favorably with streptomycin and para-aminosalicylic acid in its antibiotic activity against *Mycobacterium tuberculosis* $H_{37}RV$.

In vivo, aureomycin proved ineffective as a therapeutic antibiotic agent in experimental tuberculosis of dba mice.

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Effect of Aminoguanidine on Formaldehyde Poisoning in Rats. (17987)

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Poisonings due to the handling of formaldehyde or the ingestion of methyl alcohol have been reported repeatedly(1). Treatment of such poisoning is symptomatic, including gastric lavage, administration of alkaline salts and morphine. The acidosis may be alleviated by intravenous infusion of glucose and sodium lactate. No specific antidote is known(2). Recently Bernheim(3) has shown that in the presence of aminoguanidine the oxidation rate of formaldehyde by rat liver is greatly increased. This suggested aminoguanidine as a possible antidote for formaldehyde poisoning. Its effect on methyl alcohol poisoning was also tested since some methyl alcohol is oxidized to formaldehyde which may contribute to its toxic effects(4).

Methods. White rats were injected intraperitoneally with minimum fatal doses of formaldehyde (180 mg/kg) and methyl alcohol (10 g/kg). Aminoguanidine sulfate, a relatively nontoxic substance, was injected in doses of 200-600 mg/kg. Since the doses of the toxic substances caused death in 5-30 minutes, it was necessary to inject the aminoguanidine shortly after the aldehyde or alcohol

TABLE I.
Effect of Aminoguanidine on Survival Time of Formaldehyde- and Methyl Alcohol-Poisoned Rats.

	No. animals used	% surviving at				
		30 min.	1 hr	8 hr	24 hr	4 days
Formaldehyde 180 mg/kg	15	0	—	—	—	—
Formaldehyde 180 mg/kg + Aminoguanidine 200 mg/kg	10	100	40	0	—	—
Formaldehyde 180 mg/kg + Aminoguanidine 400 mg/kg	20	100	100	80	60	20
Formaldehyde 180 mg/kg + Aminoguanidine 600 mg/kg	20	100	100	100	100	60
Methyl alcohol 10 mg/kg	10	0	—	—	—	—
Methyl alcohol 10 mg/kg + Aminoguanidine 600 mg/kg	15	0	—	—	—	—

1. U. S. Public Health Service Reports, Suppl. No. 181, U. S. Printing Office, Washington 1945.

2. Sollman, T., A Manual of Pharmacology, Sanders, Philadelphia, 1948.

3. Bernheim, F., *J. Biol. Chem.*, in press.

4. Williams, R. T., Detoxication Mechanisms. Willy, New York, 1947.

had been introduced. In several experiments the aminoguanidine was injected first.

Results. Following injection of formaldehyde, 200 mg/kg aminoguanidine prolonged life slightly but afforded no significant protection. On the other hand 400 mg/kg of aminoguanidine prolonged the life of 60% of the animals more than 24 hours, 20% of the animals being alive after 4 days. When aminoguanidine was administered in doses of 600 mg/kg all animals were alive at the end of a 24-hour period, 60% surviving more than 4 days (Table I). Injection of aminoguanidine previous to the administration of formaldehyde raised these figures slightly. Repeated injection of aminoguanidine was without significant effect.

When methyl alcohol was administered aminoguanidine was without effect in the doses employed. This indicates that the acute toxicity of this substance is due to the depressant effect of the alcohol *per se*, particularly on respiration, and not to the accumulation of formaldehyde. It is possible, however, that some of the effects of chronic methyl alcohol poisoning could be prevented by aminoguanidine.

Summary. Aminoguanidine protects rats against the acute toxic effects of formaldehyde. Following methyl alcohol it is without effect, which indicates that formaldehyde does not contribute significantly to the acute toxicity of this substance.

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Development of Resistance to Folic Acid Antagonists in a Transplantable Lymphoid Leukemia. (17988)

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The development of resistance or insusceptibility to specific substances is a problem of much theoretical and practical interest. The production of resistant microorganisms *in vitro* and *in vivo* to various antimicrobial agents *viz.* antibiotics, antivitamins and bacteriophage has been recorded(1-6). The exact mechanism of this response is not known but has been postulated. It is possible that the development of resistance results from 1) emergence of resistant organisms due to selection, 2) action of the antimicrobial agent on the organism producing a variant, or 3), the development of gene mutations responsible for the resistance but having no direct relationship to the agent used. During the course of studies on the effect of several folic acid antagonists on transplantable acute lymphoid leukemias of the mouse, it has been noted that following a relatively long period of inhibition of leukemic cell growth, there resulted eventually a precipitous exacerbation of the disease with rapid escape of lymphoblasts into the blood, a generalized systemic infiltration into many organs and rapid growth of the localized lymphoma tumor mass in subcutaneously inoculated mice. Thus it was indicated that a resistance to the antifolic compounds had developed despite continued injections of the compounds at levels near the MTD. It was the purpose of this study to 1) attempt to induce resistance in mammalian leukemic cells to PGA antagonists, and 2) to study the characteristics of

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