Antibodies to Respiratory Syncytial Virus Polypeptides and their Significance in Human Infection

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SUMMARY

The human antibody response to respiratory syncytial (RS) virus infection was investigated using radioimmunoprecipitation analysis (RIPA). A total of nine RS virus-specific proteins, VP200, VGP95, VP68, VGP48, VPN41, VP35, VP27, VP23 and VGP20 were identified by comparing 35S- or 3H-labelled extracts of infected and uninfected HEp-2 cells, and by radioimmunoprecipitation using a hyperimmune human serum. Three glycopeptides, VGP95, VGP48 and VGP20, were identified by incorporation of [3H]glucosamine, and two of these (VGP48 and VGP20) were assumed to be part of a single disulphide-bonded polypeptide since they were precipitated by a monoclonal antibody raised against a surface protein. Human serum antibodies to three major RS virus proteins, VGP95, VGP48/VGP20 and VPN41 were measured by RIPA using radioiodinated RS virus antigens. Sera from a group of mothers whose babies escaped RS virus infection during a local epidemic showed increased antibody levels to VPN41 when compared to sera from mothers whose babies had become infected with RS virus within the first 6 months of life. In infants who remained uninfected with RS virus during the first 12 months of life the maternal gift of antibody decayed to about 50% at 3 months with traces of antibodies detected in a few sera at 12 months. The antibody levels detected in the sera of infants less than 3 months old convalescent from primary RS virus infection did not exceed the mean levels present in the serum of uninfected babies. Infants between the ages of 6 and 12 months were able to mount an IgG response to VPN41 and VGP48 but, unlike adults and older children, a particularly striking finding was their failure to produce antibodies to VGP95.

INTRODUCTION

Respiratory syncytial (RS) virus inevitably infects all infants, with 1 of every 50 babies born in urban areas becoming sufficiently ill with bronchiolitis or pneumonia to require hospital treatment (Sims et al., 1976). The peak prevalence of severe infection lies between the ages of 6 weeks and 5 months (Gardner, 1973; Parrott et al., 1973), suggesting that maternal IgG persisting in the babies' blood confers little or no protection and perhaps even contributes to disease by interaction with RS virus antigen in the lung (Chanock et al., 1970). A pathological role for immune complex formation is supported by the finding that older children with high levels of circulating antibody induced by immunization with inactivated RS virus developed more severe disease than their unvaccinated counterparts when naturally infected with RS virus (Kim et al., 1969). Nevertheless, a protective role for maternal IgG is implied by the facts that RS virus infections of the lung are rare during the first 4 weeks of life (Neligan et al., 1970) and that babies born to mothers with high levels of antibody reactive in the membrane fluorescence test were protected for several months (Ogilvie et al., 1981). Such anomalies can be explained if antibodies to the RS virion surface or the infected cell membrane protect against infection, whereas antibody to other virus components fails to protect and may even lead to immune complex reactions.
Recent studies have shown that the RS virus genome codes for at least seven polypeptides (Huang & Wertz, 1982) with two major glycoproteins expressed at the virus surface (Pringle et al., 1981; Bernstein & Hruska, 1981; Fernie & Gerin, 1982). We have used radioimmunoprecipitation techniques to quantify IgG antibodies to the immunodominant surface glycopeptides and major capsid protein, comparing the maternal gift of antibodies in protected and susceptible babies, the rate of antibody decay and the antibody response to primary RS virus infection in babies.

METHODS

Cells. HEp-2 cells were grown in Dulbecco’s minimal essential medium (MEM) supplemented with 10% (v/v) foetal calf serum (FCS, Flow Laboratories) at 37 °C in 5% (v/v) CO₂.

