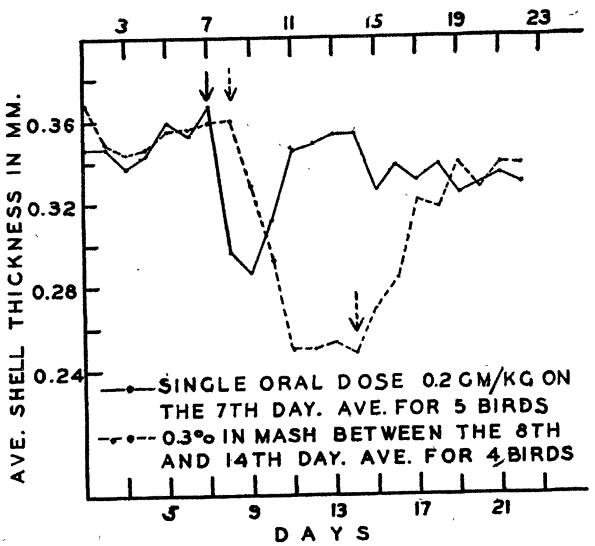


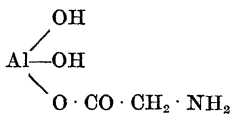
FIG. 1. Effect of sulfapyridine on shell thickness in the domestic fowl.

RICHARD BERNARD
P. GENEST

DEPARTMENT OF BIOLOGY,
LAVAL UNIVERSITY,
QUEBEC

ORAL PENICILLIN WITH BASIC ALUMINUM AMINOACETATE

RECENTLY in this laboratory[1] a new antacid, basic aluminum aminoacetate, was synthesized and studied pharmacologically and clinically. The structure proposed for the compound is



Having established the value of the compound as a rapidly active antacid with high buffer capacity, the thought of using it to protect penicillin from destruction by gastric acid occurred to us. Libby[2] has shown that effective concentrations of penicillin may be obtained in dog's serum after the oral administration of the drug suspended in oil.

Penicillin was acidified with artificial gastric juice[3] and other samples were treated with gastric juice buffered with basic aluminum aminoacetate to pH 4 to 4.5. The activity of each sample of penicillin was determined by the agar cup against staphylococcus aureus as compared with the untreated drug by the method of Abraham[4] *et al.* Gastric juice destroyed completely the activity of the drug. The penicillin treated with gastric juice buffered with the antacid was from 50 to 70 per cent. as active as the untreated penicillin.

Twelve individuals were given 100,000 units of penicillin mixed with 3 grams of basic aluminum aminoacetate, suspended in 100 to 150 cc of water. The mixture was administered in the morning on a fasting stomach. Blood samples were taken 2, 3, 5 and 7 hours after administration and in these serum levels of penicillin were determined by the method of Rake and Jones.[5]

Wide variations were found in the rates of absorption and/or excretion. Effective levels were obtained soon after ingestion and the presence of the drug in the serum, in some cases, could be detected 7 hours after ingestion. Table 1 gives average serum concentrations with respect to time in these 12 individuals.

TABLE 1

SERUM LEVELS OF PENICILLIN
Oxford units per 100 cc serum

Time after ingestion	2 hrs.	3 hrs.	5 hrs.	7 hrs.
Units	39	68	37	17

By the Abraham[4] method penicillin was shown also to be present in the urine 2 hours after ingestion.

SUMMARY

This method appears to be suitable for the oral administration of penicillin. Basic aluminum amino-

[7] R. Benesch, M. R. A. Chance and L. E. Glynn, *Nature*, 155: 204, 1945.

[1] J. C. Krantz, Jr., D. V. Kibler and F. K. Bell, *Jour. Pharmacol. and Exp. Therap.*, 82: 247, 1944.

[2] R. L. Libby, SCIENCE, 101: 178, 1945.

[3] J. C. Krantz, Jr., and A. A. Silver, *Annal. Int. Med.*, 4: 441, 1931.

[4] E. P. Abraham *et al.*, *Lancet*, 2: 177, 1941.

[5] G. Rake and H. Jones, *Proc. Soc. Exp. Biol. and Med.*, 52: 136, 1943.

acetate seems admirably suited for this purpose. It is neutral and buffers gastric acidity to pH 4 to 4.5. While this work was in progress McDermott *et al.*[6] successfully employed magnesium trisilicate in this manner.

Clinical work is now in progress using the combination in infections known to be susceptible to parenteral penicillin therapy.

JOHN C. KRANTZ, JR.
WILLIAM E. EVANS, JR.
JAMES G. MCALPINE

SCHOOL OF MEDICINE,
UNIVERSITY OF MARYLAND,
BALTIMORE, MD.

