were studied as well as certain other organs which showed some tendency to be changed in a 6-month group of spayed rats which were studied earlier in this laboratory. The vagina opened in the control rats at an average age of 42 days. The body weight of the spayed rats became significantly greater than that of the controls when they were between 6 and 7 weeks of age. In this group of rats the percentage difference in body weight between the spayed and controls constantly increased until 13 weeks of age when the difference was 20.5%. The spayed rats at 3 months of age had a significantly greater body length and tail length than the controls. The following parts were significantly heavier in the spayed rats: head, hypophysis, thyroid, thymus, lungs, heart, alimentary group, stomach, liver, spleen, and kidneys. These differences were all greater than those found at 6 months, which seemed to indicate that ovariectomized rats go through their growth changes more rapidly than controls. The suprarenals were significantly smaller in the spayed rats, but the difference was less than at 6 months.

## 9149 P

## Action of P-Aminobenzenesulfonamide on Type III Pneumococcus Infections in Mice.

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The discovery of prontosil by Domagk[1] has resulted in a new and very effective means of treating certain infections caused by hemolytic streptococci. Hörlein,[2] in reviewing Domagk's work, claimed that this compound was also effective against Type III pneumococcal infections, but failed to publish in detail the experimental results which led either to this conclusion, or to his grouping the Type III pneumococci with the streptococci on chemotherapeutic grounds.

The work of Tréfouël and his associates,[3] confirmed by Buttle, Gray, and Stephenson,[4] indicated that *p*-aminobenzenesulfonamide, a part of the prontosil molecule, was as effective against hemolytic streptococcal infections as the more complicated compounds. Cole-

[1] Domagk, G., *Deutsche med. Wchnschr.*, 1935, **61**, 829.

[2] Hörlein, H., *Proc. Royal Soc. Med.*, 1936, **29**, 321.

[3] Tréfouël, J., and Tréfouël, J. Mme., Nitti, F., Bovet, D., *Compt. Rend. d. Soc. de Biol.*, 1935, **120**, 756.

[4] Buttle, G. A. H., Gray, W. H., and Stephenson, D., *Lancet*, 1936, **1**, 1206.

brook and Kenny[5] and the present authors[6] have found *p*-aminobenzenesulfonamide even more efficacious than prontosil.

In view of these results, the therapeutic effectiveness of the *p*-aminobenzenesulfonamide* was determined against Type III pneumococcal infections in mice.

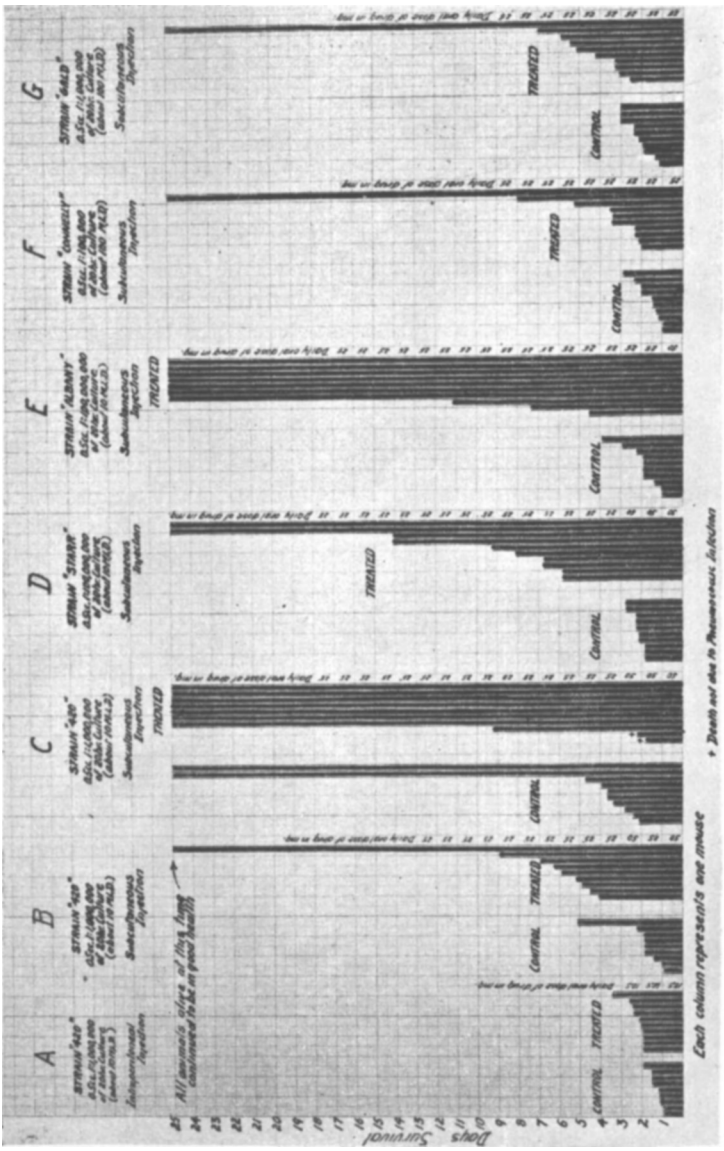


FIG. 1.
Graphic representation of results obtained by the oral administration of *p*-aminobenzenesulfonamide in mice infected with various strains of Type III pneumococcus.