Growth of virus and preparation of nucleocapsids. The virus strain was a local epidemic strain isolated in 1977 (Ogilvie et al., 1981). Virus-infected cells were maintained in Dulbecco’s MEM supplemented with 1% FCS. For the preparation of nucleocapsids, monolayers in 2.5 litre roller bottles were infected with RS virus at a multiplicity of infection (m.o.i.) of 10. Cells were harvested 40 h post-infection by treating each roller bottle with 20 ml 10 mM-Tris–HCl pH 7-4 containing 0-18 mM-NaCl, 0-25 mM-EDTA and 0-1 mM-phenylmethylsulphonyl fluoride (PMSF) for 15 min at 37 °C. Detached cells were collected by centrifugation at 5000 g for 15 min and resuspended to 10⁶ cells/ml in lysis buffer [10 mM-Tris–HCl pH 7-4, 0-1 mM-EDTA, 0-1 mM-PMSF, 0-5% (v/v) Nonidet P40 (NP40)] at 4 °C. After 20 min at 4 °C, cells were ruptured with a Dounce homogenizer, NaCl added to 0-1 M and the intact cells and cell nuclei removed by centrifugation at 600 g for 2 min. Nucleocapsids were pelleted by centrifugation at 10 000 g for 30 min and washed once in lysis buffer followed by a further wash in 10 mM-Tris–HCl, 0-1 mM-EDTA pH 7-4 (TE buffer). Nucleocapsids were purified from the crude pellet by isopycnic centrifugation on a 15 to 55% (w/w) potassium tartrate gradient in TE buffer at 100 000 g for 16 h.

Radioiodination of viral proteins with 35S or 3H. Subconfluent monolayers of HEp-2 cells in Costar 6-well trays were infected with RS virus at a m.o.i. of 10 p.f.u./cell. After an adsorption period of 6 h the medium was replaced and, following a further 18 h incubation, actinomycin D (Sigma) was added to 2-5 μg/ml and the cells were incubated for a further 2 h. For labelling proteins with 35S, the medium was replaced with fresh medium containing actinomycin D and one-tenth the normal concentration of methionine and cysteine. L-[35S]Methionine (50 μCi/ml; 1230 Ci/mmol) and L-[35S]Cysteine (25 μCi/ml; 990 Ci/mmol) (Amersham International) were added and the cells were incubated for a further 16 h until the cytopathic effect (c.p.e.) was extensive. Glycoproteins were labelled by incubating infected cells with D-[1-3H]Glucosamine (50 μCi/ml; 4-1 Ci/mmol) in Eagle’s MEM (Flow Laboratories) containing 2-5 μg/ml actinomycin D until c.p.e. was extensive. Labelled cells were washed in phosphate-buffered saline (PBS; Oxoid) and solubilized for 2 h at 37 °C in 10 mM-Tris–HCl pH 7-4 containing 0-1 mM-EDTA, 0-1 mM-PMSF, 0-5% (v/v) NP40 and 10% (w/v) sodium cholate. Insoluble cell debris was removed by centrifugation at 100 000 g for 25 min (Airfuge, Beckman Instruments).

Radioiodination of RS virus proteins. Subconfluent monolayers in 75 cm² flasks were infected with RS virus (m.o.i. of 10) and incubated for 40 h until c.p.e. was extensive. Cells were detached and washed in PBS containing 0-1 mM-PMSF and resuspended in 1 ml PBS. Cells were iodinated by the lactoperoxidase method (Marchalonis et al., 1971) using 1 μCi Na125I (15 μCi/μg; Amersham International). The reaction was stopped by washing the cells in serum-free tissue culture medium containing 2-5% cysteine. Cell membranes were solubilized for radioimmunoprecipitation assay (RIPA) in 10 mM-Tris–HCl pH 7-4, 0-1 mM-EDTA, 0-1 mM-PMSF, 0-5% (v/v) NP40 at room temperature for 2 h. Insoluble material was removed by centrifugation at 100 000 g for 1 h.

Partially purified RS virus nucleocapsids were radioiodinated using the chloramine-T method (Greenwood et al., 1963). Nucleocapsids (5 mg protein) were mixed with 1 μCi Na125I in TE buffer. Chloramine-T (100 μg) was added and after 5 min the reaction was terminated by the addition of 2-5 mg sodium metabisulphite and 5 mg carrier potassium iodide. Unreacted iodide was removed by dialysis against TE buffer. Radioiodinated nucleocapsids were solubilized for RIPA in 1% (w/v) sodium cholate at 37 °C for 2 h followed by centrifugation at 100 000 g for 1 h.

