

Incidence of Parapertussis in the Grand Rapids Area as Indicated by 16 Years' Experience with Diagnostic Cultures

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IN 1937 a report^{1 a, b} was made to the Society of American Bacteriologists on a group of cultures resembling, but not identical with, *Hemophilus pertussis*. The cultures, which were tentatively referred to as parapertussis bacilli, were first observed in 1935 as unusually large colonies on diagnostic cough plates from children with suspected whooping cough. About the same time, Bradford and Slavin² reported a group of eight parapertussis cultures isolated in the area of Rochester, N. Y. In a report in 1941, Miller³ said that he had observed similar organisms in Denmark, where they were known as "green strains" of *H. pertussis* because of the dark zone produced in blood medium. Since 1937, parapertussis cultures have been received in our laboratory from such widely scattered sources as California, Kentucky, Virginia, Illinois, New York, Mexico, Denmark, and England.

For a number of reasons the parapertussis bacillus has been of peculiar interest to bacteriologists. Its close antigenic relationship to both *H. pertussis* and *Brucella bronchiseptica* emphasizes that the pertussis bacillus is a misfit in the genus *Hemophilus*, and suggests the suitability of including these three species in the same genus. In considering the

organism in relation to the immunization program, several workers including Rambar⁴ have suggested the use of a mixed pertussis-parapertussis vaccine.

For an adequate discussion of the problem we need to consider the incidence and character of parapertussis infections. Some information on incidence is available for the Grand Rapids area from our laboratory records of diagnostic cultures, which have been used since 1932. Since 1935, when parapertussis cultures were first isolated, we have searched for these organisms on all diagnostic cultures from patients with suspected whooping cough. The records of these 16 years form the basis for this report.

CHARACTERISTICS OF PARAPERTUSSIS CULTURES IN COMPARISON WITH *H. PERTUSSIS* AND *BR. BRONCHISEPTICA*

To review briefly the characteristics of the parapertussis bacillus, especially in comparison with the related species *H. pertussis* and *Br. bronchiseptica*, the three organisms are small Gram-negative coccoid bacilli, indistinguishable morphologically. On Bordet-Gengou medium the colonies are similar—pearly white, raised, entire, and surrounded by a hemo-

lytic zone—but the parapertussis and bronchiseptica colonies grow more rapidly and are much larger than pertussis. Biochemically they are all relatively inert; carbohydrates are not fermented; indol is not formed; and acetylmethylcarbinol is not produced. In liquid medium the final reaction is strongly alkaline. Table 1 outlines the differential characteristics.

TABLE 1

Differential Cultural Characteristics of H. pertussis, Parapertussis Bacilli, and Br. bronchiseptica

Characteristic	<i>H. pertussis</i>	<i>Para-</i> <i>pertussis</i> <i>Bacilli</i>	<i>Br.</i> <i>bronchiseptica</i>
Growth on blood-free peptone agar	—	+	+
"Browning" of peptone medium	—	+	—
Motility	—	—	+
Ability to split urea	—	+ ¹	+
Citrate utilization	—	+	+

¹ Occasionally negative

Parapertussis bacilli differ from *H. pertussis* in their ability to grow readily when first isolated on agar medium without blood. They differ from *Br. bronchiseptica* in their lack of motility and in the production of a brown color in peptone medium. Parapertussis and bronchiseptica bacilli utilize citrate and usually split urea, while *H. pertussis* does not.

Serologically, antisera produced against any one of the organisms will show more or less cross-agglutination with the other two. In fact, bronchiseptica and parapertussis antisera frequently agglutinate the heterologous antigen to titer, but reciprocal agglutinin absorption tests indicate that the antigens are not identical. A more complete antigenic analysis of this group of cultures is needed and presents an interesting problem for future work.

The toxin of *H. pertussis* has been a subject for study and discussion ever

since Bordet's work. It is therefore of interest that Bruckner and Evans⁵ in England prepared toxins from *H. pertussis*, *Br. bronchiseptica*, and parapertussis bacilli which were similar in their effect on animals and were indistinguishably neutralized by pertussis antitoxic serum. The role of these toxins, whether in disease or in immunity, is still not entirely clear.

