# NOTES

## EVALUATION OF ORAL AUREOMYCIN FOR INTESTINAL ANTISEPSIS

WILLIAM I. METZGER AND JOSEPH B. SHAPSE

*Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York, and Departments of Pathology and Surgery, Harlem Hospital, New York 30, N. Y.*

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The usefulness and limitations of currently used intestinal antiseptics have been discussed in a recent publication by Spaulding, Madajewski, *et al.* (J. Bact., **58,** 279, 1949). Although streptomycin and certain sulfonamides are effective in preoperative bowel preparation, it is recognized that a more efficient agent is desirable for this purpose.

Aureomycin was considered in this connection because (1) encouraging results were obtained by Wright, Metzger, *et al.* (Am. J. Surg., **78,** 15, 1949) in a series of peritonitis cases in which the drug was beneficial in controlling mixed bacterial infections of intestinal origin, (2) the drug is effective *in vitro* against a variety of gram-positive and gram-negative organisms, including many intestinal bacteria (Pelcak, Metzger, and Dornbush: Harlem Hosp. Bull., **2,** 47, 1949), (3) acquired bacterial resistance to the drug has not been demonstrated (Paine, Collins, and Finland: J. Bact., **56,** 489, 1948), and (4) the drug may be administered orally in relatively large doses over fairly long periods of time with little or no toxicity (Wright and Schreiber: J. Natl. Med. Assoc., **41,** 195, 1949).

Pulaski and Connell (Bull. Army Med. Dept., **9,** 265, 1949) have reported the intraluminal effect of oral aureomycin on three patients. Each patient received 2.0 g of the drug daily. They found that the *Escherichia coli* count was reduced, but not to the level obtained with sulfonamides or streptomycin. The remaining flora was not affected. They concluded that aureomycin appears to be of little promise as an intestinal antiseptic. In view of this report, it was decided to investigate the problem further on a small number of patients and to expand the study later if indicated.

This report describes the results obtained from five hospital patients, two of whom were normal individuals (from a gastrointestinal viewpoint) from whom daily stool counts were made. The other three patients had functioning colostomies from which frequent cultures were obtained. The first two individuals were each given 1.0 g of oral aureomycin three times daily for 5 days. Aerobic and anaerobic counts were made in the usual way upon a known weight of wet stool. Both patients showed a definite reduction in the coliform count, one after 1 to 2 days of aureomycin treatment and the other after 3 to 4 days. In both cases the count was reduced to 20,000 to 30,000 coliforms per gram of wet stool, amounting to a decrease of approximately 100-fold in one patient and 1,000-fold in the other patient. This degree of suppression is inferior to that obtained with either sulfonamides or streptomycin. Following the reduction of coliforms, both patients

showed an immediate and marked increase in *Proteus* organisms. This increase was of such a degree that the total gram-negative count far exceeded the normal count. The total gram-positive count, *Streptococcus faecalis*, and *Bacteroides* were not affected by aureomycin in either patient. Anaerobic spores were slightly reduced in one patient and were unaffected in the other. Therefore the net effect of reducing the coliforms was an increase in the total over-all count due to the rapid proliferation of *Proteus* organisms.

The three patients with functioning colostomies were all receiving therapeutic doses of aureomycin throughout the period of study. Successive cultures from the drainage site of one patient revealed *E. coli* and *S. faecalis* over a period of 10 days. A second patient yielded *E. coli*, *Proteus*, and *Bacteroides* over a period of 3 weeks, and the third patient revealed *E. coli*, *Proteus*, and nonhemolytic streptococci over a 1-month period. In no case was there a suggestion of a diminution of any of the organisms concerned.

Although this study is limited in scope, the results are clear-cut enough to warrant the conclusion that aureomycin alone does not appear to be an efficient agent for reducing the colonic flora prior to surgery. The results obtained here are in close agreement with those of Pulaski and Connell. Among other reasons, the failure of aureomycin against certain organisms in the colon as opposed to its efficiency *in vitro* may be due to its rapid absorption from the gastrointestinal tract, as shown by the comparative blood levels obtained after oral and intravenous administration of aureomycin (Logan, Metzger, *et al.*: Am. J. Surg., *in press*). On the other hand, Dornbush and co-workers (personal communication) have shown that approximately 500 to 600 μg of aureomycin are present per gram of wet stool after the oral administration of 1.0 g of the drug.

As demonstrated here, the suppression of the coliform flora may actually be deterimental by stimulating the development of a highly resistant flora. Whether or not *Proteus* and allied organisms alone or in a mixed flora are dangerous in large bowel surgery from a pathogenic viewpoint is still to be determined.

## CHANGES INDUCED IN ESCHERICHIA COLI BY CEPHARANTINE

JEAN DUFRENOY AND ROBERTSON PRATT

*University of California College of Pharmacy, The Medical Center, San Francisco, California*

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Cepharantine, an alkaloid ($C_{37}H_{38}O_6N_2$) derived from *Stephania cepharanta* and other Formosan species of *Stephania*, has attracted interest in recent years as a chemotherapeutic agent, especially in the Orient.

Hasegawa (Japan. J. Exptl. Med., **20**, 69, 1949) has published an extensive account of the successful clinical use of the alkaloid and its salts in a large number of cases of tuberculosis, leprosy, and lupus vulgaris. He reported that the drug is relatively nontoxic, the MLD being about the same for cepharantine as for quinine