which, however, was maintained. Division of the sciatic and femoral nerves of the affected area did not have any significant effect upon the pressor phenomenon. The vasodepressor effect of hypertonic solutions administered by the venous route was also studied. Bilateral vagotomy did not prevent the fall of blood pressure, suggesting the presence of other factors in this reaction. This investigation has not yet disclosed the nature of the factors involved.

The phenomenon of vasopression following the administration of hypertonic solutions of sodium chloride by the intraärterial route can be attributed to a stimulation of the peripheral nerve endings in the involved area with a resultant generalized vasoconstriction effected by the central nervous system. The degree of stimulation of the peripheral nerves of the extremity varies directly with the amount and hypertonicity of the solution used. In view of this fact, the demonstrable relationship between water metabolism and chronaxie of nerve[9] is interesting. The release of protein-containing tissue fluid from the extremity, resulting in an increase in the circulating blood volume, is of lesser importance, in spite of recorded losses in weight up to 100 gm. of areas studied in several experiments.

Summary. A prolonged elevation of blood pressure occurs after the intraärterial administration of hypertonic solutions of sodium chloride. This pressor effect appears to be predominantly nervous in origin, inasmuch as it disappears after section of the spinal cord.

9487

Treatment of Pneumococcal Infections in Rabbits with Sulfanilamide.

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A number of studies have been made to show the curative effect of sulfanilamide in rats, mice, guinea pigs and rabbits, infected with pneumococci by various routes. Because of the difference of opinion concerning the efficacy of the drug in the treatment of infections caused by this microörganism, it was considered timely to investigate further its effects on controlled pneumococcal infection. For this

[9] Achelis, J. D., *Pflüger's Arch.*, 1930, **226**, 212.

purpose, infection was induced in rabbits by injecting Type I pneumococci endermally according to the method of Goodner,[1] which permits accurate observations of the fever, bacteremia and of the lesion produced locally.

The inoculum consisted of 0.1 cc. of a 1:1000 dilution of an 18-hour blood-broth culture injected endermally in the shaved skin of the abdomen. Rectal temperature was recorded twice daily and blood cultures were made daily until the animal died or recovered. In each of 6 sets of experiments, 4 rabbits were studied; 2 animals were treated and 2 served as controls.

For treatment, sulfanilamide (para-amino-benzene-sulphonamide) was chosen in preference to prontosil because previous experience had shown that the latter drug exerted little influence on the course of pneumococcal infection in rabbits. The limited solubility of prontosil requires the injection of larger volumes of fluid than is practical. The sulfanilamide (supplied by E. R. Squibb & Sons) was prepared in 1% solution and was administered by means of a stomach-tube—100 cc. twice in 24 hours. This daily dose is equivalent to a total of 2.0 gm. of sulfanilamide and is well within the limits of that tolerated by rabbits weighing 2 kg. According to Raiziss, Severac and Moetsch,[2] a dose of 1.5 gm. per kilo of body weight was tolerated by 94% of the rabbits, while a dose of 2 gm. per kilo was tolerated by 50% of the animals.

The strain of Type I pneumococcus used proved to be exceptionally virulent for rabbits. All of the untreated control animals died, usually between the second and fourth day after inoculation. Bacteremia with high fever was present in each case. The local lesion about the point of inoculation consisted of a swollen, indurated area about 30 mm. in diameter with erythema extending to 80 or 90 mm.

In the various series, treatment was started at different intervals after injection of the pneumococci—6, 8, 18, 20, 30 and 48 hours after inoculation, respectively. In the last series (48 hours) 2 rabbits were dead at the time treatment was started on the 2 remaining animals. Both of the latter succumbed, although one lived 9 days. At the time of death, the blood culture showed no growth of any organisms and the local lesion had disappeared entirely. Death may have been due to the toxic effects of the drug.