SDS–polyacrylamide gel electrophoresis (SDS–PAGE). Proteins were separated by SDS–PAGE using the discontinuous buffer system of Laemmli (1970) as described by Heckels (1981). The separating gel (16 cm × 12 cm × 0-75 mm) comprised a linear gradient (10%, w/v to 25%, w/v) of acrylamide containing a constant proportion (2-5%, w/w) of methylene bisacrylamide. Gels were run at a constant 200 V for 20 h at 4 °C. Samples for electrophoresis were mixed with an equal volume of dissociating buffer [0-25 mM-Tris–HCl pH 6-8, 4%, SDS, 20% (v/v) glycerol, 10% (v/v) 2-mercaptoethanol, 0-002% bromophenol blue], and heated at 100 °C for 5 min. Gels were fixed and stained as previously described (Fairbanks et al., 1971). Molecular weight marker proteins (Sigma) were: myosin, 205K; β-galactosidase, 130K; phosphorylase b, 98K; catalase, 58K; actin, 42-3K; DNase I, 31K; trypsinogen, 24K; myoglobin, 17-2K.

autoradiography and fluorography. Gels with radioiodinated proteins were dried and exposed to Kodak XAR-5 autoradiography film with an intensifying screen at -70 °C.
For fluorography, destained gels were soaked in APEX (Jen & Thach, 1982), which contains 55% acetic acid, 1% (w/v) PPO, 15% ethanol and 30% xylene, for 1 h. Gels were rinsed in water, dried and exposed to pre-flashed Kodak XAR-5 film at -70 °C.

**Radioimmunoprecipitation assay (RIPA).** Radiolabelled antigen samples were diluted in RIPA buffer: 10 mM-Tris–HCl pH 7.4, 0.15 M-NaCl, 0.1 mM-EDTA, 0.5% (w/v) Empigen BB (Albright & Wilson Ltd., Whitehaven, U.K.), 0.1% SDS. Antigen samples containing approximately $10^5$ ct/min were mixed with 10 μl of serum in a total vol. of 200 μl. Protein A–Sepharose beads (Sigma) [50 μl 10% (w/v) suspension in PBS] were then added and the mixture incubated at 4 °C for 4 h. The solid-phase Protein A immune complexes were washed extensively in RIPA buffer, resuspended in dissociating buffer and analysed by SDS-PAGE. The amount of specific radiiodinated antigen precipitated was determined by excising the band from the dried gel and γ-counting. The quantification of the antibody response was reproducible; one serum tested on ten occasions gave a mean count of 435 ct/min with a standard deviation of 18.5 ct/min for the 41K band. The counts were corrected for background by subtracting values obtained by excising portions of the gel track between the viral bands. Corrected values falling within 2 standard deviations of the background were taken to be equal to background. The counts immunoprecipitated by a high titre serum diluted over a 1000-fold range were determined for triplicate samples. Plots of the logarithm of counts against serum dilution revealed a linear relationship for the surface glycoproteins and nucleocapsid antigens. The RIPA antigen was assumed to be in excess since hyperimmune human serum precipitated at least tenfold more antigen than the maternal and infant sera used in the study.

Fig. 1. SDS–PAGE showing RS virus protein synthesis in HEp-2 cells labelled with $[^35S]$methionine plus $[^35S]$cysteine. Lane V, virus-infected cells; lane C, mock-infected control cells.

Fig. 2. RIPA and SDS–PAGE of RS virus polypeptides from extracts of infected HEp-2 cells using 1 μl of a human RS virus pneumonia hyperimmune serum. (a) Cells labelled with $[^35S]$methionine plus $[^35S]$cysteine; (b) cells labelled with $[^3H]$glucosamine. Lanes V, RS virus-infected cells; lanes C, mock-infected control cells. Bands arrowed represent polypeptides which were consistently revealed during repeat analyses.
Sera. The human sera used were collected during local RS virus epidemics (Ogilvie et al., 1981). Proof of infection was by direct isolation of RS virus from nasopharyngeal secretion and by a membrane fluorescence test.