CORNEAL VASCULARIZATION IN RATS ON A TRYPTOPHANE DEFICIENT DIET[1]

IN a previous publication[2] we have reported that both weanling and adult rats developed vascularization of the cornea within two to three weeks on a tryptophane deficient diet. Inasmuch as corneal vascularization has also been repeatedly reported to be a manifestation of riboflavin deficiency in the rat and man,[3] the need for an inquiry into the apparently dual etiology of the symptom was obvious. Since the animals maintained on the tryptophane-supplemented tryptophane deficient diet grew normally and failed to show ocular lesions, it was felt that this diet contained adequate quantities of riboflavin and the possibility that the vascularization might arise from increased riboflavin requirement which was not met by the tryptophane deficient diet needed investigation.

To test this possibility, 18 normal weanling male and female rats (50–60 gm) from a hybrid albino and hooded Norwegian rat colony were divided into two groups of 9, which were fed on the tryptophane deficient diet.[4] One of these groups was given daily a freshly prepared riboflavin solution (30 γ per cc) to drink from amber-colored, glass-graduated drinking tubes, and the other group, serving as a control, received tap water instead. Despite an average daily intake of 120 γ of riboflavin, the rats of the riboflavin supplemented group developed corneal vascularization and cataracts[5] with a rapidity and incidence equal to that of the control group. Moreover, the weight losses and general poor appearance of the animals in both groups were similar to those previously reported. After 5 weeks, the riboflavin supplementation for the first group was discontinued and both groups of animals were fed the tryptophane-supplemented tryptophane deficient diet.[4] On this regimen, the animals gained weight rapidly, and complete recovery from the corneal lesions with partial disappearance of the cataracts was noted.

The results of this experiment suggest that tryptophane deficiency exerts some direct effect upon the cornea, rather than inducing a deficiency of riboflavin. The recent reports of corneal vascularization in man which failed to respond to riboflavin therapy[6, 7] suggest the possibility of an exogenous or endogenous deficiency of tryptophane and the employment of tryptophane as a therapeutic measure.

ANTHONY A. ALBANESE
DEPARTMENT OF PEDIATRICS,
THE JOHNS HOPKINS UNIVERSITY

THE SOLUTION OF SOIL MINERALS IN DILUTE ACIDS

MANY soil minerals, particularly those of the montmorillonite group, are known to dissolve or disperse readily in water solutions containing 0.01 to 0.4 per cent. acid.[1] The evaporated clear sol has approximately the composition of the residue and of the mineral from which it was derived, going from sol to gel to amorphous solid as evaporation proceeds. Solubilities as high as 60 per cent. of the clay have been found by the writer for halloysite and montmorillonite. High solubility requires sufficient acid to take the bases and sufficient water to dissolve the silica set free by removal of the bases. The solubility of an ordinary salt does not depend upon the amount of salt present, but that of a clay may vary by a factor of 4, as clay alone is varied.

The problem is to find definite relations between the amount of sol formed and the amounts of acid, clay and water present. Analyses of residues, of the dried sols and of the water-soluble portion of the latter indicate the nature of the attack and of the preferred recombination. Any exact relations found supply a foundation for theoretical generalizations.

Such an investigation of the simple mineral halloysite has been reported by the writer[1] and formed the basis of the present work on montmorillonite by the same method. Starting with a pure halloysite analyzing $Al_2O_3 \cdot 2SiO_2 \cdot 3.4\ H_2O$ under room conditions after grinding to 0.1 mm, the washed sol after drying at 160° C was found to be $2Al_2O_3 \cdot 3SiO_2 \cdot 7H_2O$

[6] W. McDermott *et al.*, SCIENCE, 101: 228, 1945.

[1] This investigation was aided by grants from the Rockefeller Foundation and Nutrition Foundation, Inc.

[2] A. A. Albanese and W. Buschke, SCIENCE, 95: 584, 1942.

[3] O. A. Bessey and S. B. Wolbach, *Jour. Exp. Med.*, 69: 1, 1939; V. P. Sydenstricker, W. H. Sebrell, H. M. Cleckley and H. D. Kruse, *Jour. Am. Med. Asn.*, 114: 2437, 1940.

[4] A. A. Albanese, L. E. Holt, C. Kajdi, J. E. Frankston, *Jour. Biol. Chem.*, 148: 299, 1943.

[5] We are indebted to Dr. Wilhelm Buschke for some of these examinations.

[6] H. Scarborough, *Brit. Med. Jour.* 11: 601, 1942.

[7] T. E. Machella and P. R. McDonald, *Am. Jour. Med. Sci.*, 205: 214, 1943.

[1] The formation of colloid from halloysite in dilute acid solutions, *Jour. Wash. Acad. Sci.*, April 15, 1944, contains references to previous work.