lysodeikticus. (2) Sulfanilamide in concentrations up to 1000 mg % and sulfapyridine and sulfathiazol in concentrations up to 100 mg % do not interfere with the lytic activity of lysozyme (egg white). (3) The combined use of lysozyme (egg white) and sulfamido compounds (sulfanilamide and sulfapyridine) exerts somewhat greater bactericidal effects upon *M. lysodeikticus* than either agent alone.

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II. Effects of Sulfanilamide and Sulfapyridine upon Experimental Streptococcal Infections.

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Having obtained a suitable method for determining the virulence of *Streptococcus hemolyticus* in small laboratory animals, we proceeded to study the therapeutic effect of sulfanilamide and sulfapyridine upon infection. The infection consisted of injecting 0.03 cc of an 18-hour serum broth culture intracerebrally. In the experiment on the effect of sulfanilamide upon hemolytic streptococcal infection, strain SA_{17} was used. Two different dilutions of organisms were given and for each dilution the animals were divided into 2 groups. One group received the treatment and the other group served as a control. Each group consisted of 6 white mice and 3 hamsters. In the study on the effect of sulfapyridine upon hemolytic streptococcal infection, strain 232 was used instead. The animals were similarly divided and similarly infected except that only white mice were used and the number of animals employed for each group was 8. In the case of sulfanilamide, 3 mg in 1 cc normal saline was given intraperitoneally 2, 6, 10, 14, 24, 32, 50, 72, 96, 120, and 144 hours after the infection. The control group received parallel injections of 1 cc of normal saline each time. In the case of sulfapyridine, the drug was given by the oral route. The drug was suspended in a mixture containing one part of mucilage of tragacanth and one part of distilled water. The dosage was ½ cc containing 30 mg of the drug. The first treatment was given at the time of infection and subsequently 7, 24, 48, and 72 hours after the infection. The controls received similar amounts of diluted mucilage of tragacanth at the same time. All the animals were kept under observation for 2

TABLE I.
Effects of Sulfanilamide upon Intracerebral Route Infection with Strain SA_{17}.

No. org. inj.	2,660		266	
Treatment / Animals	Treated	Control	Treated	Control
White mice	+3	1	S	2
	S	2	S	2
	S	2	S	3
	S	2	S	3
	S	2	S	3
	S	3	S	4
Hamsters	S	1	S	1
	S	1	S	2
	S	1	S	2

TABLE II.
Effects of Sulfapyridine upon Intracerebral Route Infection with Strain 232.

No. org. inj.	690,000		69,000	
Treatment / Animals	Treated	Control	Treated	Control
White mice	+2	1	S	1
	3	1	S	1
	S	1	S	1
	S	1	S	1
	S	1	S	1
	S	1	S	1
	S	2	S	2
	S	2	S	2

weeks. Those that died were immediately autopsied and cultures from the brain were made. In all the autopsied cases the cultures were positive except those in the group treated with sulfapyridine, which showed no growth. The results are shown in Tables I and II.

Knowing that both sulfanilamide and sulfapyridine have good therapeutic effect on hemolytic streptococcal infection, we made a comparative study. The infection consisted of injecting 0.03 cc of an 18-hour serum broth culture intracerebrally. Animals were divided into 3 groups. The first group received sulfapyridine, the second group received sulfanilamide, while the third group received mucilage of tragacanth 1:3 dilution to serve as a control. Each group consisted of 9 white mice weighing from 16-18 g. For each group 3 different dilutions of organisms were given and for each dilution 3 animals were used. Sulfanilamide or sulfapyridine was suspended in a mixture containing one part of mucilage of tragacanth and 2 parts of distilled water and given by the oral route. The dosage was 0.5 cc containing 7.5 mg of the drug. The first treatment was given at the time of infection and subsequently 3, 7, 24, 32, and 48 hours after the infection. The results are shown in

TABLE III.

Comparative Therapeutic Effects with Small and Large Doses of Sulfapyridine and Sulfanilamide upon Intracerebral Route Infection with Strain 232 in White Mice.

Treatment	mg per dose	No. org. injected 1,300,000	130,000	13,000
Sulfapyridine	7.5	*4,S,S	S,S,S	S,S,S
	30	S,S,S	S,S,S	S,S,S
Sulfanilamide	7.5	1,S,S	S,S,S	S,S,S
	30	2,2,3	2,S,S	S,S,S
Control for	7.5	2,2,2	2,2,3	2,3,3
	30	2,2,3	2,2,3	2,3,5

*Each numeral represents days of survival of the animal after the infection and "S" represents the survival of the animals for 14 days.

Table III. All the control animals died within 3 days after the infection, while in the group receiving sulfanilamide or sulfapyridine there was only one death each. Postmortem cultures of the brain in the control group showed numerous colonies of *Streptococcus hemolyticus*. In the group receiving sulfanilamide, the brain culture of the animal that died yielded only 4 colonies while in the sulfapyridine-treated group the culture of the brain of the dead animal was sterile. The above experiment shows clearly that both drugs gave about the same degree of protection when given in doses as small as 7.5 mg. A similar experiment was performed with a larger dose on both drugs to study their toxic effect. The dosage was 0.5 cc containing 30 mg of the drug, and the treatment was given at the time of infection and subsequently 7 hours and one and 2 days after the infection. The results are shown in Table III. All the animals in the control group died, but none succumbed in the sulfapyridine-treated group. In the group receiving sulfanilamide 77% of the animals developed toxic symptoms in the form of paralysis of all 4 limbs. The paralysis occurred within 20 minutes after the administration of the drug. Some animals developed the symptom following the first administration, while some following the second. The paralysis gradually disappeared 4-6 hours later and reappeared after subsequent administrations of the drug. There were 4 deaths in the sulfanilamide-treated group which were apparently due to the toxicity of the drug. There was no toxic symptom in the sulfapyridine-treated group.

Conclusion. The method here presented appears satisfactory for chemotherapeutic investigation. The beneficial therapeutic effect of both sulfanilamide and sulfapyridine on hemolytic streptococcal infection in white mice and hamsters is presented. Sulfapyridine is

definitely superior to sulfanilamide in that it is less toxic. A very large dose of sulfapyridine can be given at one time to sterilize the infection without producing any toxic symptoms. These experiments also indicated the prompt penetration of the drug into the brain tissue.

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Relation of Water Metabolism to Porphyrin Incrustations in Pantothenic Acid-Deficient Rats.

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It had previously been observed that the material which accumulated on the fur and noses of pantothenic acid-deficient rats exhibited a red fluorescence. This symptom had been erroneously described as "nose bleed"[1] and "blood-caked whiskers".[2] This fluorescent material contained large amounts of porphyrin, and the chemical tests for blood were negative.[3, 4] It was clearly demonstrated by an ablation experiment that the Harderian (lacrimal) gland is the source of this porphyrin secretion.[5]

During the preliminary preparation for the above experiment, it was observed that the water bottles in 2 of the cages had failed to deliver water. There were six 21-day-old albino rats in the 2 glass cages. Thick incrustations of fluorescent material were observed on the noses and near the medial angles of the eyes and smeared on the fur of all 6 rats. The other 18 rats with abundant water did not show this. Thus within a period of 3 days normal rats deprived of water developed what appeared to be one of the symptoms of pantothenic acid deficiency. When the rats were given water, they

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