

Nurse-led respiratory syncytial virus immunisation



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Respiratory syncytial virus in pre-term babies. Setting up a nurse led clinic to give Synagis (immunisation) with implications for nursing practice. From the neonatal nurse's view point.

Introduction

The respiratory syncytial virus is identified as a labile paramyxovirus which produces a histologically characteristic effect of causing fusion of human cells in tissue culture – hence the term “ syncytial”. It is commonly sub-classified into types A and B. The B strain is generally asymptomatic in the majority of the population whereas the A subtype tends to produce the more severe illnesses which tend to predominate in the majority of clinically significant outbreaks (Bar-on ME et al 1996). It has an incubation period of 4-6 days and the infection typically lasts from 7-14 days, but does occasionally last up to three weeks. If it becomes necessary to hospitalise a child with respiratory syncytial virus infection, the admission period is typically 5-7 days.(Hentschel J et al 2005)

Contagion in the form of virus shedding is its highest levels during days 2-4 of the illness but the active viral particles will continue to be shed for up to 14 days after the clinical onset of symptoms.

The respiratory syncytial virus is known to affect both upper and lower respiratory tracts although the most clinically significant manifestations arise in lower respiratory tract infections, bronchiolitis and pneumonia being perhaps the most significant. Bronchiolitis is a particularly severe illness in the pre-term infant by virtue of the fact that it causes very significant small airways obstruction. (Sigurs N et al 1995)

The respiratory syncytial virus is currently the commonest identified cause of lower respiratory tract infections in children under the age of three world-wide. Serological studies have identified that, at least in the UK, that virtually all children will have had at least one episode of infection by the age of three. In the infant and neonate age groups, it is currently the numerically largest cause of both pneumonia and bronchiolitis (Krillov L R et al 1997), and is also thought to play a role (as yet not fully understood), in the aetiology of both asthma and chronic obstructive airways disease.(Pullan C R et al 1998) For those patients who have concurrent immunodeficiency states it is a very significant cause of both morbidity and mortality (Long C E et al 1995)

Clinical presentation

In our considerations here we shall confine our discussion to those clinical manifestations common in the neonatal group and accept that the comments made do not necessarily apply to those older children and adults who may also contract the virus.

The respiratory syncytial virus is currently the commonest cause of pneumonia in young children with the greatest preponderance in the under three age range. (Jeng M-J et al 1997)

The initial phases of an infection are generally characterised by symptoms of a transient upper respiratory tract infection such as runny nose, watery eyes and mild pyrexia. This typically progresses to produce symptoms of cough, wheeze (although this may be absent in the neonate), high pyrexia, dyspnoea, central cyanosis - characterised by a bluish tinge to the skin, lips and fingernails, increased respiratory rate and occasionally visible utilisation

of the accessory muscles of respiration and sub-costal retraction, all of which indicate lower respiratory tract involvement. (Brunell P A 1997). In severe cases it can progress to the point of respiratory failure.

In the context of our discussion here, these developments can be extremely dangerous in the pre-term infant who has significantly smaller airways than older children or adults, and also less in the way of respiratory reserve, so that any embarrassment of the respiratory function is of proportionally greater clinical significance. (Graham S M et al 2002)

Particular risk factors for a severe bout of the disease are:

- Prematurity
- Young age (especially those less than six weeks old)
- Pre-existing heart conditions (congenital malformations)
- Pre-existing lung conditions (bronchopulmonary dysplasia and cystic fibrosis)
- Immune system malfunction
- Low socio-economic status and especially those who live in
- Overcrowded housing conditions
- Passive exposure to cigarette smoke
- Day care or childcare attendance
- Presence of older children in the same household
- Lack of innate immunity from failure to breast feed.

(after Thompson et al. 2003)

Mode of infection

After each bout of infection the body develops a degree of immunity to the virus. This is less of a factor in the neonate, whose immune system has not developed to the same degree as in the older child. In the pre-term infant, the immune response is (in practical terms) almost non-existent. In any event the immunity is never complete as the virus is capable of subtle mutations of its protein coat which allows it to partially evade the immune system. Re-infections are common but they do tend to be less severe than the original attack. (Panigar J, et al 2004)

The mode of spread is through droplet spread and from direct contact with infected nasal or oral fluids. It can enter the body most easily through the epithelial surfaces of the eyes and nose.

