cyte response was noted. The blood values reached normal levels on the 68th day. Ten days later the patient was placed on 12 mg of CF intramuscularly, twice weekly. At the end of 117 days she appeared entirely well (Fig. 2). No alteration in neurologic status was noted.

Discussion. From the foregoing data it is clear that intravenously administered CF in doses of 3.0 mg a day induced clinical remissions and a moderately good to a complete hematologic response in two patients with pernicious anemia in relapse. It would appear that in one case (I. R.) the excretion rate surpassed the utilization rate because when the route of administration was changed to the intramuscular one the hemoglobin and erythrocytes rose to normal levels. There was no instance of development or progression of nervous system changes in either patient after 3 to 4 months although one of them (I. R.) showed evidence of spinal cord disease before treatment was begun. Recently we have observed rapidly developing alterations in the central nervous system after 3 months of oral treatment of a patient with pernicious anemia using 6.0 mg of CF daily(5). The present hematologic results also differ from our earlier report in that in this group normal blood counts were attained(2). The reticulocyte response was absent or submaximal in the 2 cases presented and this confirmed the observations made when patients were treated by the intramuscular route(2).

Summary. The daily intravenous administration of 3.0 mg of CF to two patients with pernicious anemia in relapse was followed by a satisfactory clinical remission, poor reticulocyte response, suboptimal hemoglobin and red blood cell levels in one case and a normal blood count in the other. The subsequent intramuscular injection of the same dose to the first patient resulted in a good hematologic remission.

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Effect of Intravenous Aureomycin on the Intestinal Flora of Dog and Man.* (18995)

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With increasing experience it is becoming evident that the toxic effects of aureomycin on the gastrointestinal tract may occur when the drug is given intravenously as well as orally(1,2). Since this may be due to excretion of the drug into the gastrointestinal tract, its administration parenterally may exert an antibacterial effect on intestinal flora. This report deals with a study of effects of intravenous aureomycin on the normal intestinal flora of dog and man.

Effect of aureomycin on intestinal flora of dogs. Method. Sixteen healthy mongrel dogs† received aureomycin intravenously daily for a period of 10 days. Four of them were given 1000 mg, six 600 mg, and six 400 mg, in 2 equal doses each day. The bacterial flora of the stools in all dogs was examined(3) before treatment was started, daily during the course of treatment, and for a few days thereafter.

Results. (a) 1000 mg/day. This dose proved to be toxic, as previously reported(4). Two of 4 dogs died in 3 days without any

* Aided by a grant from Lederle Laboratories Division, American Cyanamid Co.

1. Rutenburg, A. M., Jacob, S., Schweinburg, F. B., and Fine, J., *N. Eng. J. Med.*, in press.

2. Rutenburg, A. M., unpublished data.

† Each weighed about 10 kg.

3. Schweinburg, F. B., Rutenburg, A. M., Milrod, S., Glotzer, P., and Fine, J., *Ann. Surg.*, 1951, v133, 208.

demonstrable change in the fecal flora. The other 2 died in 5 days. One of these showed no coliform bacilli in the stool; the other showed a reduction to about 1/150 of the original count.

(b) 600 mg/day. All 6 dogs in this group survived, although by the 7-8th day they stopped eating and lost weight. Recovery was rapid following cessation of therapy. In 4 dogs the coliform bacilli disappeared from cultures in 7-8 days, and in the remaining 2 the coliform count was markedly reduced. Strains of *E. coli* still present after 10 days of treatment were sensitive *in vitro* to aureomycin.

(c) 400 mg/day. The number of coliform organisms was definitely reduced in all 6 dogs, but in only 2 of the 6 were the bacilli completely eliminated after 10 days of therapy.

In all 16 dogs the Clostridia and Enterococci were moderately reduced, but did not disappear from cultures.

Comment. These results and data reported elsewhere(3) indicate that intravenous aureomycin has a definite antibacterial action on the normal fecal flora of the dog, but its suppressive effect was inferior to that of the oral preparation.

Effect of aureomycin on intestinal flora of man. Method. Twenty-five patients with a variety of surgical infections received 1000 mg of aureomycin intravenously in 2 equal doses for 3 to 25 days. No other antibacterial agent was given to these patients. The stools were cultured before, during, and occasionally, after cessation of therapy.

Results. In 15 of the 25 patients the coliform bacilli and Enterococci disappeared from the stools in about 3 to 7 days. The Clostridia were completely suppressed in only 7 of the 15, and markedly reduced in 2 others. In 5 other patients there was a marked reduction in the counts of the coliform bacilli, Clostridia, and Enterococci. The remaining 5 showed no change in the coliform counts but partial to complete suppression of Clostridia in all, and partial suppression of Enterococci in 2. There was no reduction in the number of colonies of *B. proteus vulgaris* or *Pseudomonas* in any of the 25 patients.

Toxicity. Gastrointestinal side effects occurred in 8 patients (31%). Of 6 patients with diarrhea, 2 had severe protracted diarrhea which upset the fluid and electrolyte balance. Two other patients had nausea and vomiting. No other toxic effects were observed.

Comment. The results indicate that intravenous aureomycin is more effective in man than in the dog in the suppression of the normal intestinal flora. Thus, coliform organisms were completely or partially suppressed in 20 patients: Clostridia in 19; and Enterococci in 22 of the 25 patients.

Discussion. The suppression of the fecal flora and the occurrence of gastrointestinal side effects following the administration of aureomycin intravenously is presumably due to the excretion of the drug into the gastrointestinal tract in man via the bile and salivary glands. Aureomycin administered intravenously has been shown to be excreted in bile in high concentration(5,6); and the oral lesions following intravenous aureomycin suggest excretion in the saliva(2).

The inferior antibacterial action of aureomycin on the intestinal flora of the dog as compared to man may be related to the much higher concentration of sodium taurocholate in the bile of the dog(7). It is notable that following oral therapy, the effect of aureomycin on the intestinal flora is identical in both man and dog(3,8).

Summary. 1. Aureomycin administered intravenously results in partial suppression of the intestinal flora in both man and dog. The effect in patients is superior to that in dogs. 2. The drug is presumably excreted into the intestinal tract via the salivary glands and bile.

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6. Zaslow, J., Hewlett, T. H., and Goldsmith, R., *Gastroenterology*, 1950, v16, 479.

7. Tejerina-Fotheringham, *Gastroenterology*, 1948, v10, 687.

8. Rutenburg, A. M., Schweinburg, F. B., and Fine, J., *Ann. Surg.*, 1951, v133, 344.

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