Reduced Absorption of Aureomycin Caused by Aluminum Hydroxide Gel (Amphojel). (17579)

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Aureomycin given orally is effective in many microbial infections. The simultaneous oral administration of aluminum hydroxide gel and aureomycin will in some instances reduce the epigastric distress, nausea, and vomiting that occasionally occur when aureomycin is given alone. It has been recommended that this antibiotic should be prescribed along with a preparation of aluminum hydroxide suspension.(1,2) However, it has been found that solutions of aureomycin had very little antibacterial activity following exposure to aluminum hydroxide gel.(3) This observation suggested that if aluminum hydroxide were administered concurrently with aureomycin, similar loss of activity might occur in the bowel and greatly diminish the anticipated levels of the drug in the blood and tissues. The present report is therefore concerned with the influence of an orally administered aluminum hydroxide suspension† upon the absorption of aureomycin as measured by aureomycin blood levels obtained before and after aluminum hydroxide was instituted.

Method of Study. Daily levels of aureomycin in the serum of 5 hospitalized patients and 6 normal male subjects were determined. Aureomycin was administered for 3 consecutive days. This was followed immediately by a 3-day period during which aureomycin and aluminum hydroxide suspension were both administered. The dose of aureomycin was 500 mg taken orally every 6 hours. Two tablespoons of aluminum hydroxide were given immediately after each dose of aureomycin. Blood for the serum levels was drawn with sterile technique each morning and promptly refrigerated. The serum was separated by centrifugation within 3 hours after the blood was obtained and placed in a deep freeze unit where it was stored at −4°C. Aureomycin levels were determined by a modification of the broth dilution method of Dornbush.(4) Bacillus No. 5,‡ a strain of *Bacillus cereus,* was used as the test organism. Two-fold dilutions of the sera were made in broth, and .5 ml of a 1:100 dilution of an 18-hour broth growth of the organism was inoculated into each tube. The mixture was incubated for 4 hours at 37°C. The concentrations of aureomycin in the sera were calculated by multiplying the last dilution of serum that inhibited visible growth of the test organism by the sensitivity of that organism as determined at the same time. The sensitivity of the test organism varied from .01 mg per ml to .039 mg per ml. All the sera from each individual were examined simultaneously in order to avoid the effect of slight daily variation in the sensitivity of the test organism.

Results. In 4 patients, there was a fall in the level of aureomycin in the serum within 24 hours after they started to take aluminum hydroxide gel with aureomycin. After 48 hours of the combined medication, all serum levels were less than one mg per ml. Aureomycin without amphojel produced levels which averaged 5.9 mg per ml and ranged from 1.2 to 10.2 mg per ml. The fifth patient maintained a level of 5 mg per ml in spite of the aluminum hydroxide. One patient suffered a recurrence of her urinary tract infection on the third day of combined treatment which promptly subsided when the aluminum hydroxide was discontinued.

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1. Ross, S., Schoenbach, E. B., Burke, F. G., Bryer, M. S., Rice, E. C., and Washington, J. A., *J. A. M. A.*, 1948, v138, 1213.

2. Schoenbach, E. B., and Bryer, M. S., *J. A. M. A.*, 1949, v139, 275.

3. DiGangi, F. E., and Rogers, C. H., *J. Am. Pharm. Assn.*, in press.

† Wyeth, Inc.

‡ Strain was obtained from the Lederle Laboratories Division of the American Cyanamid Co.