Epidemiology

The respiratory syncytial virus produces characteristic patterns of infection which are epidemics of up to five months duration. They typically occur in the winter months and records show (since 1990) that they typically begin in the time span between October to mid-December with a marked peak in January and February. In the UK, the respiratory syncytial virus is responsible for about 125, 000 episodes of hospitalisation (Leader S et al 2002). and about 2, 500 deaths (NCHS 2002). These factors are of particular importance in our considerations when we are considering the timing of any protection programme.

These figures translate into the fact that 20% of all hospital admissions for lower respiratory tract infections are due to respiratory syncytial virus infections, and if looked at as an annual incidence rate, admission for <https://assignbuster.com/nurse-led-respiratory-syncytial-virus-immunisation/>

respiratory syncytial virus infection is currently 28.3 per 1,000 infants and 1.3 per 1,000 for children under the age of 4 years. (Muller-Pebody B et al 2002)

The highest rate of clinically significant infection occurs at ages between 2 and 6 months with a significant peak in the 2-3 month age range.

Respiratory syncytial virus is typically brought into the home by an older (school age) child who then passes it onto the younger child in the family. In child care and crèche facilities it is quite common to observe 100% infection rates in both children and staff. On a practical note, respiratory syncytial virus infection has also been seen to spread throughout a hospital environment infecting patients and staff alike. (Shay, D K et al 2001),

We shall specifically consider the implications of vaccination later in this essay, but there are other issues of prevention that require examination. We have already discussed the mode of common infection through the respiratory and ocular epithelial surfaces. It follows that there are certain measures which, while not eradicating the possibility of spread, will certainly help to reduce it. In the home environment, it is sensible to frequently wash hands after coming into contact with nasal or oral secretions and before handling a young child. Frequent handwashing will reduce the risk of contamination by direct spread. School age children should be kept as separate as practically possible from a neonate if they have symptoms of a "cold". Sneezing into a handkerchief will also help to reduce the possibility of droplet transmission. In its droplet form, the virus will live on household surfaces for many hours and is therefore still capable of transmission. In

terms of the work of the neonatal community nurse, such patient education should be seen both as part of an empowerment and education programme every bit as much as a prophylactic measure for the neonate. (Hogston, R et al 2002).

In the more controlled environment of a hospital, it is possible to institute barrier measures if there is significant risk such as the immuno-compromised patient or the child at risk with congenital heart disease. Frequent pre-touching hand washing is essential to help prevent cross transmission (Ng D K et al 2000).

Specific preventative treatments

Palivizumab (or Synagis - Trade name) is a medication that is commonly given to infants at highest risk of complications of respiratory syncytial virus infection, for example those who were born prematurely or those with chronic heart and lung disease. It is given by monthly injection through the at-risk winter months and provides significant levels of protection. This protection however, is comparatively short lived and has to be repeated on a yearly basis until the child is judged to be no longer at high risk of significant sequelae of infection. (PPTI 2005). It is also extremely expensive. (see on).

Palivizumab is the first of what may become a series, of monoclonal antibodies, which have been developed to specifically target and combat one specific infection. Its current indications include prevention of serious lower respiratory tract disease caused specifically by the respiratory syncytial virus.

There are currently a number of papers that have studied its safety and efficacy in a number of situations such as bronchopulmonary dysplasia (BPD), infants with a history of premature birth (≤ 35 weeks gestational age), and children with hemodynamically significant CHD. (Meissner H C et al 1999),

Technically it is a humanised monoclonal antibody of IgG1k type which is produced by recombinant DNA methods. It targets an A antigenic site of the F-protein covering of the virus. It is primarily derived from human antibody sequences and has two light and two heavy chains with a molecular weight of about 148, 000 Daltons.

The viability of nurse-led respiratory syncytial virus immunisation programme.

