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Antigenic Relation of Type B *H. Influenzae* to Type 29 and Type 6 Pneumococci.*

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In January, 1942, infant R.B. was admitted to the hospital with purulent meningitis. *Hemophilus influenzae* type B was isolated from the spinal fluid and type 6 pneumococcus from his nasopharynx. The child was treated with sulfadiazine and anti-*H. influenzae* type B rabbit serum (Squibb), recovered completely and was discharged. He was re-admitted with symptoms of meningitis in May, 1942, when a type 6 pneumococcus was recovered from his spinal fluid and from his nasopharynx. Because the child had previously recovered from *H. influenzae* meningitis, the type 6 pneumococcus from the spinal fluid was tested against type B anti-*H. influenzae* horse serum supplied by the Massachusetts State Health Department. The quellung obtained with the *H. influenzae* serum was quite definite but not so marked as that obtained with the type 6 pneumococcus serum. Conversely, it was found that a type B *H. influenzae* organism recently isolated from the spinal fluid of another child quelled in the presence of type 6 anti-pneumococcus therapeutic rabbit serum (Lederle), although it did not do so when tested against type 6 anti-pneumococcus typing serum (Table I). We have since tested 3 other recently isolated type 6 pneumococci against type B anti-*H. influenzae* horse and rabbit sera. Two of these organisms were quelled by these sera. We have also tested stock strains of pneumococci from Type 1 through 33 against anti-*H. influenzae* type B rabbit and horse serum. It was found that in addition to type 6 pneumococcus, type 29 pneumococcus gave marked quellung in the presence of both these sera, but none of the other types tested have so reacted (Table I). We have since found that 3 other strains of type 29 pneumococcus recently isolated from

the nasopharynx of children with pneumonia have also shown marked capsular swelling in the presence of anti-*H. influenzae* type B horse and rabbit serum. In addition, we have found that type 29 pneumococcus rabbit therapeutic serum (Lederle) causes quellung of *H. influenzae* type B. This reaction is more marked with the type 29 pneumococcus serum than it is with the type 6 serum (Table I). Seven strains of *H. influenzae* isolated since May, 1942, have also exhibited marked capsular quellung in the presence of type 29 anti-pneumococcus therapeutic rabbit serum (Lederle), and to somewhat lesser degree also in the presence of type 6 anti-pneumococcus therapeutic rabbit serum (Lederle) (Table I).

We have also tested strains 62B and 191, type B *H. influenzae*, furnished us by Dr. John Dingle and Dr. Leah Seidman. Both strains showed marked capsular swelling with type 29 anti-pneumococcus therapeutic rabbit serum, but gave only a doubtful quellung reaction with the type 6 anti-pneumococcus therapeutic rabbit serum.

Because of the rather remote possibility that the commercial sera which had been employed might have been derived from animals which had been inoculated at different times with both pneumococci and *H. influenzae*, it was thought advisable to prepare sera in our own laboratory. Two rabbits were given a course of intravenous inoculations with 6-hour cultures of the 62B strain and 2 other animals received a similar course with the 191 organism. Both rabbits which had been inoculated with the 62B organisms yielded sera which caused very great capsular swelling of type 29 pneumococci. The serum of the 2 rabbits vaccinated with the 191 strain caused only very slight or negative capsular swelling with type 29 pneumococci. None of the 4 rabbit sera produced definite capsular swelling of

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TABLE I.

Quellung Reactions Obtained with Various Strains of Type 6 and Type 29 Pneumococci, and Type B *H. influenzae* When Mixed with Various Commercially Prepared Sera.

Organism	Type	Type B <i>H. influenzae</i> horse serum (Mass. State)	Type B <i>H. influenzae</i> rabbit serum (Squibb)	Type 6 rabbit pneumococcus typing serum (Lederle)	Type 6 rabbit pneumococcus therap. serum (Lederle)	Type 29 rabbit pneumococcus typing serum (Lederle)	Type 29 rabbit pneumococcus therap. serum (Lederle)
Pneumo. (R.B.) 6	6	+ quellung	+ quellung	4+ quellung	4+ quellung	Neg.	Neg.
" (C.F.) 6	6	+	+	4+	4+	"	"
Pneumo. (Lederle)	6	+	+	4+	4+	"	"
Pneumo. (Sydenham)	6	—	—	4+	4+	"	"
Pneumo. (Lederle)	29	3+	3+	Neg.	Neg.	4+ quellung	4+ quellung
Pneumo. (Strain 1)	29	3+	3+	"	"	4+	4+
Pneumo. (Strain 2)	29	3+	3+	"	"	4+	4+
Pneumo. (Strain 3)	29	3+	3+	"	"	4+	4+
<i>H. influen.</i> (Strain 1)	B	4+	4+	"	+ quellung	Neg.	3+ quellung
<i>H. influen.</i> (Strain 2)	B	4+	4+	"	+	"	3+
<i>H. influen.</i> (Strain 3)	B	4+	4+	"	+	"	3+
<i>H. influen.</i> (Strain 4)	B	4+	4+	"	+	"	3+
<i>H. influen.</i> (Strain 5)	B	4+	4+	"	+	"	3+
<i>H. influen.</i> (Strain 6)	B	4+	4+	"	+	"	3+
<i>H. influen.</i> (Strain 7)	B	4+	4+	"	+	"	3+
<i>H. influen.</i> (Strain 62B)	B	4+	4+	"	±	"	3+
<i>H. influen.</i> (Strain 191)	B	4+	4+	"	±	"	3+