In experimental animals, suspensions of living organisms of all three species produce skin reactions of hemorrhagic necrosis, and all three injected intraperitoneally in suitable dosage kill guinea pigs and mice in approximately 24 hours. In mice inoculated intracerebrally with selected smooth strains of *H. pertussis* or *Br. bronchiseptica*, the picture is that of a true infection. The animals are killed by relatively small doses after an incubation period of 5 or more days. Parapertussis strains, on the other hand, are relatively avirulent when injected intracerebrally.

DATA

During the 16 years, 22,135 cultures have been examined. The number and percentage of positive findings are shown in the second table. No differentiation was made between cough plate and nasopharyngeal swab cultures.

TABLE 2

Results of Diagnostic Cultures for H. pertussis and Parapertussis Bacilli

Cultures	Number	Per cent
* Total	22,135	100.0
Negative	17,652	79.7
<i>H. pertussis</i> found	4,377	19.8
Parapertussis found	106	0.5

* Excluding 1396 unsatisfactory cultures.

The average number of cultures examined per year was 1,384, but the numbers varied widely, from 132 in 1944 to 4,609 in 1940. Eighty per cent of the cultures were negative. *H. pertussis* was found in 4,377, or 19.8 per cent, and parapertussis in 106, or 0.5 per cent. These figures represent specimens, not

patients, since frequently more than one culture was obtained from the same child. Of the positive cultures, one in every 42 was parapertussis.

It is of interest to know what proportion of the reported cases of whooping cough are included among the patients from whom positive laboratory findings were obtained. This correlation is given in Table 3.

TABLE 3
Reported Cases of Whooping Cough Correlated with Numbers of Patients with Positive Cultures

Period	Reported Cases	Patients with Positive Cultures	
		<i>H. pertussis</i>	Parapertussis bacilli
1935-1939	2,277	1,367	21
1940-1944	2,293	1,235	13
1945-1949	1,379	519	16
1950	321	142	15
1935-1950	6,270	3,263	65
Average per year	392	204	4

The reported cases of whooping cough in Grand Rapids, from 1935 through 1949, are given by 5 year periods; those for the year 1950 are listed separately. The total for 16 years is 6,270, with the average per year of 392. An attempt was made to eliminate from the tabulations of patients all duplicate specimens from the same child, but undoubtedly a few have been overlooked. Also, a few patients from outside the study area are included. The totals show that positive cultures were obtained on approximately half of the reported cases throughout the period. The 65 patients from whom parapertussis bacilli were isolated comprise 2 per cent of the total patients with positive laboratory findings. Certain facts of interest are not shown by the summarized figures. For example, there were 5 years, not consecutive, in which no parapertussis cultures were isolated. The 15 patients found during 1950 represent the largest number in any one year; there were 12 in 1948, 10 in 1940 (the year of the largest number of reported cases of

whooping cough), and smaller numbers in the other years.

CLINICAL CHARACTERISTICS OF PARAPERTUSSIS

Unfortunately, all 65 patients with parapertussis infection located during the 16 year period of observation were not studied by precisely the same criteria under the same diagnostician. Our judgment is based upon notes by the visiting nurse, comments by the mother recorded on the information blanks accompanying the specimens for culture, clinical impressions of different physicians who saw some of the children, and 23 detailed clinical histories obtained by the nurse in relation to other field study series.

The clinical picture was usually that of a mild pertussis-like disease. All the children coughed, and in most cases the coughs were described as paroxysmal, although actual whooping was known to occur in only seven. When whooping was observed it was recorded as rare—once or twice in the course of the disease, or occurring only for a few days or a week. The average duration of disease was three weeks. In one extreme case, a three-month-old baby coughed for three months, and in another a positive culture was obtained during the seventh week of disease. At the other extreme were a number of children with mild symptoms lasting only a week or ten days. One patient, from whom both *H. pertussis* and parapertussis bacilli were isolated, whooped for a month and had a marked weight loss. In the entire series of 65 cases there were no complications and no deaths.