Monoclonal antibodies. BALB/c mice were immunized intraperitoneally (i.p.) with $10^7$ RS virus-infected HEp-2 cells and boosted i.p. on day 10. The murine myeloma cell line BALB/c NS1/1 (NS-1) was cultured in TCM [RPMI 1640 medium (Flow Laboratories), buffered with sodium bicarbonate, containing 15 µg penicillin/ml, 15 µg gentamicin/ml, 1 mM-sodium pyruvate, 2 mM-L-glutamine and 15% (v/v) foetal calf serum]. Incubations were at 37 °C in a humidified incubator in an atmosphere of 5% (v/v) CO$_2$ in air. Cell suspensions were prepared from the spleens of immunized animals in TCM and were fused with NS-1 cells using 50% (w/v) polyethylene glycol 4000 (Merck) containing 5% (v/v) dimethyl sulfoxide as the fusing agent (Fazekas de St. Groth & Scheidegger, 1980). Spleen cells ($3 \times 10^7$) and NS-1 myeloma cells ($3 \times 10^7$) were mixed together and centrifuged at 200 g for 10 min. The pellet was equilibrated at 37 °C for 1 min and then 1 ml 50% polyethylene glycol was added slowly. The mixture was further incubated for 90 s at 37 °C when fusion was stopped by the slow addition of 20 ml TCM. Cells were centrifuged, washed once with TCM and were distributed in flat-bottomed 96-well microtitre plates (Costar) at $2 \times 10^5$ cells/well in HAT medium (TCM plus 100 µM-hypoxanthine, 16 µM-thymidine, 0.4 µM-aminopterin). All incubations were done in the presence of macrophage feeder layers prepared the day before the fusion. Each well contained 0.5 - 1 x $10^4$ peritoneal macrophages from normal mice. After 6 days, 50 µl of fresh HAT medium was added to each of the wells. At 9 to 12 days after the fusion, culture supernatants were tested for antibody activity by ELISA using RS virus antigen to determine the specificities of the secreted antibodies. Hybrids that produced the required antibody were cloned by limiting dilution in 96-well trays with macrophage or spleen cells as feeder layers. They were considered to produce monoclonal antibody only when the reactivity against VGP48 antigen remained the same upon further cloning. The procedure was repeated and hybrids were considered stable when 95% of the progeny clones produced the antibody. These stable clones did not require further cloning for the maximum time employed: 8 weeks growth in culture.

(a) (b)

Fig. 3. RIPA and SDS–PAGE of RS virus polypeptides from extracts of infected HEp-2 cells using an ascitic fluid containing a monoclonal antibody to VGP48. Infected cells were labelled with [35S]methionine plus [35S]cysteine. (a) Sample derivatized for SDS–PAGE in the presence of 2-mercaptoethanol; (b) sample derivatized for SDS–PAGE in the absence of 2-mercaptoethanol.
RESULTS

Identification of RS virus-specific proteins

RS virus-specific polypeptides were characterized by labelling infected HEp-2 cells with \([^{35}\text{S}]\)methionine and RS virus-specific glycoproteins by labelling with \([^{3}\text{H}]\)glucosamine. Three RS virus-specific proteins (Mr, 41K, 27K and 23K) were identified by comparing extracts of infected and uninfected cells on SDS–polyacrylamide gels (Fig. 1). A further six proteins were identified by a RIPA using a convalescent serum from a 5-year-old boy with RS virus pneumonia (Fig. 2). HEp-2 cells infected with RS virus and labelled with \([^{35}\text{S}]\)methionine revealed nine RS virus-specific proteins with Mr, 200K, 95K, 68K, 48K, 41K, 35K, 27K, 23K and 20K. Three of these polypeptides (VGP95, VGP48 and VGP20) were shown to be glycoproteins by their incorporation of \([^{3}\text{H}]\)glucosamine. Two of the glycoproteins (VGP48 and VGP20) plus VP23 were immunoprecipitated by a monoclonal antibody (Fig. 3). Evidence that VGP48, VP23 and VGP20 were components of a single RS virus protein was shown by demonstrating that when the monoclonal RIPA was derivatized and separated by SDS–PAGE under non-reducing conditions a single diffuse band of Mr, 75K was revealed (Fig. 3). The exact relationship between the VGP48, VP23 and VGP20 is unknown at present, although the behaviour on SDS–PAGE suggests that the polypeptides are held together by disulphide bonds, as is the case for the 'fusion proteins' of paramyxoviruses (Fernie & Gerin, 1982; Gruber & Levine, 1983).
Fig. 5. Maternal serum antibody levels to (a) VGP95, (b) VGP48 and (c) VPN41. Relative antibody levels were determined by RIPA of 125I-labelled antigen. Antigen bands were located by autoradiography, excised and γ-counted. A (●), sera from 15 women whose children were not infected by RS virus although exposed to a local epidemic. B (○), sera from 11 women whose children subsequently developed RS virus infection before the age of 6 months. The horizontal bars represent mean antibody levels.