> From the literature and the evidence that we have presented so far we can point to the fact that the respiratory syncytial virus is a significant risk to neonates, especially those who have significant risk factors for the development of lower respiratory tract complications. (Berwick D 2005)

Although we specifically have not considered treatment in this essay, we should note that, in the context of a discussion on the role of prophylaxis, that the treatments available for neonate infection with respiratory syncytial virus are severely limited. In the words of Jon Friedland, an eminent professor of infectious diseases in London:

Treating respiratory syncytial virus bronchiolitis remains a good example of therapeutic nihilism — nothing works except oxygen. Adrenaline, bronchodilators, steroids, and ribavirin all confer no real benefit.

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(quoted in Handforth J et al 2004)

If we accept that this is the case and we also accept the significant morbidity and mortality rates quoted earlier in this essay, then it clearly makes sense to consider the role of prophylaxis in respiratory syncytial virus infections.

It clearly therefore also makes sense to consider what active measures can be taken in order to try to reduce the possibility of infection or prevent the damaging and serious sequelae of infection.

Sadly, this is far from straightforward. One could reasonably hope that a immunologically based vaccine would have been developed to help with this problem. Despite the fact that the first formalin inactivated respiratory syncytial virus vaccine was developed over forty years ago, progress in this field appears to have been painfully slow.

Recently published literature on the subject of the effect of vaccines against respiratory syncytial virus found that there was no significant benefit conferred in terms of preventing either the infection or the complications. (Simoes E A et al 2001). We should note that this was not a small study but a meta-analysis of five major studies on the subject and therefore has considerable weight if we are considering an evidence base for our findings. (Green J et al 1998).

If we accept the premise that a successful respiratory syncytial virus vaccine should be able to prevent severe lower respiratory tract disease and the morbidity consequent upon it, and should also ideally protect against both A and B strains of the virus, we would also have to postulate that it would have

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to be given directly after birth in order to prevent immediate primary infection from the environment. In general terms, this presents the nub of the problem as neonates have very poorly developed immune response mechanisms and the bulk of their immunity is passively derived from the trans-placental maternal antibody production and the immunoglobulins present in the maternal milk. (Kim H W et al 1969).

Active immunisation in very early life proves to be fruitless, as the immature neonatal immune system cannot generally produce either an adequate T-cell response or effective antibody levels. It is also the case that the maternal antibodies themselves, also interfere with the infant's ability to mount an antibody response of its own. (Clements M L et al 1996)

In order to combat these problems there are a number of immunological strategies currently under investigation.

One strategy is to vaccinate the mother during the third trimester in order to try to boost the naturally occurring antibodies and thereby increase the natural passive immunity. This is unlikely to give significant immunity beyond the first six weeks of birth unless the child is breast fed, in which case the immunity would last for longer (see below). It would however, have the advantage of protecting the most vulnerable individuals at a critical time. Initial trials of this method using a purified F protein subunit vaccine was found to be safe in a trial of 35 third trimester vaccinations. (Munoz FM et al 2003).

The trial showed a disappointing, but detectable, response and the infants had increased IgG against respiratory syncytial virus up until 9 months of

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age. Clearly this strategy would be ineffective against children born with a significant degree of prematurity and who therefore, are at greatest risk

A second approach was tried with live attenuated genetically modified vaccine. This approach was found to work in adults and older children but could not be sufficiently attenuated to produce a safe and sufficient response in neonates. (Piedra P A 2003).

The third approach was to try live recombinant viral vectors which expressed respiratory syncytial virus proteins. Thus far, the results have been disappointing both in terms of immunogenicity and there are also safety concerns with iatrogenic oncogene activation. (Haller A A et al 2003)

In terms of our potential nurse run clinic, all of these options have very significant drawbacks and none are therefore likely to represent a realistic immunisation option.

Clarke (S J et al 2000) suggest that although huge strides have been taken with a number of vaccine products - especially the live attenuated vaccines, it will probably be a minimum of another decade before routine effective vaccination becomes widely available.

It is perhaps because of this failure to present a solution of a vaccine that has caused researchers to examine other avenues of investigation for workable prophylactics.

A line of investigation into passive immunity with IV hyperimmune globulins against respiratory syncytial virus has shown positive results in initial trials against preventing severe forms of respiratory complications in high risk

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children (Groothuis J R et al 1999). This particular formulation can only be given intravenously and therefore is of limited use outside of a hospital environment. It is clearly of no use in a community setting.

