
SHORT REPORT

Humoral immunity to respiratory syncytial virus in young and elderly adults

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SUMMARY

Respiratory syncytial virus (RSV) has been demonstrated to cause substantial disease in elderly and immunocompromised subjects. The relationship of serum antibody to RSV infection and the risk of infection in elderly subjects is controversial, thus we evaluated the presence of neutralizing antibodies to RSV in healthy people of different age groups and the correlation with viral protection. Baseline blood samples from 197 subjects aged 20–80 years were analysed for the presence of anti-RSV antibodies either by indirect immunofluorescence and microneutralization test. The percentage of people who had neutralizing antibodies to RSV was significantly higher ($P=0\cdot001$) in the youngest group (92·51%) compared to the frail group (36·21%). The RSV antibody level tends to wane in some older people; this factor could determine proneness to RSV re-infections in the elderly who are at a greater risk of developing severe respiratory disease.

Key words: Antibodies, elderly, RSV, young.

Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis and pneumonia in children aged <1 year [1–3]. RSV also causes repeated infections, including severe lower respiratory tract disease, throughout life and in the elderly or those with compromised immune systems [4]. A better understanding of the immune mechanisms offering protection against RSV infection and the correlation between the presence of specific antibodies and protection could be useful for the development of a vaccine. Previous studies [5] have shown that humoral responses were intact in elderly persons and suggested that severe clinical manifestations of RSV infections in elderly people could not be explained by a defect in antibody. At

present, serum-neutralizing titres correlate with the status of protection from primary infection in children and young adults; however, few published data are available on immunity in the elderly [6, 7].

It is important to understand the correlates of immunity in order to monitor adult populations and identify the individuals at risk for RSV infection. In this study, we tested the humoral response to RSV in different adult age groups and have shown that older and frail elderly adults have a lower neutralizing antibody titre than young adults, which declines with age.

A total of 197 subjects recruited from the local hospital were enrolled in this study; informed consent was obtained from participants. None was hospitalized for respiratory tract infections. They were divided into four groups on the basis of age. The first group consisted of individuals aged 20–60 years, the second of older people aged 61–70 years, the third of subjects aged 71–80 years and the fourth of frail adults aged

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Table 1. *Baseline respiratory syncytial virus (group A) humoral immunity in a human population*

Age (yr)	Total	IFA Pos/Neg*	MNA Positive*	MNA Negative	MNA mean titre \pm s.d.
20–60 (42·55)	40	38/2 (95)	37 (92·5)	3	4·65 \pm 1·15
61–70 (65·78)	45	40/5 (88·8)	25 (55·5)	20	4·36 \pm 1·13
71–80 (74·32)	54	49/5 (90·7)	28 (51·8)	26	3·97 \pm 1·01
>80 (83·70)	58	50/8 (86·2)	21 (36·2)	37	3·63 \pm 0·91

IFA, Immunofluorescence assay; MNA, microneutralization assay.

* Values in parentheses are percentage of positive subjects.

>80 years. Subjects with chronic infections or inflammatory diseases and those using immunosuppressive drugs were excluded. Serum samples were analysed for anti-RSV antibodies by indirect immunofluorescence (IFA) and microneutralization assay (MNA).

The mean differences were statistically analysed using StatView statistical software (Abacus Concepts, USA). Multiple comparisons were made using one-way analysis of variance (ANOVA). Means between groups were compared by *t* test. A probability (*P*) value of <0·05 was considered statistically significant.

One hundred and ninety-seven subjects, aged 20 to >80 years, unaffected by respiratory tract infections were enrolled during the winter/spring season of 2008 for serological studies on the humoral response to RSV. A baseline RSV humoral response analysis was performed *vs.* RSV type A in order to evaluate, in general, the role of specific antibody immunity in adults. The IFA showed that specific antibodies may wane with age, in contrast to previously published data [5]. In fact, as shown in Table 1, the percentage of individuals who are seronegative to RSV is significantly higher ($P=0\cdot001$) in the frail group (13·79%) and, in general, in adults aged >60 years, compared to the youngest group (5%). This data was more evident when the sera were assayed with MNA. The percentage of subjects with neutralizing activity is highest in the young group (92·5%) but tends to decrease in the other groups (Table 1). It is worth noting that the presence of specific antibodies does not correlate with the neutralizing activity. In fact, in the frail group, 86·2% tested positive for anti-RSV antibodies, but only 36·2% had neutralizing antibodies. Moreover, the mean MNA titre also decreased with age, being twofold lower in the frail group compared to the youngest group ($3\cdot63 \pm 0\cdot91$ *vs.* $4\cdot65 \pm 1\cdot15$). The

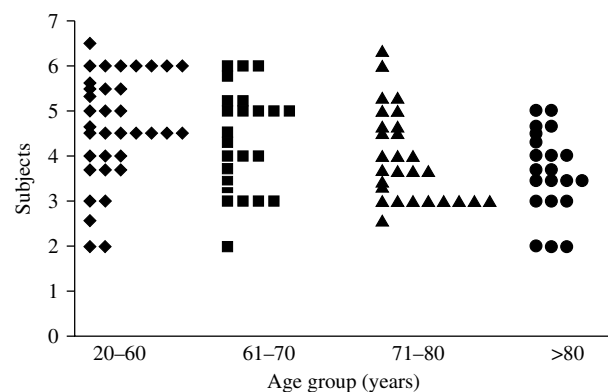


Fig. 1. Distribution of individual neutralization titres to respiratory syncytial virus in four groups of volunteers.

distribution of individual neutralization titres to RSV in the four age groups shows that subjects in the first two groups (20–60 years) have a similar pattern of distribution with some heterogeneity, while the remaining subjects, including people aged >70, have lower titres and, therefore, an increased risk of RSV infection ($P=0\cdot001$) (Fig. 1). This study analysed the baseline humoral response to RSV in subjects of different ages and has shown that the neutralizing antibody level is quite low or absent in elderly subjects, in spite of the presence of specific antibodies. Consequently, it seems very important to test the neutralizing antibody titres in patients in order to evaluate their potential protective level against RSV.

These findings suggest that elderly adults with low serum neutralizing titres to RSV may be more likely to develop symptomatic RSV infection than elderly subjects with higher titres. Although controversial, some data suggest that circulating neutralizing antibodies to RSV are beneficial, that antibody titres

directly correlate with protection [8] and that IgG prophylaxis for RSV infections may ameliorate severe infection [9]. In previous studies, a trend towards low neutralization titres and more severe disease was noted in elderly subjects [6]. In this study, the RSV antibody level, particularly neutralizing antibodies, waned in some older people; this could be due to immunosenescence or the lack of recent exposition to the virus, but this factor could determine the proneness to RSV re-infections in elderly subjects. Since infection can and does occur in the presence of circulating antibodies, the RSV-specific T-cell response plays a major role in the clearance of the virus and in the clinical outcome of RSV infection [10]; however, a balanced immune response, including RSV-specific neutralizing antibodies, are necessary for maintaining protective immunity in the host. Further studies of the RSV immune response and its epidemiology are required in order to develop a safe RSV vaccine that would be efficacious in boosting the immune response in the elderly population.

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DECLARATION OF INTEREST

None.

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