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# Prevention of nosocomial spread of respiratory syncytial virus infection in infants and children: a review

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## Introduction

Nosocomial outbreaks of respiratory syncytial virus (RSV) in neonatal intensive care units (NICU) can be particularly severe, with unexpected clinical manifestations and high mortality. The current literature proposes that this is due to increased susceptibility of young infants, easy transmission of RSV and its high virulence. Infants with RSV infection commonly present with fever, dyspnoea, rhinitis and cough. In premature neonates, however, RSV infection is frequently atypical and manifests as nonspecific symptoms such as apnoea, conjunctivitis, vomiting, diarrhoea, poor feeding, lethargy and irritability.[1,2] Reports of infants under the age of 2 years who contacted RSV, estimated that 20-45% acquired the infection and inevitably developed acute respiratory disease.[1,3,4] About one third of neonates with nosocomial RSV infection developed pneumonia and hospitalization was prolonged to a mean of 21.5 days, as compared to 9.2 days in uninfected contacts.[3] Kilani reported that during one particular RSV outbreak in an NICU, eight preterm infants <30 weeks gestational age were infected with RSV, whereas 12 other infants of >30 weeks gestational age were not. Four of the infected infants required aggressive ventilator support, and two of them developed acute respiratory distress syndrome which resulted in one death.[5] A similar observation was also recently reported by Abadesso who showed infants below 32 week gestational age had 4.65 times higher risk of becoming seriously ill than those above 32 weeks of gestation.[6] Cross-infection in pediatric wards is a common problem as infected infants can shed large amounts of virus in their respiratory secretions for around 7 days and up to 21 days. Hall et al. documented that during a community outbreak, 56% of health care workers became infected with RSV. Upper respiratory tract symptoms occurred in 86% of those infected personnel leading to 46% being absent from work. The staff were found to shed the virus for an average of 3 days and up to 11 days.[4]

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## Mode of transmission

In a sequence of articles by Hall in the early 1980's, the various possible modes of transmission of RSV in a hospital ward were carefully studied. Fresh secretions from infants admitted with RSV bronchiolitis or pneumonia were allowed to contaminate a variety of surfaces around their bed. These surfaces were then sampled to determine the amount of virus present at specific intervals. Survival of RSV was found to be longest on gloves and countertops, at 2 and 7 hours, respectively. However, viability was diminished to an average of 1 hour on cloth, skin and tissue paper. Subsequent to contact with contaminated paper, facial tissue or hands, RSV could still be recovered from the skin after an average of 3 and up to 10 minutes. Hands that touched RSV-contaminated countertops had infectious virus for an average of 20 to 25 minutes. These experiments showed that contaminated nonporous surfaces such as countertops, glass and rubber gloves allowed RSV to survive for many hours, and they were significant medium for transmission.[7] From the above results, Hall et al. then proposed three possible routes of RSV transmission: 1) by close contact with direct inoculation of large infected particles or droplets; 2) by self-inoculation after touching contaminated surfaces (formites); and 3) by aerosols containing particles small enough (<10 microns) to travel distances of 6 feet or more. The transmission routes were tested by exposing 3 groups of adult volunteers to infants infected with RSV in a hospital ward. The first group, "cuddlers", cared for the babies in the usual manner, which included feeding, bathing, and playing with infants. They wore gowns but no masks or gloves. The second group, "touchers", were exposed only to surfaces contaminated with baby's secretions and then proceeded to touch the mucous membranes of their eyes and nose. The third group, "sitters", were exposed to infected babies by sitting more than 6 feet from the infant's bed. They wore gowns and gloves but no masks, and were allowed to read while touching nothing else for 3 hours. Thus, the "cuddlers" were potentially exposed to all three routes of transmission, whereas "touchers" only by means of fomites and self-inoculation, and

"sitters" only by small-particle aerosols. Infections were then found to occur in the cuddlers and touchers, but not in the "sitters", thereby suggesting that RSV is spread via the first two modes of transmission.[8]

## Control measures

During a community outbreak in winter of 1976, infants with proven RSV infection were admitted to a new hospital facility in Rochester to study control measures limiting nosocomial spread of the virus. The hospital contained separate wards each consisting of 9 rooms that had an individual bathroom and a sink near the entrance. Within each room, one to three cribs were then arranged radially around the central nursing station. The staff were advised to adhere to the following preventative procedures: 1) isolation of infected infants; 2) handwashing with a povidone compound when entering or leaving the room, and between contact with different infants in the same room; 3) use of gowns in all rooms containing infants with respiratory illness, and to change gowns between contact with different infants in the same room; 4) cohorting of staff to infants; 5) isolation of high-risk infants; and 6) limitation of visitors. In this two-month study period, thirty-six infants were admitted with RSV respiratory tract infection. Another 87 infants were admitted with unrelated illnesses and they were assumed potentially susceptible to nosocomial RSV infection. Forty-two infants were hospitalised for more than seven days. These infants were the "contacts" according to the study definition. Eight (19%) of the 42 contact infants became infected with RSV during their hospital stay as compared to 45% infants in previous study. The rate of acquisition of RSV infection in hospital personnel was 56%.[3,4]

