

3. Title: Cytomegalovirus Infection of the Respiratory Tract

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#### OBJECTIVE

To determine the significance of cytomegalovirus in the respiratory tract of children, and measure serological responses in infected children.

#### PROGRESS

During the months of January–December 1968, 342 nasopharyngeal swabs from children seen at the Out–Patient Department with febrile upper respiratory tract disease were satisfactorily studied for cytomegalovirus. Overall 62, or 18.1% were positive. The age distribution of those positive for virus (Table 1) suggested that this virus is acquired very early in life; recovery of virus was unusual over the age of three years. Of those under the age of 12 months, 39.5% of whom were positive for virus, cytomegalovirus was recovered as early as two months of age (Table 2). On the basis of the number studied, it appears that the peak incidence is around 7–9 months of age.

During the months of August 1968 to January 1969, a separate study of the viruses associated with clinically diagnosed whooping cough was in progress. 100 patients were studied, and eleven yielded cytomegalovirus from nasopharyngeal swabs. The age distribution of these patients was similar to that of the URI group (Table 3).

For a control group study, nasopharyngeal swabs from 66 asymptomatic children under the age of 12 months were obtained. All children were first examined and selected for study only if well by history and physical examination. 10, or 13.3%, of these were positive for virus. However, since the monthly age distributions are significantly dissimilar the aggregate prevalence rate cannot be compared between the two groups.

In order to rule out the unlikely possibility that the presence of virus was a reflection of congenitally acquired infection, urine specimens were obtained from 187 randomly selected, normal newborns. The sample was centrifuged, and after treatment with antibiotics the supernatant tested for virus. Only 2 specimens were positive, both from infants apparently normal during the neonatal period.

Previous workers have not demonstrated cytomegalovirus to be a primary pathogen of the respiratory tract, and there is no evidence to suggest this here, either. Overall, in the URI group other established pathogenic respiratory viruses were isolated in addition to cytomegalovirus in 27.4% of the cases. Even assuming no interference in cell cultures between other agents and the growth of cytomegalovirus, this figure is biased toward the minimum, since early destruction of cultures by such agents as adenoviruses, rhinoviruses would preclude the detection of the more slowly appearing CPE of cytomegalovirus. Moreover this 27% recovery rate of other respiratory viruses compares favorably to the overall isolation rate of 32.5% from those patients not yielding cytomegalovirus (Table 4).

Table 1. Age Distribution, CMV Positives

<u>Age</u>	<u>No. Cultures</u>	<u>No. Positive</u>	<u>% Positive</u>
< 1 yr	81	32	39.5
1-2	66	17	19.8
2-3	51	6	11.8
3-4	37	5	13.5
> 4	<u>87</u>	<u>2</u>	<u>2.3</u>
Total	342	62	18.1%

Table 2. CMV Positives, Less Than 12 Months Old

<u>Age (Mo.)</u>	<u>No. Cultures</u>	<u>No. Positives</u>	<u>% Positive</u>
2	1	1	100
3	2	1	50
6	7	4	57
7	13	9	69
8	17	8	47
9	11	2	18
10	17	3	29
11	<u>13</u>	<u>2</u>	<u>15</u>
Total	81	32	

Table 3. CMV Positives, Patients with Whooping Cough

<u>Age</u>	<u>No. Cultures</u>	<u>No. Positives</u>	<u>% Positive</u>
< 1 yr	12	4	33.3
1-2	19	3	16.0
2-3	14	2	14.3
3-4	12	1	8.3
> 4	<u>43</u>	<u>1</u>	<u>2.3</u>
Total	100	11	11%

Table 4. Association with Other Respiratory Virus

Total Number	Patients	
	CMV+	CMV-
	62	280
Parainfluenza	6	34
Adenovirus	2	14
Influenza A2	3	16
Rhinovirus	2	11
Coxsackie B <sub>2</sub>	2	9
Rubella	2	4
Misc. — Polio (1), Echo (3), Rubeola (1), RS (2), Reovirus (1)	1	7
Total	17	91
	27.4%	32.5%

Table 5. Complement—Fixing Antibody in Sera of Virus Excretors.

	No. Sera	No. Sera CF+ (1;4 dilution)	No. Sera Titer
URI Group	34	6	0
Pertussis Group	9	4	2

Table 6. Neutralizing and Fluorescent—Antibody in Sera of Virus Excretors

Neutralizing Antibody	30/34
IFAT, Anti—Gamma Glob.	29/34
IFAT, Anti—IGM Fraction	22/34
CF neg. sera: IGM pos.	21/28
Neut. Ab+, IGM—CF+	5/9

The most frequently utilized test to assess the incidence of experience with cytomegalovirus has been the complement-fixation test. Sera obtained from children in the URI and pertussis groups at the time virus excretion was demonstrated were accordingly tested for CF Ab in duplicate. In one test, commercial antigen prepared from the prototype AD-169 strain was employed, and in another test antigen prepared from a local isolate was used. Results indicated no difference between these strains, and also revealed a very low incidence of CF antibody (Table 5). However, assay for neutralizing antibody at a serum dilution of 1:4 and indirect fluorescent antibody (serum dilution 1:10) indicated a considerably higher frequency of these types of antibody to be present in sera during virus excretion (Table 6). In addition, 32 of the sera also contained IGM macroglobulin anti-CMV antibody by indirect immunofluorescence. 21 of the 28 CF antibody negative sera were positive for IGM antibody. Of the 3 sera containing antibody not in the IGM immunoglobulin class, 5 were CF positive.

#### SUMMARY

Cytomegalovirus has been found to be commonly excreted from the respiratory tract of Bangkok children. Such infections are most common in children less than 1 year of age the frequency declining thereafter so that virus is rarely recovered from children over 3 years of age. Evidence indicates these infections are acquired early in life. Measurements of CF antibody fail to indicate the frequency of infection, although neutralizing and fluorescent antibody are present even during active virus excretion.