intravenously was studied in 6 rabbits. Daily injections, except for Sunday, were continued for 8 weeks. Three rabbits received 5 mg per kilo daily for 26 days. For the next 13 days the dosage was raised to 15 mg, and finally to 20 mg for the next 13 days. Three other rabbits were given 10 mg daily for 26 days, and 20 mg daily for the next 26 days. There were no fatalities in these experiments on subacute toxicity.

The symptoms observed in these toxicity studies will be discussed in a later publication dealing with the tissue changes produced by citrinin, and with the pharmacological data covering effects on blood, circulation, respiration, and smooth muscle structure.

Conclusions. The lower toxicity values reported by Robinson, as compared with those reported by Timonin and Rouatt and those reported here, may be due to a low rate of absorption of citrinin from a suspension in gum acacia solution.

Citrinin in solution is rapidly absorbed, regardless of the mode of administration, as shown by the toxicity data.

The production of tissue changes and the fact that citrinin may result in delayed deaths, up to fourteen days, would make a statement regarding an LD_{50} dose misleading.

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Effect of Streptomycin on Avian Malaria.

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Streptomycin, an antibiotic produced by the soil actinomycete *Streptomyces griseus,* was first described by Schatz, Bugie, and Waksman.[1] Unlike penicillin, streptomycin has been shown to have a high order of activity against certain gram negative infections both *in vitro* and *in vivo*.[2,3,4] Streptomycin has also been found to be active against the acid fast organism *Mycobacterium tuberculosis* both *in vitro*[5] and in the experimental animal.[6] In this communication we are reporting the results of studies on the activity of this antibiotic against avian malaria.

Trophozoite induced *Plasmodium gallinaceum* infections were established in 50 g Single Comb White Leghorn chicks by an intravenous inoculum of 200,000,000 parasitized erythrocytes per kilogram. The tests for suppressive activity against both trophozoite induced *P. cathemerium* and *P. lophurae* malaria were performed on 50 g Pekin ducklings inoculated intravenously with 500,000,000 parasitized erythrocytes per kilogram. The sporozoite induced *P. gallinaceum* infections used for the prophylactic tests were established in 50 g Single Comb White Leghorn chicks by the intravenous inoculation of 0.2 cc per bird of a suspension of sporozoites prepared by grinding 100 infected mosquitoes in 20 cc of chicken plasma.

The streptomycin used in these experiments was supplied by Merck & Co., Inc. and came from batch 162 which had a potency of 440 units per mg.[2] In all cases the streptomycin was administered as an aqueous solution intramuscularly every 3 hours. Birds inoculated with the trophozoites of *P. cathemerium, P. gallinaceum* and *P. lophurae* were treated for 5 days while the birds inoculated with the

1 Schatz, A., Bugie, E., and Waksman, S. A., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 66.

2 Jones, D., Metzger, H. J., Schatz, A., and Waksman, S. A., *Science*, 1944, **100**, 103.

3 Robinson, H. J., Smith, D., and Graessle, O., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 226.

4 Heilman, F. R., *Proc. Staff Meet., Mayo Clinic*, 1944, **19**, 553.

5 Schatz, A., and Waksman, S. A., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 244.

6 Feldman, W. H., and Hinshaw, H. C., *Proc. Staff Meet., Mayo Clinic*, 1944, **19**, 593.

TABLE I.
Ineffectiveness of Streptomycin Against Trophozoite-Induced Avian Malaria Infections.

No. of birds	Drug	Dose	Route	% r.b.c parasitized at peak of infection
P. cathemerium in Pekin ducklings.				
5	Streptomycin	4 × 100,000 units/kg	i.m.	33.4
5	,,	2 ,, ,,	,,	41.2
5	,,	1 ,, ,,	,,	29.3
5	Quinine	80 mg/kg	p.o.	0.3
5	Controls	——	—	37.2
P. gallinaceum in Single Comb White Leghorn chicks.				
5	Streptomycin	4 × 100,000 units/kg	i.m.	70.7
5	,,	2 ,, ,,	,,	70.2
5	,,	1 ,, ,,	,,	68.9
5	Sulfadiazine	0.05% ,,	diet	1.1
10	Controls	——	—	66.5
P. lophuræ in Pekin ducklings.				
5	Streptomycin	4 × 100,000 units/kg	i.m.	73.6
5	,,	2 ,, ,,	,,	73.4
5	,,	1 ,, ,,	,,	74.5
5	Quinine	40 mg/kg	p.o.	0.1
5	Controls	——	—	74.6

TABLE II.
Effect of Streptomycin Against Sporozoite-Induced *P. gallinaceum* Malaria.

No. of chicks	Drug	Dose, units/kg or % in diet	Route	% r.b.c. parasitized on 9th day
5	Streptomycin	40 × 10,000	i.m.	17.7
5	,,	20 ,,	,,	26.9
5	,,	10 ,,	,,	31.8
5	,,	5 ,,	,,	38.5
5	,,	2.5 ,,	,,	40.8
	Sulfadiazine	0.2%	diet	0
	,,	0.1%	,,	0
10	Controls	—	—	35.1

sporozoites of *P. gallinaceum* were treated for 3 days. Treatment was invariably begun within an hour following the inoculation. In the experiments with each infection, groups of 5 birds were given 400,000, 200,000, 100,000, 50,000 and 25,000 units respectively per kilogram per day. In each experiment 5 infected birds served as untreated controls and 5 infected birds were given either quinine or sulfadiazine.

The effect of streptomycin therapy was judged by parasite counts made on the fifth day in the *P. cathemerium* experiment and on the eighth day *P. lophurae* experiment. Parasite counts on the trophozoite induced *P. gallinaceum* infection were made on the fifth day, while the counts on the sporozoite induced infection were made on the ninth day. The parasite counts were made by determining the number of parasitized erythrocytes among ten thousand erythrocytes on Giemsa stained thin blood smears.

Streptomycin at a dose as high as 400,000 units per kilogram per day showed no suppressive activity against *P. cathemerium, P. gallinaceum* or *P. lophurae* infections (Table I). The partially purified streptomycin used in these experiments did, however, have a slight effect on the sporozoite induced *P. gallinaceum* infection (Table II). While the group of birds on each dose level was so small that the differences among the average parasite counts are not in themselves significant, the linear relationship between the dose of the drug and the parasite count is noteworthy.