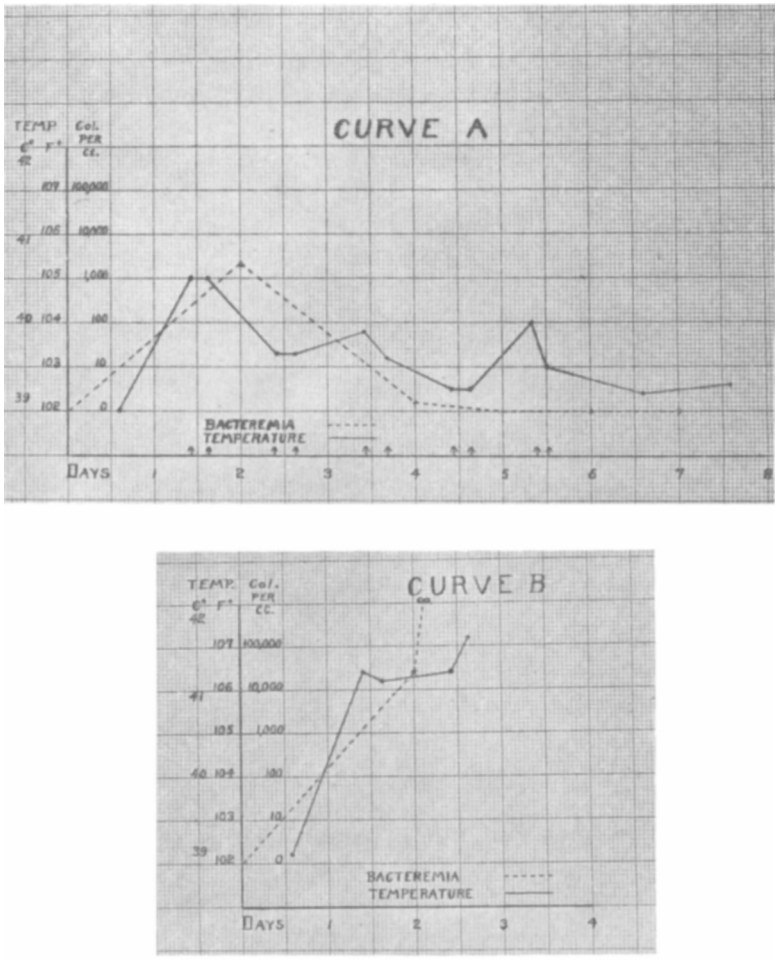
The results of treatment of 10 rabbits in the other 5 experiments were more encouraging—7 of the animals survived. The blood cul-

1 Goodner, K., *J. Exp. Med.*, 1928, **48**, 413.

2 Raiziss, G. W., Severac, M., and Moetsch, J. C., *J. Chemotherapy*, 1937, **14**, 1.

tures of *all* the treated animals became negative in 3 to 5 days, their temperatures dropped to normal and the local lesions promptly healed. Yet 3 died, possibly because of the toxicity of the drug.

The set of rabbits in which treatment was started 20 hours after inoculation may be described as typical of the results obtained in the other experiments. At the time treatment was instituted the temperatures of the 4 rabbits ranged between 105.0° and 106.4°F. and blood cultures revealed many pneumococci—the lowest count being 3200 colonies per cc. of blood while the plates made from 2 of the rabbits were uncountable. In addition to this well established bac-



The temperature and the number of pneumococci per cc. of blood at various intervals in a rabbit (A) treated with sulfanilamide, as indicated by arrows, and in an untreated control (B).

teremia, each animal had a local lesion (80 to 90 mm. in diameter) about the point of inoculation which presented an intense erythema and marked induration. Two of the rabbits were given 100 cc. of a 1% solution of sulfanilamide by mouth twice each day. After 3 days, the blood cultures showed no growth and at the end of 5 days the temperature had returned to normal and the local lesions had healed. Each rabbit received a total of 10 gm. of the drug during the period of treatment. It should be noted that the dose used was far in excess of that recommended in human therapy.

Both of the untreated rabbits died in 2 days. There was no reduction in the bacteremia or extent of the local lesions; neither was there a drop in the temperature of either animal. (See chart.)

Conclusion. Sulfanilamide, when given orally to rabbits in adequate doses, early in the course of experimental dermal pneumococcal infection, eliminates this microörganism from the blood stream, reduces the fever, cures the local lesion and favors recovery in most of the treated animals.

9488

Presence in Milk of the Extrinsic Factor of Castle.

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The extrinsic factor of Castle has been found in several protein-containing foods, such as beef muscle,[1] autolyzed yeast,[2] wheat germ,[2] and egg white.[3] From Castle's[4] more recent work, one may infer that some of the negative results obtained with protein foods other than these, were due to prolonged incubation periods, or the trial use of the materials at hydrogen ion concentrations too great for the interaction of the extrinsic and intrinsic factors. Casein[5] has been reported as giving a negative response at a pH of 2.5 to 3.5, however, more recently Taylor, *et al.*,[6] have indicated that the in-

1 Castle, W. B., Townsend, W. C., Heath, C. W., *Am. J. M. Sc.*, 1929, **180**, 305.

2 Strauss, M. B., and Castle, W. B., *New Eng. J. Med.*, 1932, **207**, 55.

3 Miller, D. K., and Rhoades, C. P., *New Eng. J. Med.*, 1934, **211**, 921.

4 Castle, W. B., and Ham, T. H., *J. Am. Med. Assn.*, 1936, **107**, 1456.

5 Castle, W. B., and Townsend, W. C., *Am. J. M. Sc.*, 1929, **178**, 764.

6 Taylor, F. H. L., Castle, W. B., Heinle, R. W., and Adams, M. A., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 566.