Fig. 6. Time course of antibody decay in sera from 10 infants (including twins) who remained uninfected with RS virus during the first year of life (sera were available from only 8 infants when aged 1 year). Relative antibody levels to (a) VGP95, (b) VGP48 and (c) VPN41 were determined by RIPA of 125I-labelled antigen. Antigen bands were located by autoradiography, excised and γ-counted. M, Maternal serum antibody levels at birth. Horizontal bars represent mean antibody levels.

Detection of antibodies to RS virus in normal adult sera

In order to detect levels of anti-RS virus antibodies in normal human sera the sensitivity of the RIPA was increased by radiolabelling RS virus antigens with 125I. Partially purified nucleocapsids were radioiodinated using chloramine-T and RS virus glycoproteins were labelled by surface-iodinating intact HEp-2 cells 40 h post-infection, using hydrogen peroxide and lactoperoxidase. The results in Fig. 4 show that antibodies to five RS virus polypeptides could be
detected in a range of normal adult female sera; in particular, there were relatively high antibody levels to the 41K capsid protein (VPN41) and the two glycoproteins VGP95 and VGP48. In two sera (1 and 3, Fig. 4), antibodies to VP68 were detected.

A comparison was made of counts immunoprecipitated by the serum of 11 mothers whose infants had become infected with RS virus before the age of 6 months and 15 mothers whose babies had escaped infection during an epidemic period (Fig. 5). Sera were obtained from the women at or just before delivery of their babies, and the antibody levels to VGP95, VGP48 and VPN41 were determined by $^{125}$I-RIPA. Bands on SDS–polyacrylamide gels were located by autoradiography, excised and counted in a $\gamma$-counter. Sera from mothers whose babies did not become infected with RS virus, although exposed to a local epidemic, showed a significantly increased level of anti-capsid antibody ($P < 0.02$ by Student's $t$-test).

**Decay of maternal antibody in infants**

A number of mothers and their infants were followed in a 12 month trial to determine the decay of maternal anti-RS virus antibodies in infants. Blood samples were taken from each child at 3, 6 and 12 months after birth and a sample was taken from the mother at or just before delivery of the child. A group that remained uninfected with RS virus was used for measurement of antibody levels (Fig. 6). It can be seen from the figure that the counts immunoprecipitated by placently transferred antibodies to the two glycoproteins and the major capsid protein were reduced to about 50% after 3 months and were almost undetectable by 12 months.

**Antibody response to primary RS virus infection in infancy**

Convalescent sera from RS virus-infected infants were examined by RIPA (Fig. 7). Antibodies to VPN41 and VGP48/VGP20 were detected in all samples and, as with adults,
Fig. 8. Serum antibody levels (○) in infants of various ages under 12 months recovering from primary RS virus infection. Relative antibody levels to (a) VGP95, (b) VGP48 and (c) VPN41 determined by RIPA of 125I-labelled antigen. Antigen bands were located by autoradiography, excised and γ-counted. The decay curve for the maternal gift of antibody (●) is taken from Fig. 6 and shown superimposed on the data. M, Maternal serum antibody levels at birth.

some infant sera contained antibodies to VP68. Only traces of antibodies reactive with VGP95 could be detected. Quantification of the antibody response to VPN41, VGP95 and VGP48 is shown plotted against patient age (Fig. 8) with the mean antibody levels in uninfected infants (solid line, Fig. 8) superimposed on the data for infected babies. During the first 3 months of life, antibody levels in convalescent sera were essentially those of the maternal gift whereas over this age an immune response to both VPN41 and VGP48 was seen. The striking feature of these data was the apparent failure of infected infants to respond to VGP95.

