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Urinary Excretion of Aureomycin.*

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Aureomycin is a new antibiotic which is active against many gram-positive and gram-negative bacteria and also against certain viral and rickettsial infections.[¶] As part of a clinical trial of this antibiotic in a number of infections, bacteriologic and pharmacologic studies were also carried out in this laboratory. The results of the bacteriological studies are reported elsewhere.[1] In this paper are presented some preliminary findings on the urinary excretion of aureomycin after single and multiple doses.

Two normal adult male subjects were given a single dose by mouth in the morning on a fasting stomach; one was given 0.5 g and the other 0.75 g. Each subject emptied his bladder just prior to taking the dose and the urine thus voided was used as a control. The bladder was then emptied at intervals, the volumes of urine recorded and aliquots immediately filtered,** frozen and stored at −20 C. After all the urines had been collected, each specimen was assayed for aureomycin by a method similar to that used by Rammelkamp for penicillin.[2] The test organism, *Streptococcus* No. 98, was completely inhibited by 0.5 μg per ml and partially inhibited, as evidenced by growth on subculture, by 0.25 to 0.125 μg per ml. The control urine specimens, obtained before and several days after the dose, failed to inhibit the growth of the test organism.

The results for the subject receiving 500 mg are shown in Fig. 1 and those for the subject receiving 750, who had a much greater volume of urine output, are shown in Fig. 2. The greatest rate of aureomycin excretion occurred in both instances between 4 and 8 hours. If similar absorption and excretion take place from repeated oral doses, the intervals between such doses should be about 8 hours in order to maintain maximum absorption and excretion rates. Concentrations of aureomycin sufficient to completely inhibit the test organisms when the urine was diluted 16-fold or more were excreted for at least 33 hours. The aureomycin was still being ex-

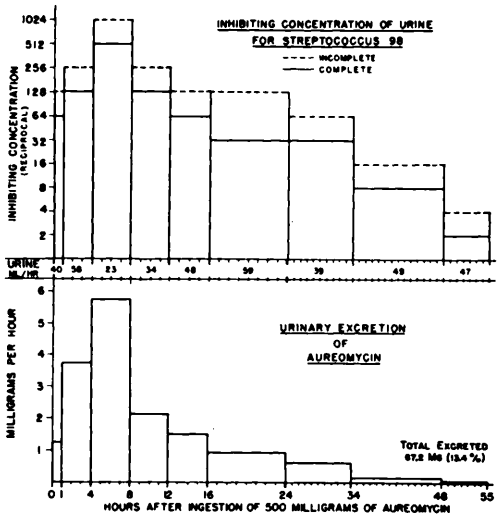

FIG. 1.

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¶ Reports on the method of isolation of aureomycin, its pharmacology and activity will be made by workers of the Lederle Laboratories Division of the American Cyanamid Company at the New York Academy of Sciences, July 21, 1948. Some of the data were made available by these workers in personal communications to the authors.

1 Paine, T. F., Jr., Collins, H. S., and Finland, M., *J. Bact.*, 1948, **56**. Submitted for publication.

** Filtration through Seitz, Mandler or sintered glass filters did not remove any of the antibiotic.

2 Rammelkamp, C. H., Proc. Soc. Exp. Biol. and Med., 1942, **51**, 95.

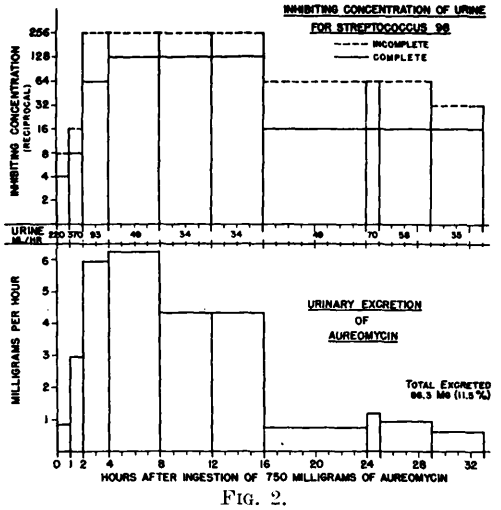

FIG. 2.

creted in both subjects at 55 and 33 hours, respectively, when the studies were terminated. The total amount recovered was 13.4% of the 500 mg dose in 55 hours and 11.5% of the 750 mg dose in 33 hours.

Blood levels carried out with the same organism were unsatisfactory since the maximum amount of antibiotic in the serum inhibited the test organism only in a final dilution of 1:2 or 1:4.

Total urinary excretion studies were made in 2 patients who were receiving 2 doses of aureomycin by mouth each day for several days. The urines were collected at 12-hour intervals and all voidings were stored at 5 to 10°C during the intervals. The tests were otherwise carried out in the same manner as before. In one of these patients who received 0.25 g twice a day for 10 days the concentrations of antibiotic in the urine were sufficient completely to inhibit the test streptococcus in dilutions of 1:4 to 1:16, and partial inhibition occurred in dilutions of 1:8 to 1:32. In the patient who received 0.5 g twice a day for 7 days the concentrations of aureomycin in the urine ranged from 10 to 32 μg per ml. In these 2 patients the total amount recovered was 5% and 2%, respectively of the amount administered. Antibiotic activity was present in the urine up to 72 hours and longer after the last dose. Control urines from these patients, obtained before and several days after the antibiotic was given failed to inhibit the test strain.

Both of the patients were acutely ill and the differences in the percentage recoveries may have been related to poor absorption of the drug associated with the illness. Technical difficulties may also have accounted, in part, for the discrepancies.

Summary. After a single oral dose of 0.5 or 0.75 g of aureomycin given to fasting normal subjects antibiotic activity was recovered in the urine for more than 33 to 55 hours. The antibiotic was excreted in high concentrations between 2 and 16 hours and the largest rate of excretion occurred between 2 and 8 hours. The findings suggest that the optimum intervals between oral doses of aureomycin should be about 8 hours.

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Stereoencephalotomy.*

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Using the previously described stereotaxic apparatus (stereoencephalotome) for the production of subcortical lesions in the human brain,[1] the following procedures have been developed.

I. *Dorsomedial thalamotomy* in mental dis-

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[1] Spiegel, E. A., Wycis, H. T., Marks, M., and Lee, A. J., *Science*, 1947, **106**, 349.