We recall here the report of Zuelzer and Wheeler⁶ of two deaths of very young infants with bronchopneumonia in which parapertussis organisms were isolated at autopsy. It would be misleading, we believe, to place too much emphasis on these interesting but probably very rare findings.

SOURCE OF INFECTION

As to the source of the infections, very little information could be obtained. A few related cases were recognized. For example, there were three instances of three cases in a family and four instances of two. In a number of families, other children besides the one with the positive culture were reported to have similar coughs, suggesting possibly related cases. Evidence of contact outside the family was found on three occasions, when positive cultures were secured from children in two associated families. A few of the mothers stated that a playmate had had an undiagnosed cough; but in approximately half of the infections there were no known associated cases.

Of 55 of the children on whom reliable information could be secured, 32 had had pertussis vaccine, and 7 of these had also had a booster injection.

COMMENTS

The data just presented suggest that in the area studied the incidence of parapertussis infections in comparison with pertussis is low. The relative mildness of the infection, however, may prevent our obtaining a true picture as to prevalence. In New York, Bradford's study² indicated that parapertussis was the etiologic agent in 5 per cent of the whooping cough cases during a relatively short period of observation. In California, Miller³ concluded, on the basis of agglutination tests on sera from children with negative histories, that parapertussis infections, either subclinical or too mild to be called to the attention of a physician, were common. That parapertussis infections may sometimes be more prevalent is suggested by a recent experience in Copenhagen. In a letter received in February, 1951, from Dr. Hans Lautrop⁷ of the State Serum Institute, he tells of isolating 150 parapertussis cultures during three or four months at the rate of about 10 a week. The

parapertussis cultures during November and December, he stated, were 23 per cent of the positive findings from pertussis-like disease. He described in some detail the clinical course of disease, which closely resembled what has been observed here. In a recent report from England (Medical Research Council⁸), parapertussis bacilli were isolated from 24 children, in comparison with 482 with *H. pertussis* infection.

In considering the question of including parapertussis bacilli in pertussis vaccine, several points should be borne in mind. The problem needs to be considered from the standpoint of incidence and severity of disease in the particular geographic area of interest; that is, does the disease constitute a public health problem? In the Grand Rapids area the incidence of recognized infection is low and the disease mild. At the present time, therefore, the problem is not of sufficient magnitude to warrant a vaccination program. If under different circumstances a mixed vaccine were ever to be seriously considered, we would need to know the immunizing effects of the separate antigens on the two diseases; also, what effect the addition of parapertussis bacilli would have on the toxicity of the mixed vaccine. In comparison with pertussis vaccine, parapertussis vaccine is a poor immunizing agent against pertussis infection in mice.⁹ The immunizing effect of either antigen against parapertussis infection has not been studied in mouse protection tests because no culture has yet been found of sufficient virulence to be used for challenge.

SUMMARY

During the 16 years from 1935 through 1950, 22,135 diagnostic cultures have been examined for *H. pertussis* and the parapertussis bacillus. Positive findings were reported in 4,483 specimens, of which 106 were parapertussis and 4,377 were pertussis bacilli, representing,

respectively, 0.5 and 19.8 per cent of the total specimens.

The positive parapertussis cultures were from 65 patients, in comparison with 3,263 patients from whom *H. pertussis* was isolated. During the period of study there were 6,270 reported cases of whooping cough in the area.

In general the parapertussis infections were much milder and of shorter duration than those caused by *H. pertussis*. These findings indicate that in the area studied, parapertussis infections were of relatively slight public health significance.

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Laboratory Refresher Courses

The 1952 schedule of laboratory training courses to be given by the Communicable Disease Center of the U. S. Public Health Service is now available. These courses, usually two weeks in duration, in a few instances, one, three, or four weeks, are all given at the laboratory in Chamblee, Ga., except those dealing with viruses, which are

given at the virus laboratory in Montgomery, Ala. The courses are planned under the general direction of Senior Surgeon R. F. Reider, chief of the Laboratory Training Services. The schedule, application forms and further information from Chief, Laboratory Training Services, Communicable Disease Center, P. O. Box 185, Chamblee, Ga.