Adenovirus, parainfluenza virus and respiratory syncytial virus antibodies in the sera of Jamaicans

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(Received 17 February 1972)

SUMMARY

Surveys for respiratory virus antibodies in the Jamaican population have shown that adenovirus, respiratory syncytial virus and parainfluenza types 1 and 3 virus antibodies are acquired early in life. The incidence of haemagglutination-inhibiting antibodies to parainfluenza viruses increases rapidly with age and almost all adults possess parainfluenza type 3 antibody, usually in high titre. Parainfluenza type 1 antibodies are only slightly less common. Complement-fixing antibodies to the adenovirus group were also observed to increase in incidence with age.

Complement-fixing antibody to respiratory syncytial virus was less common in Jamaican sera than antibody to the other respiratory viruses described here. The highest titres were observed in the youngest age-group.

INTRODUCTION

The aetiology and prevalence of a variety of respiratory viruses in the population of Jamaica has been examined by determining the pattern of virus isolations from persons clinically ill with respiratory infections (Jennings & Grant, 1967a) and by serological surveys for antibodies to influenza viruses in sera collected from Jamaican individuals of all ages (Jennings & Grant, 1967b; Jennings, 1968). The present paper is concerned with the incidence of adenovirus, respiratory syncytial virus and parainfluenza virus antibodies in Jamaica as determined by serological surveys.

Parainfluenza viruses, respiratory syncytial virus and adenoviruses have been associated with serious respiratory diseases of children. Parainfluenza viruses have been associated with croup (Lewis, Lehmann & Ferris, 1961) and respiratory syncytial virus with bronchiolitis in infants (Channock et al. 1961). Adenoviruses have been shown to cause severe and fatal pneumonia in young children (Chany et al. 1958). In adults all these viruses can cause mild, upper respiratory tract infections (Rhodes & van Rooyen, 1968).

Studies on the prevalence of antibodies to parainfluenza and respiratory syncytial viruses in different parts of the world have indicated that such antibodies are

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fairly widespread (Jensen, Peeler & Dulworth, 1962; Hambling, 1964; Suto et al. 1965) and are acquired early in life. Neutralizing antibodies to certain adenoviruses are also acquired early in life (Potter & Shedden, 1963).

Few studies on the incidence of respiratory viruses and their antibodies in tropical or subtropical areas have been carried out although surveys in Nigeria (Njoku-Obi & Ogunbi, 1966) and Panama (Monto & Johnson, 1967) have shown that antibodies to several respiratory viruses are not uncommon.

MATERIALS AND METHODS

Sera

The sources of the sera used have been described previously (Jennings & Grant, 1967b). They were from both sexes and all age-groups of the Jamaican population. Sera from 449 individuals were examined for haemagglutination-inhibiting (HI) antibodies to parainfluenza types 1 and 3 viruses, 510 sera tested for complement fixing (CF) antibodies to the adenovirus group and 558 sera tested for CF antibodies to respiratory syncytial (RS) virus. Most sera were from infants and children under 10 years of age.

Viruses and antigens

Parainfluenza type 1 antigen was prepared in human thyroid tissue cultures from a locally isolated strain, CV 837/64. Thyroid tissue monolayers were maintained using Eagle's basal medium (Eagle, 1955) with 2% calf serum and 0.5% lactalbumin hydrolysate. Antigen was prepared from monolayers showing strongly positive haemadsorption 12–14 days after inoculation. They were frozen and thawed three times, centrifuged at 2000 rev./min. for 60 min., the supernatant removed, dispensed and stored at -70° C. The haemagglutinin titres of these fluids ranged from 1/32 to 1/128. Control antigen was prepared similarly using uninoculated thyroid cultures.

Parainfluenza type 3 antigen and control were obtained commercially from Flow Laboratories, Rockville, Maryland, U.S.A.

CF antigens from a locally isolated strain of type 3 adenovirus, RV 757 (Jennings & Grant, 1967a) and an RS strain, TRVL 1283, kindly supplied by Professor L. Spence from the Trinidad Regional Virus Laboratory were prepared in HEp-2 or HeLa cells according to methods described by Rose (1964).

Antisera

Standard HI antisera to parainfluenza types 1 and 3 viruses were obtained from Flow Laboratories.

Adenovirus group antiserum was prepared in rabbits by standard methods (Rose, 1964) using the locally isolated type 3 adenovirus strain, RV 757.

Antiserum for use in the RS virus CF test was obtained commercially from Microbiological Associates Inc., Bethesda, Maryland, U.S.A.

Serological procedures

The methods used for detecting HI antibodies to parainfluenza viruses have been described previously (Jennings & Grant, 1967a).

