monkey by means of the intracerebral inoculation of a 10% suspension of the spinal cord was successful.

These feeding experiments, considered by themselves, serve chiefly to confirm the work of Kling and his associates[7] who have long maintained that poliomyelitic virus will infect the *Mac. cynomolgus* by the oral route, but not the *Mac. rhesus*. In conjunction with the inoculations by other routes, they also indicate that the behavior of this virus is compatible with that of poliomyelitic virus, and these results thus become of supplementary value in the identification of this strain.

*Summary.* The SK. strain of poliomyelitic virus has been shown to be occasionally infectious by the intraperitoneal, intracutaneous, intratonsillar, and oral routes. The *Mac. mordax* species of monkey, as well as the *Mac. cynomolgus*, is susceptible to infection with poliomyelitic virus by the oral route.

## 10638

## Detection of Free Polysaccharide in Blood of Pneumococcic Pneumonia Patients; Prognosis and Therapy.

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Early observations by Dochez and Avery[1, 2] and by Blake[3] demonstrated the presence of specific soluble pneumococcal substance in the blood and urine of patients suffering from lobar pneumonia. The substance, a product of the growth of pneumococci, rather than of their degeneration, was identified as capsular polysaccharide by the work of Heidelberger and Avery.[4] Of a total of 44 cases studied by Dochez

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1 Dochez, A. R., and Avery, O. T., PROC. SOC. EXP. BIOL. AND MED., 1917, **14**, 126.

2 Dochez, A. R., and Avery, O. T., *J. Exp. Med.*, 1917, **26**, 477.

3 Blake, F. G., *Arch. Int. Med.*, 1918, **21**, 779.

4 Heidelberger, M., and Avery, O. T., *J. Exp. Med.*, 1923, **38**, 73.

and Avery[2] (25) and by Blake[3] (19), soluble substance was detected in the blood in 11. Ten of these patients died, the 11th having shown only traces in the blood. Blake[3] demonstrated a reciprocal relation between the amount of polysaccharide in the urine and blood, and the development of antibody. It was felt advisable to repeat these observations, particularly noting the comparative influence of sulfapyridine, specific serum, or the combination on the antigen-antibody balance, and its relation to the outcome of therapy. Conceivably, sulfapyridine might decrease the formation of polysaccharide by inhibiting bacterial growth, thus increasing availability of spontaneously produced or passively introduced antibody.

Studies were carried out in the following manner: Repeated blood cultures were taken, using 3-5 cc quantities. For antigen determination, 0.5 cc quantities of serial dilution of patient's serum (using sterile 0.85% saline as diluent) were mixed in 10 x 75 mm tubes with 0.5 cc of a 1 to 10 dilution of homologous rabbit antipneumococcal serum,† having an original antibody-titer of 5,000 to 10,000 units per cc.‡ For agglutination 0.5 cc of saline suspensions of the sediment from 18-hour broth cultures, giving an evident specific Neufeld reaction, were employed. For precipitin-detection, 0.5 cc of freshly-prepared appropriate saline dilutions§ from 1 to 1,000 or 1 to 5,000 stock solutions of homologous polysaccharide‖ were employed, and mixed with 0.5 cc of serially diluted patient's serum. Controls with heterologous polysaccharide and heterologous rabbit antipneumococcal serum; positive and negative controls showing specific and adequate activity of the polysaccharide and antiserum; and saline controls of suspensions of organisms were employed with each determination.

The antigen-antibody balance was determined repeatedly, an average of 5 times each, in 25 cases.¶ No serum polysaccharide was found in 21, all of whom recovered under therapy with sulfapyridine, serum, or both. Capsular polysaccharide was detected in the serum

† Sera used were commercial rabbit sera obtained from several manufacturers; the titers used were those determined by the manufacturers' mouse protection tests.

‡ Recent observations on the use of constant 0.5 cc portions of patient's serum with varying dilutions of added type-specific serum indicate that it is possible to detect capsular polysaccharide in lower concentrations by this procedure than by the method of Blake and of Dochez and Avery.

§ Appropriate dilutions must be determined for each type used, and for each batch of antigen. For types III and VII, 1 to 50,000 dilution was employed throughout.

‖ Supplied through the courtesy of Dr. W. G. Malcolm of Lederle Laboratories, Inc., Pearl River, New York.

¶ Detailed description of these cases will be published.

