

oped in the blood stream a ratio of phage to bacteria adequate for initiation of lysis even when the amount of phage injected was greatly in excess of the amount required to lyse the number of bacteria used. The bacterial curves in treated animals and controls exhibited no significant differences. Bacteria recovered from the blood stream both in fatal infections and in animals who survived (because they received less than the lethal dose of organisms) showed no change as regards susceptibility to phage action. That is, exposure to phage in the circulating blood did not produce phage resistant strains.

Red cells were found to be capable of adsorbing phage in quantities sufficient to make this action a considerable factor in the failure to establish a lytic threshold *in vivo*.

Our experiments indicate that: 1. Homologous anti-staphylococcus bacteriophage introduced in large quantities into the blood stream of rabbits suffering from acute experimental staphylococcal septicemia not only does not increase in amount but is rapidly eliminated from the blood stream. 2. The phage has no influence on the course of the experimental infection nor upon the quantities of bacteria found in the blood stream. 3. In the case of the infection studied it is not possible to establish in the circulating blood those conditions shown in earlier work to be requisite for bacterial lysis. 4. Phage adsorption on red blood cells effectively operates to remove considerable quantities of phage from participation in lysis. 5. Clinical failures in the treatment of staphylococcal septicemia with bacteriophage, such therapy aiming at lytic dissolution of cocci in the blood stream, are not only explicable but are to be anticipated in light of known facts concerning the bacterium-bacteriophage reaction.

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Meningococcus Precipitinogens in the Cerebrospinal Fluid.

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The demonstration of type-specific substances for Group I-III and Type II strains of meningococcus,¹ and the production of sera

¹ Rake, G., PROC. SOC. EXP. BIOL. AND MED., 1931, 20, 287.

rich in precipitins for such substances but lacking in precipitins for the non-type-specific (C and P) fractions have led to the investigation of C.S.F. (cerebrospinal fluid) from meningococcal meningitis to ascertain whether this contains type-specific precipitinogens. Vincent and Bellot^{2, 3} and others have demonstrated precipitin reactions between C.S.F. and polyvalent antimeningococcal serum. Most of the investigators noted some inconsistencies, especially cross-precipitation with C.S.F. of other forms of meningitis, notably pneumococcal. The reason for this, no doubt, lies in the fact that the polyvalent serum contains non-specific antibodies, and that the antibody for the C polysaccharide of the meningococcus will react with the similar fraction from other organisms, especially the pneumococcus. Using polyvalent serum, there is, of course, no possibility of typing the organism involved. Marie,⁴ however, states that cases of meningitis due to the meningococcus can be separated from those due to the parameningococcus by the use of monovalent serum prepared against these 2 types and used in the precipitin reaction with C.S.F.

The spinal fluid is cleared by rapid centrifugation. The precipitin test is made with equal parts of undiluted serum and spinal fluid for 2 hours at 37° C. and 15 to 18 hours in the ice-box. Both the ring method and the mixing method have been used. 0.1 cc. of each of the 3 type sera is placed in a small tube. 0.1 cc. of spinal fluid is layered on top of each specimen of serum so that the precipitate appears as a ring at the point of junction. A reading is made immediately and again after one hour at 37° C. The tubes are then agitated and returned to the water bath. At the end of 2 hours a third reading is made and the tubes are placed in the ice-box overnight for a final reading in the morning. Of all the specimens of cerebrospinal fluid tested, only those are mentioned here from

TABLE I.

C. S. F. No.	Type by Agglutination	Type I Serum		Type II Serum		Type III Serum	
		2 hr.	20 hr.	2 hr.	20 hr.	2 hr.	20 hr.
23	I-III	++	++±	0	0	+	++
28	I-III	+	+	0	0	±	+
425	I-III	+	+++	0	0	±	++
429	II	0	0	±	+	0	0
436	II	0	0	±	±	0	0
449	I-III	0	(±)	0	0	(±)	±
451	I-III	+	++	0	0	+	++±

² Vincent, H., and Bellot, *Bull. Acad. Med.*, 1909, **61**, 326.

³ Vincent, H., and Bellot, *Bull. et Mém. Soc. Hôp. de Paris*, 1909, **27**, 952.

⁴ Marie, P. L., *Bull. et Mém. Soc. Hôp. de Paris*, 1917, **41**, 259.

which the meningococcal strain involved was grown and typed in this laboratory. Seven fluids fulfill this requirement and the results of precipitin and agglutinin tests on these are given in Table I. It will be seen that the precipitin results agree completely with those of agglutination and there is no cross-precipitation. The apparent cross-precipitation between Types I and III can be explained by the fact that there is no demonstrable difference in the type-specific substance of these two types as they occur at present, if indeed the types themselves differ. The custom has therefore been adopted of referring to these strains as belonging to Group I-III rather than to either Type I or III.

The presence of the type-specific substance in C.S.F. is probably due to autolysis of the organisms and it has been found that fluids such as No. 436 and No. 449, in which the precipitin reaction is weak, show very few organisms on the smear, whereas in cases as No. 425 and No. 451, in which the reaction is strong, meningococci are present in large numbers.

It is important that C.S.F. be obtained before intrathecal serum treatment or early in the course of such treatment. Fluids positive before such therapy rapidly become negative or very weak in reaction. One must suppose that antibodies in the serum unite with the specific substance and remove it from solution. C.S.F. stored in the ice-box will continue to give a precipitin reaction for many months as will solutions of the isolated type-specific substance.

These observations offer a rapid method of typing a case of meningococcal meningitis and remove one of the chief criticisms against the use of monovalent therapeutic serum, namely, the enforced delay of 2 or more days while the strain is being grown and typed. Readings such as those in Table I can be made 17 to 20 hours after the spinal fluid is drawn, but the majority of fluids will allow of a diagnosis on removal from the water bath at the end of 2 hours. In 4 of the fluids shown in Table I a diagnosis could have been made within $2\frac{1}{2}$ hours after the fluid was withdrawn. In many cases, indeed, the precipitin reaction is immediate and sufficiently strong to allow of a diagnosis directly fluid and serum come into contact.