4. Dornbush, A. C., and Pelcak, C. J., *Ann. N. Y. Acad. Sci.*, 1948, v51, 218.

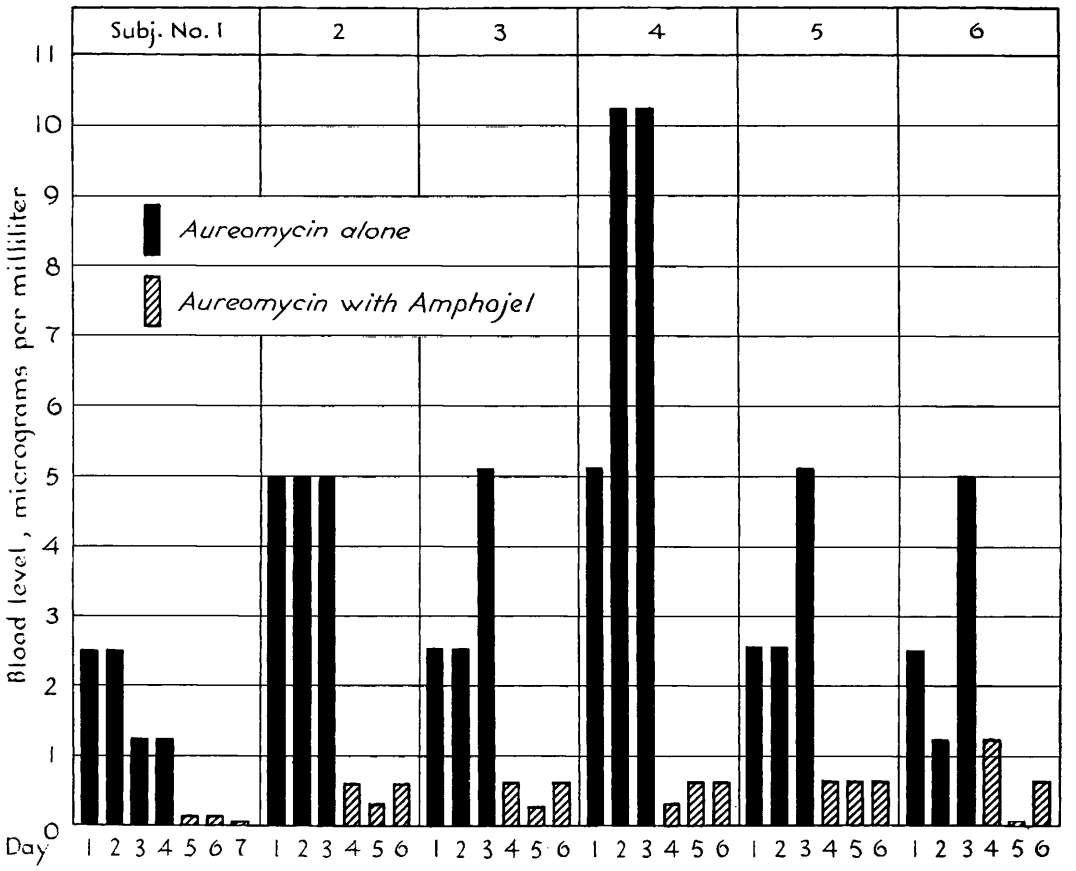

FIG. 1.
Serum levels of aureomycin in 6 normal subjects who first took aureomycin alone and then aureomycin and amphojel together.

The addition of aluminum hydroxide gel was followed by a sharp drop in the serum concentration of aureomycin in each of the 6 normal males. This drop occurred within 24 hours after they began to take aluminum hydroxide gel (Fig. 1). Levels before aluminum hydroxide gel averaged 4.2 mg per ml and ranged from 1.25 mg per ml to 10.24 mg per ml. After aluminum hydroxide gel, the average level was .49 mg per ml with a range of from .036 mg per ml to 1.25 mg per ml.

Four of the normal male subjects complained of loose unformed stools during the 6 days they were taking aureomycin. Three of them noted pruritus ani that disappeared after aureomycin was discontinued.

Discussion. These results clearly indicate that when aluminum hydroxide gel is given with aureomycin, a lowered level of aureomycin is obtained. This lowering of the serum level of aureomycin by aluminum hydroxide gel may explain some therapeutic failures in infections that usually respond to aureomycin. A possible explanation of these findings is that the colloidal particles of the aluminum hydroxide gel may adsorb the aureomycin and prevent its absorption through the gut. The possible influence by other foods and drugs on the absorption of aureomycin is worthy of further investigation.

Summary and Conclusions. Aluminum hydroxide gel (amphojel) reduced the level of aureomycin in the serum of 10 individuals within 24 hours after the gel was added to each dose of aureomycin. These findings indicate that the two drugs should not be used together.

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