Summary and Conclusions. (1) Since *Trichocephalus vulpis* eggs are stimulated in their development by previous subjection to mechanical agitation by centrifugalization, and to immersion in brine, the results of studies on these, and probably other nematode eggs subjected to these influences are not applicable to eggs developing in nature. (2) Sodium chloride in low dilutions (1/1000 N to 1/10 N solutions) stimulates the embryonation of *T. vulpis* eggs. Higher concentrations (1 to 3 N solutions) inhibit development, collapse the inner layer of the egg shell, and finally kill the embryo. It is not unlikely that other salts present in the soil in small concentrations may also influence the embryonation of these eggs. Thus, the salt content of soils may conceivably play an important rôle in the epidemiology of whipworm disease. (3) From 25% to 50% of *T. vulpis* eggs can be hatched by subjecting them in turn to artificial gastric juice for 20 hours and artificial pancreatic juice for 2 hours. The fact that eggs must remain in the gastric juice for a period of time before they will hatch in pancreatic juice suggests that the rapidity with which eggs pass through the stomach of the host may influence the rate of hatching, and thus the resulting intensity of infection in the host.

10886

Sulfanilamide and Sulfapyridine in Treatment of Experimental *B. Friedländer* (*Klebsiella pneumoniae*) Infections of Mice.

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Buttle, Parish, McLeod and Stephenson[1] found sulfanilamide in dose of 0.025 g by oral administration twice daily practically ineffective in the treatment of mice inoculated intraäbdominally with varying amounts of 18-hour broth culture of *B. friedländer;* of 70 treated mice only 12 survived the minimal amount of culture for 12 days, whereas 4 out of 40 untreated controls remained alive. All treated and control mice inoculated with larger amounts of culture perished so that the compound was found to give only temporary protection. Bliss, Feinstone, Garrett and Long,[2] using type B of

1 Buttle, G. A. H., Parish, H. J., McLeod, M., and Stephenson, D., *Lancet*, 1937, **1**, 681.

2 Bliss, E. A., Feinstone, W. H., Garrett, A. W., and Long, P. H., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 619.

B. friedländer observed essentially similar results in that none of 45 treated mice survived when inoculated with sufficient culture to cause fatal infections of 30 controls.

Our experiments were conducted with a strain freshly cultivated from the cerebrospinal fluid of a fatal case of *B. friedländer* meningitis secondary to a chronic ethmoiditis* due to the same organism. Its virulence was determined by giving mice 0.01, 0.02, 0.03, 0.04, 0.05, 0.08, and 0.1 cc of 24-hour broth culture by intraäbdominal inoculation, 2 mice being used for each dose. The 2 mice inoculated with 0.01 cc survived; both inoculated with 0.02 cc died in 5 to 6 days while the remaining mice succumbed in 1 to 4 days, all with positive heart blood cultures. In the treatment-experiments mice were inoculated with 0.05 cc of 24-hour broth culture corresponding to between 2 and 3 minimal lethal doses. All of 12 untreated controls succumbed in 24 to 72 hours with positive heart-blood cultures.

Since difficulty was experienced in giving mice accurate doses of the compounds by mouth, they were administered in solution by subcutaneous or intraäbdominal injection. For this purpose 0.4 g of sulfanilamide was dissolved in 50 cc hot saline giving 0.008 g per cc; 0.2 g sulfapyridine was dissolved in 200 cc of hot saline solution giving 0.001 g per cc.

In one experiment 16 mice were given 0.160 g sulfanilamide per kilo by *subcutaneous* injection immediately after intraäbdominal inoculation with 0.05 cc of 24-hour broth culture followed by a second dose of the drug 6 hours thereafter and repeated twice daily (10 A.M. and 3 P.M.) for 5 days. Four additional mice, which were infected but not treated, served as controls. They all succumbed in 24 to 48 hours after inoculation. Of the 16 treated animals 3 survived for 1 to 2 or 3 days beyond the untreated controls, indicating that sulfanilamide in the dose administered probably showed some slight protective effect.

In the second experiment 20 mice were inoculated with 0.05 cc of 24-hour broth culture; 4 kept as untreated controls died in 24 to 72 hours. Sixteen of the mice were given 0.160 g *sulfanilamide* by *intraäbdominal* injection immediately after inoculation, 6 hours thereafter and then twice daily (10 A.M. and 3 P.M.) for 5 days. Of the 16 treated mice 2 survived while the lives of 6 were prolonged for 3 to 6 days beyond the untreated controls, indicating some thera-

* Patient a male; age 36 years; weight 154 lbs; sulfapyridine administered orally in dose of 1.0 g every 4 hours beginning about 3 days after onset of meningitis and continued for 8 days when death occurred (necropsy denied). Marked clinical and spinal fluid improvement during first 4 days of treatment.

peutic effect probably because of more rapid absorption than occurred after subcutaneous injection.

In a third experiment 20 mice were inoculated with 0.05 cc of 24-hour broth cultures; 4 kept as untreated controls died in 24 to 72 hours. Sixteen of the mice were given 0.160 g *sulfapyridine* by *intraäbdominal* injection immediately after inoculation with a second dose 6 hours later and thereafter twice daily (10 A.M. and 3 P.M.) for 5 days. Of these, 4 survived for 12 days when the experiment was terminated while the lives of 6 were prolonged 1 to 5 days beyond the untreated controls.

Summary. Sulfanilamide by subcutaneous injection in dose of 0.160 g per kilo slightly prolonged the lives of 3 out of 16 mice when given immediately, 6 hours later and thereafter twice daily for 5 days after intraäbdominal inoculation with *B. friedländer* in a dose fatal in 24 to 72 hours. When the compound in the same dose was given by intraäbdominal injection in the same manner to 16 mice, 2 survived 12 days when the experiment was terminated, while the lives of 6 were prolonged for 3 to 6 days beyond the untreated controls. Of the total of 32 treated mice, 2 survived and the lives of 9 were prolonged, whereas all of 8 untreated controls succumbed in 1 to 3 days after inoculation.

Sulfapyridine was somewhat more effective. Of 16 mice given 0.160 g by intraäbdominal injection immediately after inoculation, 6 hours later and thereafter twice daily for 5 days, 4 survived while the lives of 6 were prolonged 1 to 5 days beyond the survival of 4 untreated controls which succumbed in 24 to 72 hours after inoculation. All treated and untreated mice succumbing gave positive heart-blood cultures. All drug controls given both sulfanilamide and sulfapyridine by subcutaneous and intraäbdominal injection survived the period of 12 days, when the experiments were terminated.

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Sulfanilamide and Sulfapyridine in Treatment of Experimental *B. coli* (*Escherichia coli*) Infections of Mice.

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Clinically sulfanilamide has proven useful in the treatment of some cases of urinary-tract infections due to *B. coli* as well as in some cases of septicemia due to this organism. It is possible, how-