type 6 pneumococci. It should be noted that all of these sera were unconcentrated (Table II).

Rabbit sera were also prepared by us against type 6 and type 29 pneumococci. The 2 strains used had been obtained from Lederle Laboratories in May, 1941. One rabbit was given a course of intravenous inoculations with living type 6 pneumococci while another rabbit received heat-killed type 6 organisms. Similarly, 2 rabbits were inoculated with living and one with heat-killed type 29 pneumococci. As can be seen in Table II, the animal inoculated with living type 6 pneumococci yielded serum which caused very marked capsular quellung with the homologous organism but did not cause any capsular swelling of the type 29 pneumococcus. When tested against an 18-hour culture of recently

isolated type B *H. influenzae*, a limited but definite quellung of the capsule of this organism occurred. The serum obtained from the rabbit inoculated with heat-killed type 6 pneumococci caused capsular swelling of only the homologous pneumococci. The sera of the 2 rabbits vaccinated with living type 29 pneumococci did not cause quellung of the type 6 pneumococci. They did, however, produce marked quellung of both type 29 pneumococci and type B *H. influenzae*. The serum of the rabbit vaccinated with heat-killed type 29 pneumococci caused marked quellung of type 29 pneumococci and a definite but much less marked reaction with type B *H. influenzae*.

Discussion. It appears that the capsule of type B *H. influenzae* has an antigen in common with the capsule of at least some strains of the type 29 and type 6 pneumococcus, but

TABLE II.
Quellung Reactions with Unconcentrated Rabbit Sera Prepared by Authors.

Rabbit serum No.	Vaccine used in preparation of serum	Culture used in quellung test		
		Type 6 pneumo.	Type 29 pneumo.	Type B <i>H. influenzae</i>
1316	Living type B <i>H. infl.</i> (62B)	Neg.	2+ quellung	4+ quellung
1317	" " " " " "	"	2+ "	4+ "
1318	" " " " " " (191)	"	± "	4+ "
1319	" " " " " "	"	Neg.	4+ "
1386	" " 6 pneumococci	4+ quellung	"	+ "
1387	Heat killed type 6 pneumococci	4+ "	"	Neg.
1388	Living type 29 pneumococci	Neg.	4+ quellung	4+ quellung
1389	" " " " " "	"	4+ "	4+ "
1390	Heat killed type 29 pneumococci	"	4+ "	+ "

in the latter instance this relationship is much less clear cut. This and other evidence thus far accumulated indicates that the antigenic components involved in these cross reactions are not identical. The clarification of the relationship involved must await absorption experiments. Types of *H. influenzae* other than type B are being investigated. It is very probable that other relationships between *H. influenzae* and the pneumococcus group will be uncovered as they are sought. In fact, while this article was being prepared for pub-

lication, Chapman and Osborne¹ stated that they had discovered a mutual quellung reaction between pneumococcus type 6B and *H. influenzae* type A. These authors also described the quellung of *H. influenzae* type C in type 21 anti-pneumococcus rabbit serum.

Conclusion. Four strains of type 6 pneumococci and 4 strains of type 29 pneumococci have been encountered which appear to have one or more capsular antigens in common with 7 strains of type B *H. influenzae* which have recently been recovered from the spinal fluid or blood of infants. This relationship has been demonstrated by the capsular quellung method.

¹ Chapman, O. D., and Osborne, W., *J. Bact.*, 1942, **44**, 620.

14138

Effect of Thymoxyethyldiethylamine on Various Pain Thresholds with Special Reference to Referred Pain.*

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Observations that the phenol ether, thymoxyethyldiethylamine, administered to unanesthetized dogs produced a generalized elevation of the cutaneous threshold for pain stimuli without evident signs of central narcosis¹ suggested to the authors its possible

utility in the experimental study of visceral pain.

Method. Adult untrained dogs were used. The threshold for pain was determined by electrical stimuli supplied from a Harvard inductorium with 4.5 v on the primary circuit. Faradic stimuli of graded intensity were applied by means of bipolar electrodes in contact with the shaved abdominal skin, the parietal and visceral peritoneum of the abdomen, me-

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¹ Rosenthal, S. R., and Minard D., *J. Exp. Med.*, 1939, **70**, 415.