The other line of passive immunity has developed into the intramuscular form of IgG humanised monoclonal antibody described above (palivizumab). Clinical trials already published have already shown that monthly injections of palivizumab in high risk infants have been able to reduce the hospital admissions for respiratory syncytial virus-related disease by more than 50% (IRSVSG 1998). This was a well designed double-blind placebo controlled randomised study and, in addition to apparently demonstrating its efficacy, it also showed an impressive safety record.

This particular formulation appears to have a very good side-effect profile and clinical experience appears to confirm the initial trial results. Given the fact that respiratory syncytial virus places a heavy financial and economic burden on the NHS, a 50 % reduction in these levels is quite substantial. Cost-effectiveness is clearly a major question in any consideration of a national vaccination programme and studies elsewhere in Europe, (Roeckl-Wiedmann I et al 2003) have called into question the costings and have therefore also called into question the need for further evaluation.

These considerations are given further credence if we consider the fact that if we take as a marker the number of hospital laboratory reports of respiratory syncytial virus, there appears to be a marked downward trend in the UK between 1990 and 2003. (Fleming D M et al 2003). It may be that there are other active factors here such as changes in clinical or laboratory

practice, but it would appear to reflect a definite downward trend. This comment is actually given further credence when one considers the epidemiological data from the primary health care sources which also show a fall in acute respiratory infections over the same period. (Neuzil K M et al 2000)

Passive immunisation is currently considered to be the best option in terms of providing immunity in the community although many authorities consider that it is currently only an option for the high risk infant.

In the terms of our consideration here for a nurse run immunisation clinic, we should consider a set of guidelines, (that were actually produced in the USA), which could be adopted as they are based on the current best evidence available. (AAP 2003)

The guidelines suggest that passive immunisation (palivizumab) should be currently considered for premature infants born at less than 32-35 weeks gestation or for infants younger than 2 years with chronic lung disease. Although this is clearly a rational view, we have to note that it is based upon American statistics and American costings and is applicable primarily to American culture. It does not imply that the recommendations are necessarily transferable to the UK situation.

The NHS has been more cautious. The current NHS guidelines were considered and formulated by the joint committee on vaccination and immunisation of the Department of Health. (JCVI 2002). Their report notes that:

Palivizumab seems safe, well tolerated, and effective in reducing admissions to hospital, but it remains very expensive, at a cost of around £2500 for five doses over the season for respiratory syncytial virus.

In the UK, the statistics seem to suggest that readmission rates associated with respiratory syncytial virus infection-related bronchiolitis show that palivizumab is only cost effective if it is used in infants born prematurely with chronic lung disease and receiving oxygen at home (which is actually a very expensive undertaking in any event). (Feldes T F et al 2003). If this opinion is taken in conjunction with the suspicion that the rates of respiratory syncytial virus infection are actually falling, this will actually weight the cost-effectiveness argument further against the use of palivizumab.

It is noted that a more recent study of palivizumab in infants who have congenital heart disease has been completed, but the information collected is insufficient in terms of readmission rates, morbidity and cost-benefit analysis, to allow a confident recommendation for use in this population. (Feldes T F et al 2003)

The neonatal nurse's viewpoint.

In this essay we have considered much of the current literature on the subject of community immunisation for respiratory syncytial virus. There is little doubt that the virus represents a significant threat to a small proportion of neonates and a minor threat to the rest. (Crowe JE Jr 1995). It is also clear from the evidence that the prospect of active immunisation of the at risk groups has been aggressively pursued over a time scale of about four decades with very little in the way of positive practical results. In essence,
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this means that the only realistic prospect of giving the at-risk neonate a degree of protection against the respiratory syncytial virus, is by means of increasing the levels of passive immunity.

We have considered the role of the only viable therapeutic agent in this area (palivizumab), and have come to the conclusion that the evidence base for its use is sound if it is given on a monthly basis through the winter months when the at risk populations are at greatest risk of significant morbidity, and indeed mortality. Against this statement we have to weight the cost-effectiveness of what is a very expensive agent. (Handforth J et al 2000).

