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.

10887

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

JOHN A. KOLMER AND ANNA M. RULE.

From the Research Institute of Cutaneous Medicine, Philadelphia, Pa.

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-

ever, that not all strains are equally susceptible to the effects of this compound *in vitro* and *in vivo* and for this reason an *in vitro* test for bacteriostatic and bactericidal effects of sulfanilamide upon strains of *B. coli* isolated from the urine of urinary-tract infections, may be helpful in determining the dosage to employ in treatment.

In experimental *B. coli* infections of mice produced by intraäbdominal inoculation Cooper, Gross, and Lewis[1] found sulfanilamide effective, 55% of 40 treated mice surviving inoculation with fatal amounts of culture. They also observed that sulfapyridine was somewhat more effective since 80% of a group of 10 mice survived.

The strain employed in our experiments was cultivated in pure culture from the urine of a case of pyelonephritis of 5 years' duration occurring in a boy 17 years of age. A concentration of about 0.5% sulfanilamide in 5 cc of broth seeded with approximately 200,000 bacilli was required for bacteriostatic effects while a concentration as high as 1% was not completely bactericidal, indicating that this particular strain was above the average in resistance to sulfanilamide. Its virulence for mice was determined by giving 0.02, 0.05, 0.1, 0.2, 0.3, and 0.4 cc of 24-hour broth culture intraädominally, 2 mice being used for each dose. Amounts of 0.2, 0.3 and 0.4 cc proved fatal in 1 to 3 days with positive heart-blood cultures while mice inoculated with the smaller doses survived. For the therapeutic tests mice were inoculated intraäbdominally with 0.3 cc of 24-hour broth culture, corresponding to between 1 and 2 minimal lethal doses, which proved fatal for all untreated controls in 24 to 48 hours after inoculation.

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

In one experiment 10 mice were given 0.160 g per kilo of *sulfanilamide* by *subcutaneous* injection 2 hours after intraäbdominal inoculation with 0.3 cc of 24-hour broth culture followed by a second dose 4 hours later and thereafter by 2 doses daily (10 A.M. and 3 P.M.) for 5 days. None of the mice survived although the lives of 3 were prolonged for 1 to 3 days beyond those of 4 untreated controls, all of which succumbed in 1 to 2 days after inoculation. The

[1] Cooper, F. B., Gross, P., and Lewis, M., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 34.

unfavorable results in treatment were probably due to the unusually high resistance of the strain to sulfanilamide as indicated by the results of the *in vitro* tests.

Essentially similar results were observed in a second experiment in which 10 mice were given 0.160 g of *sulfanilamide* per kilo by *intra-abdominal* injection 2 hours after inoculation with 0.3 cc of 24-hour broth culture, followed by a second dose 4 hours later and thereafter by 2 doses daily (10 A.M. and 3 P.M.) for 5 days. None of the mice survived, although the lives of 3 were prolonged 2 to 3 days beyond those of 4 untreated controls, all of which succumbed in 1 to 2 days after inoculation.

Treatment with *sulfapyridine* did not yield any better results with this strain. Of 10 mice given 0.160 g per kilo by *intraäbdominal* injection 2 hours after inoculation with 0.3 cc of 24-hour broth culture, followed by a second dose 4 hours later and thereafter twice daily (10 A.M. and 3 P.M.), for 5 days, none survived although the lives of 4 were prolonged by 1 to 3 days beyond the survival of 4 untreated controls, all of which succumbed in 1 to 2 days after inoculation. In each experiment all treated and untreated mice succumbing gave positive heart blood cultures; two treatment controls survived 12 days, when the experiment was terminated.

Summary. Sulfanilamide by subcutaneous and intraäbdominal injection and sulfapyridine by intraäbdominal injection in dose of 0.160 g per kilo slightly prolonged the lives of some mice when given 2 hours after intraäbdominal inoculation with *B. coli* in a dose fatal in 24 to 48 hours, followed by a second dose 4 hours later and thereafter twice daily (10 A.M. and 3 P.M.) for 5 days. All of the treated mice succumbed with positive heart-blood cultures and the unfavorable results are believed to be due to the fact that the strain of *B. coli* employed was one unusually resistant to the bacteriostatic and bactericidal effects of sulfanilamide as indicated by the results of *in vitro* tests. All treatment-controls lived for 12 days, when the experiments were terminated.