

5. Title: Etiology of Pertussis Syndrome in Children

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OBJECTIVE

Recent evidence indicates that in at least some instances the clinical syndrome of whooping cough may be the result of viral infection. Recent reports raising this question, however have been of isolated cases. The relative roles of Bordetella pertussis and virus remain unknown.

DESCRIPTION

Patients initially admitted to the study met the following criteria: absence of high fever, clinical symptoms of severe paroxysmal cough with facial suffusion, inspiratory whoop and vomiting following the paroxysm. Upon admission to the study each patient received the following: (a) physical examination (b) cough plate and nasopharyngeal culture for bacteriology studies, (c) blood for antibody, white blood cell count and differential count. Convalescent serum was obtained two weeks later (d) Nasopharyngeal swabs were obtained and immersed in 2.0 ml of 1% bovine albumin in balanced salt solution. These were then treated with Penicillin, Streptomycin, Fungizone and Kanamycin before inoculation into EE (esophageal epithelium), Hela M and WI-38 cells. Medium were changed on the following day and cytopathogenic effect (CPE) were observed. Isolations failing to show CPE on day 7 were hemadsorbed with 0.4% guinea pig red blood cells for evidence of hemadsorbing viruses. Isolates with CPE were processed as routine method for virus identification.

Paired sera were tested for antibodies against:

Cytomegalovirus, Adenovirus, Respiratory syncytial virus, Herpes simplex virus, Influenza A₂-PR/64, Rubella, Parainfluenza type 1-3.

In addition, homologous neutralization antibody titers will be determined against nasopharyngeal swab isolates.

Results of the study.

100 patients were included in this study. Specimens were collected from July 1, 1968 to January 14, 1969. Table 1 shows the distribution of patients studied. Females predominated and most patients were above 3 years of age. Bordetella pertussis was isolated from only 8 patients. 4 cases were observed in

patients of 1-2 years old. The small number of positive specimens did not permit significant analysis of age and sex distribution. Viruses isolated were mostly cytomegalovirus, rhinoviruses and adenoviruses (Table 2). Among 13 cases of cytomegalovirus isolated, 8 were found in children under 2 years. The age and sex distribution of the patients are separately reported. Only 3 of 13 patients showed an increase in antibody titer by CF test. This evidence suggested that CMV virus may be isolated from any patients without causing infection and may not be the cause of a clinical syndrome similar to "Pertussis". Of the adenoviruses (ADV), isolated, none showed CF antibody conversion, but one showed seroconversion to respiratory syncytial virus. From the 8 patients from which B. pertussis was recovered, 2 of them had CMV virus isolated from nasopharyngeal swab and one of them had an increase of CF antibody to ADV virus. One patient had ADV isolation from nasopharyngeal swab without serological response to the virus. One patient had rhinovirus isolated with unknown serological response. The hypothesis that some viruses may associate with B. pertussis infection remains under question, since the number positive are small.

Studies of antibodies to B. pertussis among patients are in progress. Antibodies to some respiratory viruses were studied and results were summarized in Table 3. Increases of antibody titers found against CMV, ADV, RS, H. simplex, Flu A₂/64, Rubella and Parainfluenza type 2 and 3 viruses, suggest that virus infection of these types may sometimes be associated with a clinical syndrome similar to pertussis. The answer to this problem may be clearer when pertussis agglutinin antibody are completed.

Table 1. Age and Sex Distribution of Studied Patients.

Sex	< 6m,	6-12m.	1-2y.	2-3y.	3-4y.	4-5y.	5+y.	Total
M	2	1	10	2	5	2	16	38
F	3	5	10	12	8	6	18	62
Total	5	6	20	14	13	8	34	100

Table 2. Virus isolation from nasopharyngeal swab of patients.

Virus	No. isolated	Isolation with seroresponse	Isolation without seroresponse
CMV	13/100	3	7 (3 not done)
ADV	4/100	0	4
Rhino	8/100	—	— (not done)
Unknown	2/100	—	—
Total	31/100		

Table 3. Studies of antibodies to respiratory viruses among studied patients.

Viruses	Method	No. tested	No. rise in Antibody titer	No. detectable antibody
CMV	CF	88	6	9
ADV	CF	88	5	38
RS	CF	88	13	36
H. simplex	CF	88	2	12
Flu A ₂ /64	HAI	88	1	57
Rubella	HAI	88	1	33
Parainf. 1.	HAI	77	0	29
Parainf. 2.	HAI	77	2	30
Parainf. 3.	HAI	77	3	37