as the disturbed serum constituents upon which the positive Bradosol test is dependent. This possibility is further suggested by the above mentioned variation in results obtained in cirrhosis and nephrosis. In both of these diseases a gross alteration of total serum proteins exists, with the common finding of a low albumin level. Despite this fact, the serum protein precipitation, as demonstrated by the Bradosol reaction, revealed that only 1 out of 13 of the cirrhotics tested was positive while 4 out of 5 cases of nephrosis gave a positive reaction. It thus seems likely that factors other than quantitative variations in the serum albumin level are responsible for the positive Bradosol reaction.

The precipitation of blood sera with cationic detergents would thus appear to be another of the group of non-specific tests which have been described in recent years. This group includes the thermal coagulation test of Mayer(2) and the iodoacetate index of Huggins(4) which demonstrate a definite alteration from the normal pattern in malignancy as well as in an appreciable percentage of non-malignant disease. Some evidence was noted during this work, as indicated by the previously mentioned cases with a varying Bradosol reaction, to suggest the use of this test as a prognostic guide to the progression or regression of malignant disease. This possibility is at present the subject of further investigation.

Summary. 1. The sera of 234 subjects were tested with Bradosol, a total of 294 tests being carried out. 2. A significantly greater percentage of positive reactions was noted in malignancy than in non-malignant disease.

Received May 21, 1951. P.S.E.B.M., 1951, v77.

Effect of Aureomycin on Liver Fat and Liver Function. (18812)

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Recent observations(1-2) indicate that some patients given aureomycin or terramycin developed fatty liver. This was associated with an increase in bromsulphthalein retention in some cases. The following experiments represent attempts to study this phenomenon.

Methods. Aureomycin was administered to mongrel dogs, Sprague-Dawley rats and humans in the manner and dose indicated in Table I. Serial data from dogs and humans fed aureomycin were compared to pre-treatment data. Rats fed or injected aureomycin were compared with pair-fed or pair-injected (saline) animals. Rats and dogs were continued on commercial rations and humans on their usual diet. Histological studies including fat stains were made of liver tissue from needle biopsies(3) of dogs and necropsies from rats. Liver fat in rats was also determined chemically(4). The following liver function tests were performed on dogs and humans at weekly intervals: bromsulphthalein retention(5), serum bilirubin(6), thymol turbidity(7) and zinc sulfate turbidity(8). In

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TABLE I. Effect of Aureomycin on BSP Excretion and Fat Content of Liver in Normal Rats, Dogs, and Human Subjects.

Subject	No.	Dose/ day	Route of administration	Treatment (days)	Increase in BSP retention	Increase in liver fat histologically	Liver fat % by wt chemical analysis
Dogs	4	1 g	Oral	30	0	0	—
Rats	6	0	Saline IP	28	—	Control	—
	6	2 mg	IP	28	—	0	—
	6	5	"	28	—	0	—
	6	10	"	28	—	+, —	—
	25	0*	Oral	30, 60, 70†	—	Control	13.9 ± 1.1‡
	25	25	"	30, 60, 70†	—	0	13.8 ± 1.5‡
Humans	3	2 g	"	30	0	—	—

* Control animals pair-fed.
† 5 animals of each group sacrificed at 30 days, 15 at 60 days, 5 at 70 days.
‡ Mean ± std dev.

addition, cephalin cholesterol flocculation(9) and gamma globulin turbidity(10) tests were done on humans.

Results. (Table I). There were no significant changes in liver fat of dogs or rats as measured histologically and/or chemically after aureomycin administration for as long as 70 days. Two g aureomycin taken orally by three healthy young men for 30 days produced no changes in liver function tests in 2 subjects. One individual showed a change in bromsulphthalein retention from control values of 2% to 6% during therapy. This was not considered significant. There were no changes in the other tests done in this subject.

Comment. Dowling, *et al.*(11) observed increased liver fat and even death in some animals treated with large amounts of aureomycin. György, *et al.*,(12) has demonstrated that aureomycin actually prevents fatty liver and prolongs the survival of rats fed diets low in choline or methionine. On the other hand, clinical studies(1,2) indicate that some patients with hepatic disease or serious infections develop fatty liver after aureomycin administration, despite adequate diets. It is the purpose of this report to point out that these various effects were not obtained in normal dogs and rats maintained on adequate diets with levels of aureomycin dosage approximating the therapeutic range, and that no liver function test abnormalities developed in normal humans.

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Received June 13, 1951. P.S.E.B.M., 1951, v77.

Inhibition of Pantothenate Synthesis by Streptomycin.* (18813)

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During the past few years the mode of action of streptomycin has been studied by several groups. Thus, Umbreit(1), and Oginsky *et al.*(2) reported that streptomycin specifically inhibits an oxidative reaction, apparently the "oxalacetate-pyruvate" conden-

* This investigation was supported in part by RG 2916 from the National Institutes of Health, Public Health Service.

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