Conn(7). He found that when glutathione was injected into man with "ACTH diabetes" there was a transitory decrease in glycosuria lasting 1 to 2 hours. Studies with ACTH are now in progress.

These results emphasize that although glutathione protects the beta cell against physiologically occurring toxic compounds(3) it may also have diabetogenic effects due to its action on steroids, enzyme systems, etc. They furthermore suggest the possibility that glutathione might potentiate the therapeutic effect of cortisone in the treatment of rheumatic disease.

Summary. Glutathione, when injected into normal animals which had been force-fed a high carbohydrate diet, induced glycosuria. The amount of glycosuria decreased with increasing adaptation to the high carbohydrate diet and after feeding the diet for 2 months, glutathione produced insignificant effects. By contrast the injection of glutathione into cortisone-diabetic rats caused a marked (in some cases up to 10 fold) increase in glycosuria which has been observed even after 3 months of the high carbohydrate diet. Cysteine and ascorbic acid were also studied. Glutathione potentiates the diabetogenic effect of cortisone. The mechanism of this potentiation has been discussed and its possible significance in the treatment of rheumatic disease has been suggested.

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Chemoprophylactic Effectiveness of Aureomycin and Terramycin in Murine Bartonellosis.* (18021)

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The bartonellae resemble the rickettsiae in many of their characteristics. Previous work in this laboratory (unpublished) has shown, however, that murine bartonellosis is not prevented or made less severe by para-aminobenzoic acid or penicillin, both of which are highly effective against murine typhus infection in mice(1,2). We have also obtained negative chemoprophylactic results in murine bartonellosis with sulfanilamide, sulfathiazole, sulfapyridine, folic acid, atabrine, and several other antimalarial drugs. The purpose of this paper is to report the chemoprophylactic effectiveness of aureomycin and terramycin in this disease.

Material and methods. Two strains of white rats were used, one of which was bartonella-free while the other, like most laboratory strains, was a so-called "carrier" strain, latently infected with *Haemobartonella muris*. It is well known(3) that rats rarely develop clinical or hematological evidence of bartonellosis unless splenectomy is carried out. When bartonella-free rats are splenectomized and then injected with the organism, they become severely ill in a few days as a result of extensive parasitization and destruction of erythrocytes, and the mortality is usually 100%. When ordinary carrier rats are splenectomized, they also become severely ill, and the mortality usually ranges from 50 to 75%.

In one experiment, 19 bartonella-free rats (Sprague-Dawley strain) were splenectomized, and injected 3 weeks later with 1 cc of rat blood containing *H. muris* of high virulence. Twenty-four hours after injection, 5 of these rats were started on aureomycin, 4 on terramycin and 5 on chloramphenicol, the remaining 5 serving as controls. The aureomy-

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TABLE I (Exp. 1).
Chemoprophylactic Effect of Aureomycin, Terramycin, and Chloramphenicol on Splenectomized Bartonella-free Rats Injected with *H. muris*.

Rat No.	Dosage	Illness after inj. (hr)	Lowest hemoglobin level (mg)	Highest Bartonella count (per 100 r.b.c.)	Hemoglobinuria	Outcome
1	Control	72	10	237	+	died 5th day
2		72	6	127	+	" " "
3		72	10.5	54	+	" " "
4		72	7	99	+	" " "
5		72	6	246	+	" 6th "
6	Chloramphenicol	96	7.5	289	+	" 7th "
7	18 mg twice daily,	96	9	143	—	*S
8	9 days	96	6	241	+	died 7th day
9		72	6	102	+	" 5th "
10		72	4	315	+	" 7th "
11	Aureomycin	0	16	0	—	*S
12	10 mg twice daily,	0	15	0	—	"
13	9 days	0	12.5	<1	—	"
14		20 days	16.5	<1	—	died 20th day†
		21 "	14.5	<1	—	" 21st "
16	Terramycin	0	16.5	0	—	*S
17	18 mg twice daily,	0	17	1	—	"
18	9 days	0	15	0	—	"
19		0	16.5	<1	—	"

* S—Survived.
† Cause of death not obvious. No anemia and no bartonellae in blood at time of death.

cin was dissolved in distilled water and injected subcutaneously in the dosages indicated in Table I. The terramycin and the chloramphenicol were relatively insoluble in water and were given partly in aqueous suspension by the subcutaneous route.

In a second experiment, 30 carrier rats of the St. Louis University strain were splenectomized. Twenty-four hours later, 10 of these rats were started on aureomycin, 10 were started on terramycin, and 10 were left as controls. The drugs were given subcutaneously, as described above, and in the dosages shown in Table II.