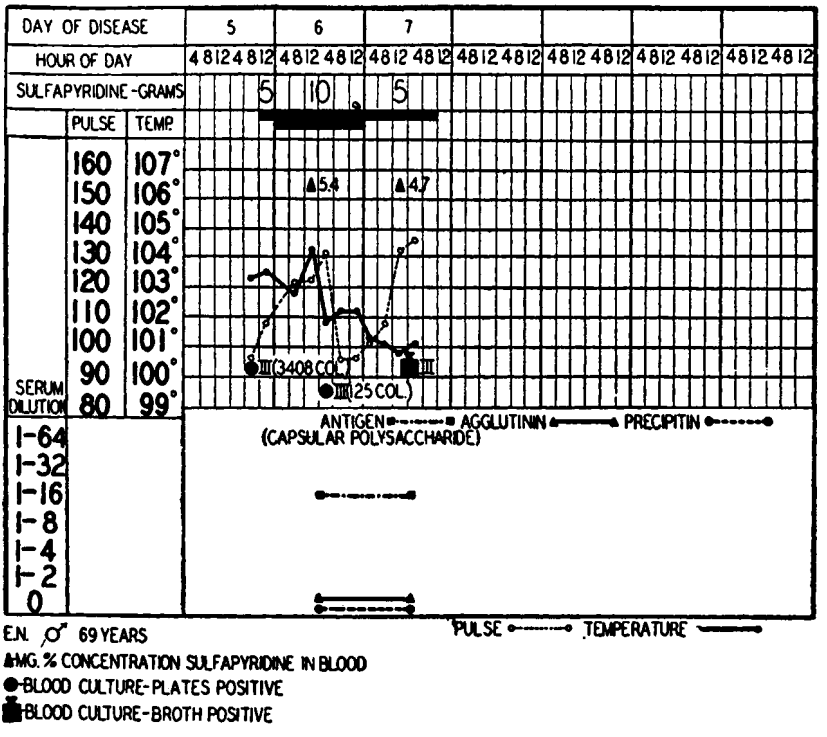
DAY OF DISEASE
HOUR OF DAY
SULFAPYRIDINE-GRAMS
PULSE
TEMP.
SERUM DILUTION
ANTIGEN
AGGLUTININ
PRECIPITIN
(CAPSULAR POLYSACCHARIDE)
PULSE
TEMPERATURE
E.N. ♂ 69 YEARS
MG. % CONCENTRATION SULFAPYRIDINE IN BLOOD
BLOOD CULTURE-PLATES POSITIVE
BLOOD CULTURE-BROTH POSITIVE

FIG. 1.

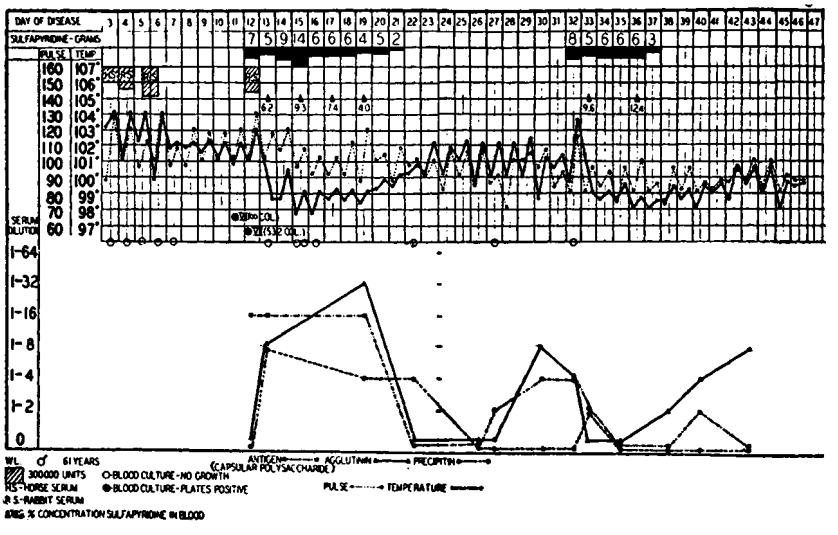
DAY OF DISEASE
SULFAPYRIDINE-GRAMS
PULSE
TEMP.
SERUM DILUTION
ANTIGEN
AGGLUTININ
PRECIPITIN
(CAPSULAR POLYSACCHARIDE)
PULSE
TEMPERATURE
300000 UNITS
BLOOD CULTURE-NO GROWTH
BLOOD CULTURE-PLATES POSITIVE
MG. % CONCENTRATION SULFAPYRIDINE IN BLOOD