**Masks** were found to have little benefit in controlling the nocosomial spread of RSV infection to infants or to ward personnel.[9] This was because the RSV portal for infection was via the eyes and nose, but not the mouth. Self-inoculation from contaminated hands might still occur by touching the eyes, but this can be prevented by the use of **eye-nose goggles**. Gala et al. showed that eye-nose goggles significantly decreased nosocomial RSV infections from 43% to 6% in contact infants ($p<0.05$), and 34% to 5% in staff ($p<0.003$).[10]

Recommendations about the use of **gowns** varied between studies. Hall was unable to show any significant benefit for their use.[9] In contrast, LeClair demonstrated that the increased use (from 39% to 81%) of gloves and gowns when in direct contact with RSV reduced nosocomial infections from 6.4 to 3.1 cases per 1000 days at risk.[11] Furthermore, Madge et al. conducted a prospective controlled study on four infection control procedures, namely 1) no special precautions; 2) gowns and gloves; 3) cohorting nursing; and 4) cohorting nursing and gowns with gloves. Without special precautions the nocosomial RSV infection rate was found to be 26%. Combined cohort nursing and the wearing of gowns and gloves reduced the rate to 10%. The other two procedures alone did not reduce cross-infection significantly.[12] **Hand-washing** was another important way of controlling nosocomial infections. Isaacs evaluated the efficacy of hand-washing by placing alcohol-based hand rubs on each sink and instructing the staff on the importance of handwashing. A leaflet encouraging parents to wash their hands and to keep older siblings with common colds away from the play area was then prepared, and given to the parents of every child admitted with infection. Afterwards, children with proven RSV infection (by indirect immunofluorescence stain of nasopharyngeal secretions) were also cohorted to a six-bed area. After these interventions, the hospital acquired RSV infection rate in children <2 years old was reduced from 4.2% to 0.6%. Moreover in children <2 years old with congenital heart disease, the rate of RSV nosocomial infection was decreased from 34.8% to 3.3%.[13] Similarly, nosocomial RSV infection was minimized by sending nasopharyngeal aspirates for **rapid diagnostic testing**, followed by **cohorting** the RSV positive infants into a designated area.[14]

Although no controlled studies are yet available to support the use of palivizumab for outbreak control, it has been published in the literature for use to control RSV outbreaks in special care baby units (SCBU) and neonatal intensive care units (NICU). During one reported outbreak of RSV infection affecting seven premature infants in a SCBU, eight other babies with extreme prematurity or whom were at risk of severe lung disease if they contacted RSV were given palivizumab (15 mg/kg) by intramuscular injection and a second dose four weeks later. No further injections were then offered because the RSV season had ended. There were no further cases of RSV in the unit and none of the babies given palivizumab developed RSV. The total cost of two doses of palivizumab for the eight babies were £800.15

In February 1999, a RSV outbreak occurred in the NICU of a hospital in Portugal consisting of three index cases. Standard infection control procedures were at once rigorously instituted, but nevertheless, five additional infants were infected in one month. Therefore in March 1999, palivizumab (15 mg/kg, 2 doses at 4 week intervals) was administrated to 19 infants in the NICU. Cumulative incidence (CI; proportion of children at risk that became ill) and second attack rate (SAR) were determined for four periods of 15 days. CI was 2.4% in the first 15 days and 10.5% in the second, it dropped to zero after the administration of palivizumab. SAR was 2.9% in the first 15-day and 14.1% in the second 15-day period. It further decreased to 0% in the third and fourth 15-day periods. The total cost of palivizumab administration was 7619 euros (401 euros per patient).[6] These two reports concluded that in addition to meticulous infection control procedures, the use of palivizumab might have contributed to stop an uncontrolled RSV nosocomial outbreak in a large NICU.

The Center of Disease Control (CDC) advises the use of contact precautions, in addition to standard precautions, for RSV infections. The CDC recommends hand-washing (water with soap or antibacterial agent or waterless hand rub), personal protective equipment (gloves, masks with eye protection, and gowns), housing patients infected with RSV in private rooms or in a cohort isolated from other patients, and the use of dedicated patient-care equipment. They classify the evidence for the above recommendations as "category I-B", which is based "on strong rationale and suggestive evidence" and is "strongly recommended" and "reviewed as effective by experts in the field". The CDC also suggests screening visitors for illness and restricting them during RSV season, and assigning specific staff to care only for patients with RSV infection although lacking high level supportive evidence for these recommendations.

## Conclusions

Various infection control measures can be used to prevent RSV infection. In the hospital environment, re-infection among staff and otherwise healthy individuals may spread the infection to those at risk of life threatening disease. The most important method for reducing the transmission is frequent and consistent hand washing. Other methods, such as personal protective equipment and cohort isolation are useful in controlling nocosomial RSV infection, but may not be practical when used in a busy and crowded general paediatric ward. Nevertheless, they should be considered if an RSV outbreak occurs in a high-risk unit (e.g., neonatal intensive care unit). Further studies are required to support the use of palivizumab for outbreak control.

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