CF tests for RS virus and adenovirus antibodies were carried out using standard methods (Lief, Fabiyi & Henle, 1958) with the exception that fixation of complement was for 90 min. at 37° C. and incubation time following the addition of sensitized cells was for 30 min.

Sera for HI tests were treated with acid-washed kaolin and absorbed with guineapig erythrocytes before testing. Sera for CF tests were inactivated at 56° C. for 30 min. The microtechnique (Sever, 1962) was employed for all serological tests. In HI tests the lowest serum dilution examined was 1/20; in CF tests it was 1/4. To estimate geometric mean titres, sera negative at 1/20 in the HI test were assigned an arbitrary titre of 1/10.

RESULTS

Sera were divided into nine groups according to age of donor. The youngest group were infants under 1 year of age. Sera from individuals 1–10 years inclusive were divided into five age-groups each spanning 2 years. Sera from persons aged 11 years and over were divided into three age-groups: 11 to < 20 years, 20 to < 40 years and 40 years and over.

Haemagglutination-inhibiting antibodies to parainfluenza virus types 1 and 3

Table 1 shows that 257 sera, about 60% of those examined for antibodies to parainfluenza type 1, were positive at or above 1/20, but up to the age of 5 years the percentage of positives was considerably lower. The incidence of HI antibody to this virus also declined in sera from persons of 40 years or over, whilst the greatest acquisition of antibody was observed in the 5 to < 7 year age-group.

HI antibodies to parainfluenza type 3 virus were very common in Jamaican sera (Table 2), and a total of 387 (86·2%) were positive. Antibodies were not detected in infants under 1 year, but were rapidly acquired with age and all sera from 5- to < 7-year-old children were positive. In older age-groups, sera without parainfluenza type 3 antibodies were rare. The highest geometric mean antibody titre level was observed in the 5- to < 7-year age-group.

Antibodies to respiratory syncytial virus

CF antibodies to RS virus were found in 208 (37·2%) of the sera tested (Table 3). Of the sera, 358 were from infants and children less than 11 years old and 130 (36·3%) of these were positive.

The incidence of antibodies to RS virus was relatively low in the sera of infants and children up to 3 years of age, but thereafter the frequency increased to about 40%, a frequency that was maintained with minor fluctuations into late adult life. However, the percentage of sera showing high titres decreased fairly steadily

Table 1. Age distribution and geometric mean titres of haemagglutination-inhibiting antibody to parainfluenza type 1 virus in the sera of Jamaicans

Age-group (years)	No. of sera tested	No. positivo	Positivo (%)	Geometric mean antibody titre
0 to < 1	21	1	4.8	13.3
1 to < 3	51	8	15.7	13.5
3 to < 5	47	16	34.0	18-5
5 to < 7	54	34	63.0	64-1
7 to < 9	64	52	81.3	49-4
9 to < 11	67	50	74·6	48.2
11 to < 20	64	51	79-7	35.5
20 to < 40	42	28	66.7	33.8
≥ 40	39	17	43.6	17.4
Tot	als 449	257	57.2	

Table 2. Age distribution and geometric mean titres of haemagglutination-inhibiting antibody to parainfluenza type 3 virus in the sera of Jamaicans

Age-group (years)	se	No. of ra tested	No. positive	Positive (%)	Geometric mean antibody titre
0 to < 1		21	0	0	10.0
1 to < 3		51	23	45-1	38.0
3 to < 5		47	38	80.9	52·6
5 to < 7		54	54	100.0	193.7
7 to < 9		64	63	98.4	161-4
9 to < 11		67	67	100.0	127.5
11 to < 20		64	63	98.4	146-7
20 to < 40		42	41	97.6	139-3
≥ 40		39	38	97.4	123.3
	Totals	449	387	86.2	

Table 3. Complement-fixing antibodies to respiratory syncytial virus in sera from the population of Jamaica

Age-group (years)	No. tested	Pos	sitivo	Sera with titre of 1/16 or above		
		No.	%	No.	%	
0 to < 1		25	4	16.0	2	50.0
1 to < 3		66	17	25.8	5	29.4
3 to < 5		76	33	43.3	6	18.2
5 to < 7		58	20	34.5	3	15.0
7 to < 9		62	25	32.0	7	28.0
9 to < 11		71	31	43.7	2	6.5
11 to < 20		81	36	44-4	2	5.6
20 to < 40		61	21	34.4	1	4.8
≥ 40		58	21	36.2	0	0
	Totals	558	208	37.2	28	

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Age-group		No. tested	Pos	Positive		Sera with titre of 1/16 or above	
(years)	No.		%``	No.	%		
0 to < 1		20	3	15.0	0	0	
1 to < 3	,	38	13	$34 \cdot 2$	${f 2}$	13.4	
3 to < 5		64	38	59·4	10	26.3	
5 to < 7		62	34	54·8	11	40.7	
7 to < 9		7 6	45	$59 \cdot 2$	18	40.0	
9 to < 11		71	44	$62 \cdot 0$	18	40.9	
11 to < 20		7 8	50	64.1	9	18.0	
20 to < 40		44	30	68-2	13	43.3	
≥ 40		57	18	31.6	6	33.3	
т	otals	510	275	53.9	87		

Table 4. Complement-fixing antibodies to the adenovirus group in sera from the population of Jamaica

as age increased and the titres, highest in the two youngest age-groups, were considerably lower in adults and adolescents.