FIG. 2.

of the remaining 4. Three of these were Type III cases, 2 bacteremic; all 3 died. One Type III patient (Fig. 1), a 69-year-old Negro male with bacteremia, died despite 48 hours of therapy with sulfapyridine alone, with no appreciable effect on the circulating polysaccharide and no development of antibody, although the colony-count from the blood culture was progressively reduced. In this case, the supernatant fluid from one of the tubes in which the serum polysaccharide had been precipitated gave evidence, when retested, of complete absorption of its type-specific antibody. The fourth case (Fig. 2) was a 61-year-old Negro male admitted on the 3rd day of a single-lobe Type VII pneumonia, non-bacteremic on admission. Studies were begun after failure to respond to more than 1,000,000 units of Type VII antiserum, both horse and rabbit. At this time the patient had an overwhelming invasion of the blood stream, and a considerable quantity of capsular polysaccharide in the serum, without evidence of antibody. Infection was controlled, and the blood promptly sterilized with sulfapyridine and additional rabbit serum, although polysaccharide persisted in the blood stream, together with detectable precipitin, for at least 8 days. Following cessation of sulfapyridine there was gradual depletion of serum-antibody and a return of detectable polysaccharide, coincident with recurrence of fever, culminating in chill, although demonstrable blood-stream invasion did not recur. However, at this time agglutinins were detectable in the blood. A second administration of sulfapyridine, at a time when both agglutinin and polysaccharide were detectable in the blood, resulted in prompt control of the infection with disappearance of polysaccharide. Cessation of drug therapy the second time was followed by the transient reappearance of polysaccharide and a slight elevation of temperature, together with increasing antibody-concentration and ultimate return of temperature to normal. The patient, though now apparently over the acute infection, has bronchoscopic evidence of a collection of granulation tissue partially obstructing the right upper-lobe bronchus with roentgenographic evidence of atelectasis, and is still under observation.

Of interest is the simultaneous occurrence of pneumococcal polysaccharide and its homologous precipitin in the blood of this patient as well as its prolonged duration. This occurrence in immune rabbits injected intravenously with homologous polysaccharide has not been observed by Downie.[5] Similar occurrences have been observed *in vitro* by Heidelberger and Kendall[6] (pneu-

[5] Downie, A. W., *J. Path. and Bact.*, 1937, **45**, 149.

[6] Heidelberger, M., and Kendall, F. E., *J. Exp. Med.*, 1929, **50**, 809.

mococcus III polysaccharide and purified homologous precipitins), and by Taylor, Adair, and Adair[7] (serum albumin and its precipitin). The former authors explained the phenomenon on the basis of the laws of mass action which they derived for the precipitin reaction. Marrack[8] reviews the observations on this occurrence and explains it on the probable existence of non-uniformity of antigen and of antibody.

*Conclusions.* The occurrence of free polysaccharide in the blood of pneumonic patients is not uncommon. Its presence is generally indicative of a severe infection, with usually fatal outcome. It would appear that sulfapyridine alone may be ineffective in the control of those pneumococcic infections which are accompanied by the production of sufficient polysaccharide to reach relatively high concentrations in the blood stream, but that it may be effective in such instances if it is combined with the administration of sufficient type-specific antibody. The observations reported suggest that sulfapyridine alone may control pneumococcic infections provided there is not too much antigen present in the blood, and some specific antibody is produced.

**10639 P**

## Group Similarity of Alpha Hemolytic Bovine Mastitis Streptococci for Lancefield's Serological Group C.

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Minett and his associates[1] included in mastitis streptococcus Group II certain streptococci which usually cause a more acute form of mastitis with less tendency to a permanent infection than Group I. In the serological study of these streptococci, Stableforth[2] found that, although grouped together on the basis of cultural and biochemical similarities, they could also be regarded as a serological group because they were directly or indirectly connected antigenically. Diern-

[7] Taylor, G. L., Adair, G. S., and Adair, M. E., *J. Hyg. Camb.*, 1932, **32**, 340.

[8] Marrack, J. R., *Medical Research Council, Special Report Series*, No. 230, 1938, pp. 146-7.

[1] Minett, F. C., Stableforth, A. W., and Edwards, S. J., *J. Comp. Path. and Ther.*, 1929, **42**, 213.

[2] Stableforth, A. W., *J. Comp. Path. and Ther.*, 1932, **45**, 185.