Criteria for the effectiveness of the drugs were: 1. presence or absence of clinical illness, 2. daily direct hemoglobin determinations (Dare) for 10 days, 3. daily bartonella counts in giemsa stained blood films for 10 days, 4. presence or absence of hemaglobinuria (obvious by inspection) and 5. mortality. Bartonella counts were recorded as organisms per 100 erythrocytes, based on observation of 400 erythrocytes.

Parenteral aureomycin was obtained from the Lederle Laboratories, and terramycin from the Charles Pfizer Co.

Results. The results of these experiments are shown in Tables I and II. In Exp. 1, (Table I) all 5 control rats and 4 of the 5 rats receiving suspensions of chloramphenicol, developed high bartonella counts, severe anemia and hematuria, and died 5 to 7 days after injection with *H. muris*. There was evidence of a slight prolongation of the incubation period in the rats receiving chloramphenicol, and the fact that one of these rats survived is possibly significant, since 100% mortality is the rule in this type of experiment. None of the rats treated with aureomycin or terramycin showed clinical evidence of anemia or hematuria. Several of these animals showed low parasite counts for a day or two, but definite anemia did not develop in any during an observation period of 30 days. (Two rats from the group receiving aureomycin died on the 20th and 21st days after injection of bartonellae. The cause of death was not clear, but these rats did not show anemia or bartonellae in the blood stream.

In Exp. 2 (Table II) all 10 control animals developed severe clinical illness, severe anemia, and high bartonella counts. The mortality was 50%, which is about average

TABLE II (Exp. 2).
Chemoprophylactic Effect of Aureomycin and Terramycin on Splenectomized Carrier Rats.

Rat No.	Dosage	Illness after splenectomy, hr	Lowest hemoglobin level (mg)	Highest Bartonella count (per 100 r.b.c.)	Hemoglobinuria	Outcome
1	Control	144	7.5	99	—	*S
2		120	5	108	—	"
3		120	3	216	—	died 9th day
4		144	5	122	—	*S
5		120	5	240	—	"
6		120	5	220	+	died 8th day
7		144	4	266	+	" 7th "
8		120	3	276	—	*S
9		120	6	211	—	died 6th day
10		168	6.5	363	—	" 8th "
11	Aureomycin	None	11	0	—	*S
12	15 mg twice daily,	"	13	0	—	"
13	8 days	"	16	0	—	"
14		"	14	0	—	"
15		"	15	0	—	"
16		"	14	0	—	"
17		"	15.5	0	—	"
18		"	15	0	—	"
19		"	12.5	0	—	"
20		"	15	0	—	"
21	Terramycin	"	14.5	0	—	"
22	15 mg twice daily,	"	16	<1	—	"
23	8 days	"	15.5	0	—	"
24		"	15.5	0	—	"
25		"	14	0	—	"
26		"	16	<1	—	"
27		"	15	<1	—	"
28		"	15	0	—	"
29		"	16	0	—	"
30		"	16	0	—	"

* S—Survived.

for this type of experiment. None of the 10 rats treated with aureomycin, and none of the 10 rats receiving terramycin showed clinical evidence of illness or significant lowering of the haemoglobin level. Bartonellae were not found in the blood of 17 of these 20 treated rats, and were present in only very small numbers in the other 3.

Discussion. Mayer, Borchardt, and Kikuth (4) found that organic arsenical compounds, including neoarsphenamine, were chemotherapeutically effective in murine bartonellosis. These agents have not given favorable results in human bartonellosis(4). Whether aureomycin or terramycin will prove to be of value in the human disease remains to be seen. It should be noted that chloramphenicol, because of its low solubility, was perhaps not given a fair trial in the experiment described above. It has been called to our attention that Dr. E. H. Payne reported the successful use of this compound in human bartonellosis to the American Society of Tropical Medicine in November, 1949.

Conclusions. Both aureomycin and terramycin, started 48 to 72 hours before the expected onset of illness and continued for 9 days were found to be effective in preventing murine bartonellosis. Rats treated with these compounds developed no evidence of illness while the morbidity in the control groups was 100%, and the mortality 50 to 100%. A few bartonellae appeared in the blood of some of the treated rats, but anemia and hemoglobinuria were prevented. The chemoprophylactic effectiveness of these 2 compounds in murine bartonellosis is in contrast to negative results obtained with a wide variety of other antibiotics.

4. Mayer, M., Borchardt, W., and Kikuth, W., *Arch. f. Schiffs-u. Tropen-Hyg.*, 1927, v31, 295.

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