mice, sacrificed after 75 days of treatment with p-anisaldehyde-thiosemicarbazone, showed only one plus gross pulmonary tuberculosis.

3. It may be concluded that p-anisaldehyde-thiosemicarbazone is an effective antimycobacterial agent in the mouse as well as *in vitro*.

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A Comparative Study of Susceptibility of Tubercle Bacillus ($H_{37}RV$) to Aureomycin, Streptomycin, and Para-aminosalicylic Acid.* (17986)

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Aureomycin, an antibiotic derived from *Streptomyces aureofaciens*, has been effective in the treatment of a wide variety of bacterial, rickettsial and virus diseases(1). For the purpose of exploring its possible usefulness as an antibiotic agent in tuberculosis, experiments with this agent were carried out to compare it with streptomycin and para-aminosalicylic acid. The latter 2 antibiotics are known to be active against the tubercle bacillus(2,3), while only brief mention of the activity of aureomycin against this organism has been made(4,5,6).

In vitro experiment. Sterile solutions of streptomycin and aureomycin were prepared in Dubos' Tween-albumin medium. The para-aminosalicylic acid was dissolved in a saturated solution of $NaHCO_3$ and then brought to pH 7.0 with M/15 phosphate buffer. The solution was Seitz-filtered and then added to Dubos' medium. The concentrations of streptomycin, aureomycin, and para-aminosalicylic acid tested, ranged from 0.1 to 30.0 μg/cc of medium. The tubes containing 5 cc of each dilution were inoculated with 0.1 cc of a 10-day $H_{37}RV$ culture from Dubos' medium. The concentrations of aureomycin were maintained by adding suitable amounts of aureomycin every 24 hours for the duration of the experiment, since its rate of deterioration is fairly constant(1). The amount of growth was graded from ++++, representing a milky growth, to 0, representing no growth. Whenever present, growth was checked by stained smears. Aureomycin compares favorably with streptomycin and para-aminosalicylic acid in inhibiting the growth of the tubercle bacillus *in vitro* (Table I).

In vivo experiments. Seventy-five dba mice, averaging 25 g in weight, were infected intravenously with 0.1 mg of $H_{37}RV$ suspended in 0.2 cc of saline. The mice were then divided into 5 groups of 15 each. Group I was untreated, Group II received 1000 μg/cc of streptomycin, injected subcutaneously, in 0.25 cc of saline every 12 hours. Group III received 1.5% para-aminosalicylic acid incorporated in the diet. Group IV and Group V received 1000 and 5000 μg/cc, respectively, of aureomycin, injected subcutaneously in

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The aureomycin was supplied by the Lederle Laboratories Division of the American Cyanamid Corp.

† Deceased.

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TABLE I.
Inhibition of the Growth of $H_{37}RV$ in Dubos' Tween-Albumin Medium.

Antibiotic	Concentration in μg/cc															
	0.1		0.2		0.5		1.0		2.0		4.0					
	6 days*	15 days	6 days	15 days	6 days	15 days	6 days	15 days	6 days	15 days	6 days	15 days				
Aureomycin	++	++	++	+++	++	+++	0	0	0	0	0	0				
Streptomycin	++	++	++	+++	+	+++	0	0	0	0	0	0				
Para-aminosalicylic acid	++	++	+++	+++	+++	+++	+	+++	0	++	0	0				

* Controls with no antibiotic were fully grown at the end of this period of time.

TABLE II.
Average Gross Tuberculosis in Lungs of dba Mice Treated with Aureomycin, Streptomycin, and Para-aminosalicylic Acid.

Group	Treatment	Avg degree of lung lesions
I	Control—none	3.5+
II	Streptomycin, 2,000 μg/day	0.8+
III	Para-aminosalicylic acid 1.5% in food	2.0+
IV	Aureomycin, 2,000 μg/day	3.4+
V	" 10,000 "	3.9+

0.25 cc of saline every 12 hours. Treatment for all groups was begun 24 hours after infection. Sixty days after infection all surviving mice were sacrificed. Treatment was continued to within 2 days of sacrifice.

At autopsy the lungs, liver, kidney, and spleen were examined grossly and were fixed in Zenker's solution for further histological study. No gross tuberculosis was observed except in the lungs. The appearance of the lesions in the lungs was graded from 0 to ++++(7). It may be seen from Table II that the degree of gross tuberculosis of the lungs in the aureomycin-treated animals was equal to that in the controls.

Microscopically, in the lungs, the lesions appeared as tuberculous broncho-pneumonia. The alveoli were filled with mononuclear cells and the walls were thickened and infiltrated. Only in the streptomycin-treated groups did the pulmonary lesions, when present, contain significant numbers of lymphocytes. In an occasional streptomycin-treated mouse fibrosis was found. Necrosis and caseation were rare and were equally distributed among Groups I, III, IV, and V.

The livers contained perivascular tubercles composed of mononuclear cells, lymphocytes, and a few epithelioid cells. In the spleen the lesions were composed of epithelioid cells and mononuclears, usually surrounded by lymphocytes. In the spleens of some of the animals multinucleated cells occurred in or at the periphery of the tubercles. Lesions in the kidney were rare and when found consisted of periglomerular collections of monocytes.

Summary. *In vitro,* aureomycin compares

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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	—	—	—	—

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