Antibodies to the adenovirus group

A total of 510 sera were examined for antibodies to the adenovirus group CF antigen, and 275 (53.9%) were positive at dilutions of 1/4 or higher.

The distribution of antibodies according to age (Table 4) shows that few infants possessed adenovirus CF antibodies. Such antibodies were present in the sera of more than half the children tested by 5 years, and although a slight decrease in frequency was noted in 5- to < 7-year-olds, adenovirus CF antibody became more prevalent as age increased up to 40 years. In older persons there was a decrease in antibody prevalence.

Table 4 also shows the percentage of positive sera with titres of 1/16 or above. Higher titres were encountered in the older age-groups, with most high-titred sera in the 20 to < 40 age-group.

DISCUSSION

The surveys for antibodies to parainfluenza types 1 and 3 viruses show they are widespread in the Jamaican population. Parainfluenza type 3 antibodies were detected in almost every serum tested from persons older than 4 years and over half also contained parainfluenza type 1 antibodies.

High incidence of parainfluenza antibodies has been reported in surveys in both tropical and temperate zones. In America, Jensen et al. (1962) found 80-90 % of children aged 1-4 years to have parainfluenza type 3 antibody in their sera and only two sera from 470 older individuals were negative in this respect. In the same survey, a third of the sera tested for parainfluenza type 1 antibodies in the 1-4 ago-group were positive and 60-70 % positives were found in older children and adults. Antibodies to parainfluenza viruses are also common in sera from Europeans (Forsgren, Sterner & Wolontis, 1965) and in tropical countries (Monto & Johnson, 1967).

The incidence of parainfluenza type 1 and 3 antibodies in Jamaican sera is thus similar to that in other areas. They are acquired early in life and are very prevalent in the adult population.

The survey for RS virus antibodies in Jamaica shows the virus is active in the island, mainly in children. However, only 43% of 76 sera from 3- to < 5-year-old Jamaican children were positive and in sera from children aged 5 to < 9 years antibody was even less frequent.

In England, the incidence of CF antibodies to RS virus is much higher. Hambling (1964) found 66% of children aged 2-4 years to be positive and Moss, Adams & Tobin (1963) detected RS antibody in 93% of sera from 14 children aged 3-5 years. In an industrial population in North America over 66% of sera from children aged 6 years contained RS virus antibody (McClelland et al. 1961). Above 6 years of age RS virus antibodies are very common in the general population (Moss et al. 1963; Suto et al. 1965).

The findings reported here suggest that antibody to RS virus is relatively uncommon in the Jamaican population but agrees with findings elsewhere in showing that such antibody is acquired up to 5 years of age, indicating that this segment of the population may be particularly susceptible to infection by this virus.

RS virus epidemics occur over short periods of time and both neutralizing and CF antibodies have short survival times in humans (Suto et al. 1965). Thus, the time of collection of the sera would affect the prevalence of antibody to RS virus and the sera used in the present survey may have been obtained during an interepidemic period. On the other hand, it has been suggested that severe infections produced by RS virus may be more frequent in industrialized regions that in less urbanized areas (Holzel et al. 1965). Jamaica, besides being a tropical area is practically free from heavy industrialization, a factor which may have contributed to the results obtained.

The survey for adenovirus group CF antibodies in Jamaica shows such antibody to be acquired early in life, the incidence increasing from 15% in infants under one year to over 50% by 5 years of age. Similar findings have been reported in England (Potter & Shedden, 1963). Although no epidemiological information on the incidence of individual adenovirus types can be obtained using the CF test, it seems probable that the antibodies observed in young Jamaicans are produced in response to infections by types 1, 2, 3 and 5 adenoviruses as these types have been recovered from sick children in Jamaica (Jennings & Grant 1967a).

Adenovirus CF antibodies continue to be acquired with age by the Jamaican population, probably through infection by different adenovirus types, up to the age of 40, after which the prevalence of these antibodies is reduced.

This study was supported by a grant from the Ministry of Overseas Development, Great Britain. I am indebted to Professor L. S. Grant and Dr E. A. Belle for their advice and constant encouragement.