DISCUSSION

The action of antibodies on cells infected with viruses has been the subject of a recent review (Sissons & Oldstone, 1980). Cells expressing viral antigens at their surface may be destroyed by IgG antibody plus complement activated either via the classical or alternative pathways. Furthermore, antibody alone modulates virus antigen expression leading to incomplete replication cycles. That such mechanisms are operative at the onset of RS virus infections is compatible with the finding that babies escaping symptomatic RS virus infection in early life possess significantly greater titres of maternally derived IgG reactive with the membrane of RS virus-infected cells (Ogilvie et al., 1981). Using the radioimmunoprecipitation technique we have demonstrated antibodies reactive with cell-associated RS virus antigens, VP200, VGP95, VP68, VGP48, VPN41, VP35, VP27, VP23 and VGP20, in the serum of a child convalescent from viral pneumonia. In the revised nomenclature of Pringle and his colleagues (1981) these proteins may correspond to VP200, GP1 (VGP95 in this study), VGP48, VPN41, VPP32 (VP35 in this study), VPM27 and VP25 (VP23 or VGP20 in this study). A protein corresponding to
VP10 was not detected in this study. Antibodies reactive with the polypeptide VP68 were detected in several sera. Although this protein was not recorded by Pringle et al. (1981), a protein of similar molecular weight has been described by other workers and shown to be immunoprecipitated by horse anti-RS virus serum (Dubovi, 1982). Fernie & Gerin (1982) have suggested that a protein of $M$, 66K was the disulphide-linked unreduced precursor of VP43 and VP19. There was no obvious association between human antibodies reactive with VP68 and the immunoprecipitation of other RS virus polypeptides, nor did a monoclonal antibody to VGP48 react with VP68. Thus, there was no evidence to suggest that VP68 shared antigenic determinants with any other RS virus polypeptides as might be the case if this were a precursor protein. VP27 was shown to be a dominant protein in RS virus-infected cells but it was poorly immunogenic for man since specific antibodies were absent from all normal adult sera and only traces were detected in a hyperimmune human serum. Of the two RS virus glycoproteins, VGP95 was shown to be a relatively poor immunogen while VGP48 and VGP20 co-precipitated, together with an additional non-glycosylated protein VP23, with a monoclonal antibody and were found to run as a single band ($M$, 75K) under non-reducing conditions.

In order to detect the traces of RS virus-specific maternal IgG present in the serum of older babies it was necessary to enhance the sensitivity of the RIPA using $^{125}$I-labelled virus polypeptides. Furthermore, $\gamma$-counting of the excised bands allowed for easy quantification of the specific antibodies reactive with the immunodominant RS virus polypeptides. The hypothesis that maternally derived IgG can protect babies from RS virus infection was tested by comparing sera from mothers of infected babies and mothers whose babies remained uninfected during a winter epidemic. Only low levels of antibody to VGP95 were detected and there was no difference between infected and protected groups. Considerable variation was found in maternal antibody levels to VPN41, with significantly higher levels in protected babies. Although 9 out of 15 protected babies had antibody levels to VGP48 above the mean value for infected babies this difference was not statistically significant. In interpreting these data it is important to appreciate that the ‘protected group’ must include an unknown proportion of babies susceptible to infection but who escaped exposure to RS virus during the trial period. Nevertheless, comparable results were reported by Glezen et al. (1981) who showed that babies born to mothers with higher levels of neutralizing antibody for RS virus developed infection at a later age and had milder illness than infants receiving low or undetected levels of antibody. Repeated infections of decreasing severity are a feature of RS virus infections in childhood. In this context it was notable that convalescent sera from babies admitted to hospital with severe RS virus infection showed no increase in antibodies to VGP95. Further work is required to establish whether antibodies to VGP95 are directed to the carbohydrate or polypeptide moieties of the molecule. This is of interest because antibodies to sugar polymers such as bacterial capsules are of IgG-2 and IgG-4 subclasses and the ability to mount IgG-2 and IgG-4 responses is particularly poor in infancy (Pabst & Kreth, 1980).

Attempts to control RS virus infection by protecting older infants using attenuated vaccine given parenterally were unsuccessful (Belshe et al., 1982), while susceptible young children could not be uniformly infected with a large dose of highly attenuated vaccine given intranasally (Wright et al., 1982). Killed virus vaccine led to cases of exacerbated disease on exposure to natural infection. Immunization of the 2 to 6 months age group at risk is unlikely to be successful since our data show a failure to produce antibody to all RSV polypeptides in response to natural infection. This is compatible with earlier findings of a poor antibody response in this age group (Richardson et al., 1978; Welliver et al., 1980). The feasibility of preventing RS virus infections in the critical 2- to 6-month-old babies by boosting the maternal gift of protective antibodies must now be considered. The key to vaccine development must be to define immunity in protected babies in terms of the maternally derived IgG antibodies in serum and secretory IgA antibodies in breast milk reactive with RS virus polypeptides. Although the present paper examines the specificity of the maternal IgG antibodies present in the serum of these babies, extensive work is required to confirm their role in immunity. This must include knowledge of the IgG subclasses involved and whether antibodies reactive with distinct epitopes on the same RS virus polypeptide differ in their ability to block infection.
REFERENCES


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