The neonatal community nurse therefore finds herself ideally placed to act as the gatekeeper in this role. By virtue of her position of having direct contact with each of the neonates in her community, she is probably the most optimally placed member of the primary healthcare team to assess and oversee the administration of palivizumab to those at greatest risk. (Scally G et al 1998)

The mechanics of the enterprise will inevitably vary from practice to practice, but the elements of any recall system will be an up to date age/sex register, a forward planning facility and good communications with the antenatal services so that prospective candidates can be assessed at the earliest opportunity. The multidisciplinary nature of the modern primary healthcare team is ideal for communication of this nature and the neonatal nurse should be able to optimally utilise the recall facilities of the practice in order to ensure maximal compliance once the decision to treat has been made. (Yura H et al 1998)

On the positive side there is the fact that Nurse led clinics, in general terms, have been proven to work both effectively and efficiently in many other areas.

On the negative side we have the practical situation that the current recommendations from the Joint Committee on Vaccination and Immunisation that the current evidence base supports the view that palivizumab should only be offered to babies in the Group I classification, which currently includes babies under the age of two years with severe chronic lung disease, on home oxygen during the RSV season. This represents about 500 babies a year nationally. Common sense would indicate that there is absolutely no practical rationale for setting up any form of clinic in primary care for this number of babies on a national basis. Even if this recommendation was extended to include those babies in Group II (those with chronic lung disease but not on home oxygen), this would only add another 1000 to the national total and again, clearly there would be absolutely no rationale for setting up a local clinic base for this type of work load. (Netten A et al. 2000)

The Committee's reasoning for offering palivizumab to the Group I babies was on the evidence that it would be likely to reduce hospitalisation by a factor of 40% and thereby be cost effective. The Committee also suggested that these guidelines should be reviewed if a more effective and cheaper vaccine became available.

If we consider, for the sake of argument, that such a vaccine has become available and that it is both practical and National policy to set up such

vaccination clinics, we can consider the leads given by papers that report experiences in other areas of childhood vaccination. Nesbitt (A et al. 1997) give a very informative overview of the practical difficulties involved in setting up a Hepatitis B vaccination clinic. They point to the problems of trying to reach the most vulnerable and potentially isolated individuals in the community and highlight the need for specific nurse initiated home visits to the persistent absentees to the clinic. (Nesbitt A et al. 1995)

They also highlight the difficulties in trying to get a level of immunity in a population that is constantly turning over. It requires a very high degree of vigilance on the part of the nurse running the clinic to ensure that all new arrivals are incorporated into the recall system with complete efficiency and without delay.

On a slightly tangential subject, the whole issue of the nurse-led clinic was reviewed and assessed for overall effectiveness and cost effectiveness by Raftery (J et al. 2005). This paper demonstrated, beyond doubt that nurse led clinics could be both effective and very cost effective. This particular paper looked at the role of the clinic in the prevention of heart disease in the adult population, which is clearly not directly applicable to our considerations here, but the important relevant considerations are that the autonomous nurse led clinic can work very effectively with auditable results that can demonstrate both positive health benefits and an efficient and cost-effective use of a nurse's time. (Polsky D et al. 1997) One of the interesting points raised in this paper which was also directly transferable to a nurse led immunisation clinic was that the increased costs noted also included an element for increased prescribing for intercurrent morbidity that was discovered at the <https://assignbuster.com/nurse-led-respiratory-syncytial-virus-immunisation/>

time of the assessment. This is a factor that is likely to be translated into increased costings for the vaccination clinic, as many mothers are likely to save up questions and minor degrees of pathology if they know that they are having an appointment with the practice nurse. (Lancaster T 2003).

This may well be translated into increased prescribing costs. Taking a holistic view however, one would hope that these costs would not be incurred without good reason and therefore one could conclude that it would be for the greater good of the patient in the long run and therefore presumably justified. (Benger J R et al. 2005)

Considering all of these issues one can see that the viability of the nurse led clinic, certainly in the areas of RSV vaccination, is totally dependant on the development of an effective and cheaper vaccine. At this point in time, the recommendations do not support the logistics of a nurse led clinic for palivizumab although it is clear that the neonatal nurse should be the prime source of the palivizumab vaccination, the numbers involved support the specific identification and targeting of the Group I babies.

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