REFERENCES

- CHANOCK, R. M., KIM, H. W., VARGOSKO, A. J., DELEVA, A., JOHNSON, K. M., CUMMING, C. & PARROT, R. H. (1961). Respiratory syncytial virus. I. Virus recovery and other observations during 1960 outbreak of bronchiolitis, pneumonia and minor respiratory diseases in children. *Journal of the American Medical Association* 176, 647.
- CHANY, C., LEPINE, P., LELONG, M., LE-TAN-VINH, SATGE, P. & VIRAT, J. (1958). Severe and fatal pneumonia in infants and young children associated with adenovirus infections.

 American Journal of Hygiene 67, 367.
- EAGLE, H. (1955). Nutrition needs of mammalian cells in tissue culture. Science, N.Y. 122, 501. FORSGREN, M., STERNER, G. & WOLONTIS, S. (1965). Antibodies against respiratory viruses among healthy children. Acta paediatrica scandinavica 54, 314.
- HAMBLING, M. H. (1964). A survey of antibodies to respiratory syncytial virus in the population. British Medical Journal 1, 1223.
- HOLZEL, A., PARKER, L., PATTERSON, W. H., CARTMEL, D., WHITE, L. L. PURDY, R., THOMPSON, K. M. & TOBIN, J. O'H. (1965). Virus isolations from throats of children admitted to hospital with respiratory and other diseases, Manchester 1962-4. *British Medical Journal* i, 614.
- JENNINGS, R. (1968). Respiratory viruses in Jamaica. A virologic and serologic study.

 3. Haemagglutination-inhibiting antibodies to type B and C influenza viruses in the sera of Jamaicans. American Journal of Epidemiology 87, 440.
- Jennings, R. & Grant, L. S. (1967a). Respiratory viruses in Jamaica: A virologic and serologic study. 1. Virus isolations and serologic studies on clinical specimens. *American Journal of Epidemiology* 86, 690.
- JENNINGS, R. & GRANT, L. S. (1967b). Respiratory viruses in Jamaica: A virologic and serologic study. 2. Haemagglutination-inhibiting antibodies to influenza A viruses in the sera of Jamaicans. American Journal of Epidemiology 86, 700.
- Jensen, K. E., Peeler, B. E. & Dulworth, W. G. (1962). Immunization against parainfluenza infections. Antigenicity of egg-adapted types 1 and 3. *Journal of Immunology* 89, 216.
- Lewis, F. A., Lehmann, N. I. & Ferris, A. A. (1961). The haemadsorption viruses in laryngo-tracheo-bronchitis. *Medical Journal of Australia* 2, 929.
- Lief, F. S., Fabiyi, A. & Henle, W. (1958). Antigenic analysis of influenza viruses by complement fixation. 1. The production of antibodies to the soluble antigen in guinea-pigs. *Journal of Immunology* 80, 53.
- McClelland, L., Hilleman, M. R., Hamparian, V. V., Ketler, A., Reilly, C. M., Cornfeld, D. & Stokes, J. Jr. (1961). Studies of acute respiratory illnesses caused by respiratory syncytial virus. New England Journal of Medicine 264, 1169.
- Monto, A. S. & Johnson, K. M. (1967). A community study of respiratory infections in the tropics. 1. Description of the community and observations on the activity of certain respiratory agents. American Journal of Epidemiology 86, 78.
- Moss, P. D., Adams, M. O. & Tobin, J. O'H. (1963). Serological studies with respiratory syncytial virus. Lancet i, 298.
- NJOKU-OBI, A. N. & OGUNBI, O. (1966). Viral respiratory diseases in Nigeria: A serological survey. II. Complement-fixing antibody levels of adenoviruses, respiratory syncytial virus, psittacosis virus. Journal of Tropical Medicine and Hygiene 69, 147.
- POTTER, C. W. & SHEDDEN, W. I. H. (1963). The distribution of adenovirus antibodies in normal children. Journal of Hygiene 61, 155.
- RHODES, A. J. & VAN ROOYEN, C. E. (1968). Textbook of Virology, 5th ed., pp. 259-270. Baltimore: The Williams & Wilkins Company.
- Rose, H. M. (1964). The adenoviruses. In Diagnostic Procedures for Viral and Rickettsial Diseases, 3rd ed. (ed. E. H. Lennette and N. J. Schmidt), p. 434. American Public Health Association Inc.
- Sever, J. L. (1962). Application of a microtechnique to viral serological investigations.

 Journal of Immunology 88, 320.
- Suto, T., Yano, N., Ikeda, M., Miyamoto, M., Takai, S., Shigeta, S., Hinuma, Y. & Ishida, N. (1965). Respiratory syncytial virus and its serologic epidemiology. *American Journal of Epidemiology* 82, 211.