[5] Colebrook, L., and Kenny, M., *Lancet*, 1936, **2**, 1319.

[6] Mellon, R. R., Gross, P., and Cooper, F. B., *J. Am. Med. Assn.*, in press.

* Kindly supplied by Winthrop Chemical Company, Inc., New York City.

In a preliminary experiment, 19 mice were inoculated intraäbdominally with approximately 10 minimal lethal doses of Strain 420 of Type III pneumococcus. Ten of the mice were given 12.5 mg., of the drug by mouth immediately after infection and every 24 hours thereafter; while the remaining 9 mice received no treatment and served as controls. A negligible prolongation of the survival time of the treated group was obtained. The data are shown graphically in *A*, Fig. 1.

A second series of 18 mice were given the same infecting dose by the subcutaneous route, and half of them treated as indicated in *B*, Fig. 1. Reference to this chart shows a marked increase in the survival-time of the treated group.

A third series of 20 mice (*C*, Fig. 1) were infected by the subcutaneous route with the same dilution of the same 420 culture which had been allowed to deteriorate in virulence. The untreated animals, with the exception of one survivor, lived approximately twice as long as the controls of the previous experiment *(B);* whereas 7 of the treated animals were alive after 25 days. Two of the treated animals died from causes other than the pneumococcal infection, while only one died of pneumococcal septicemia.

Additional experiments with 4 other Type III pneumococcal strains were conducted. Three of these (*D*, *F*, and *G*, Fig. 1), had recently been isolated from the sputum of fatal pneumonia cases. All experiments showed a definite increase in the survival-time of the treated mice. The "Albany" strain (*E*, Fig. 1), which was a stock strain, showed a 70% survival of the treated mice after 25 days.

Buttle, Gray, and Stephenson[4] have shown that *p*-aminobenzenesulfonamide was effective in bringing about recovery in mice previously infected with 10,000 lethal doses of a highly virulent hemolytic streptococcus. Our own work[6] has shown a similar high protective and therapeutic effect against experimental hemolytic streptococcal infections. Proom[7] was able to protect mice under optimal conditions against one million fatal doses of meningococci by means of this drug.

The action of *p*-aminobenzenesulfonamide in combatting Type III pneumococcal infections in mice does not appear at first to be as effective as its action on either streptococcal or meningococcal infections. The results obtained against subcutaneous Type III pneumococcal infections of less than 10 minimal lethal doses are sufficiently striking, whereas little protection is shown against heavier infecting doses. However, when the extreme susceptibility of mice to pneu-

[7] Proom, H., *Lancet*, 1937, **1**, 16.

mococci is considered, the degree of protection demonstrated possibly assumes a greater magnitude, even though the number of fatal doses against which protection was obtained is not so high numerically as in streptococcal or meningococcal infections. The results of these experiments with mice justify a therapeutic trial of *p*-aminobenezenesulfonamide in human Type III pneumococcal infections.

*Conclusions.* The oral administration of *p*-aminobenzenesulfonamide is capable of prolonging, and in some cases of saving, the lives of mice infected subcutaneously with approximately 10 minimal lethal doses of highly virulent Type III pneumococci.† ‡

## 9150

## Influence of Deuterium Oxide on Growth and Morphology of Lactobacilli.

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The biological interest in deuterium oxide or heavy water cannot be overlooked because all living cells require water for growth. Barnes[1] reported that *Spirogyra* showed some unusual and interesting effects when grown in low concentrations of deuterium oxide and that these concentrations had a stimulating effect on the growth of *Euglena.* Harvey and Taylor[2] recorded that when luminous bacteria were incubated in tubes containing mixtures of heavy water and ordinary water, the amount of oxygen used by the bacteria was in proportion to the percentage of heavy water in the mixture. Also the luminescence of the bacteria was diminished when exposed to low concentrations of heavy water. Richards[3] observed the growth of *Saccharomyces cerevisiæ* in weak concentrations of deuterium oxide which he claimed accelerated growth and development, as opposed to its lethal effect in higher concentrations.

† The authors wish to acknowledge the technical assistance of Miss Louise Peebles.

‡ After this paper went to press our attention was called to the paper by Rosenthal in *Public Health Reports,* 1937, **52**, 48, which reported results similar to ours.

1 Barnes, T. C., *Science,* 1934, **79**, 370.

2 Harvey, E. N., and Taylor, G. W., *Science News Letter,* 1934, **25**, 200.

3 Richards, O. W., *Am. J. Botany,* 1933, **20**, 679.