Respiratory infections in the newborn

Michael D Nissen

Queensland Paediatric Infectious Diseases Laboratory
Department of Infectious Diseases
Sir Albert Sakzewski Virus Research Centre
Royal Children's Hospital
Brisbane QLD 4029
Tel (07) 3636 8654
Email theniss@uq.edu.au

Theo Sloots

Queensland Paediatric Infectious Diseases Laboratory
Department of Infectious Diseases
Sir Albert Sakzewski Virus Research Centre
Royal Children's Hospital
Brisbane QLD 4029
Tel (07) 3636 8833
Email t.sloots@uq.edu.au

It is well recognised that acute respiratory tract infection (ARTI) occurs commonly in children younger than 5 years of age, with pneumonia being the most serious complication [1]. The greatest risk of death from pneumonia in childhood is in the neonatal period [2]; it is estimated that pneumonia contributes to between 0.75-1.2 million neonatal deaths annually, accounting for approximately 10% of global child mortality [3]. Of all neonatal deaths due to pneumonia, 96% occur in the developing world [4].

ARTIs in neonates can be classified as congenital or neonatal in origin, and are defined by the timeframe in which the infection or pathogen has been acquired. Congenital pneumonias are usually part of a transplacental infection, while neonatal pneumonias can evolve from intrauterine or postnatal acquisition. Neonatal pneumonia is classified as early or late onset [2]. Early onset neonatal pneumonia, in general, is defined as a clinical presentation in the first 48 hours up to 1 week of life, while late onset neonatal pneumonia occurs in the following 3 weeks.

Congenital and neonatal pneumonias are often a difficult disease to identify and treat. Clinical manifestations are generally non-specific, sharing respiratory and a range of non-inflammatory processes. Laboratory findings also have limited value, with attempts to identify specific microbes often unsuccessful due to difficulty in their recovery from intrapulmonary sites without contamination. In addition, many organisms are primarily uncultivable or uncultivable due to antimicrobial therapy.

Bacterial respiratory pathogens

The pathogens commonly associated with neonatal and congenital pneumonia include numerous bacteria, fungi and viruses (Table 1). Bacterial pneumonia derived from infected amniotic fluid or colonisation of the birth canal is linked with maternal chorioamnionitis and fetal asphyxia. It is assumed that asphyxia leads to fetal gasping and aspiration of infected amniotic fluid. This hypothesis is based on the histological finding of amniotic fluid and/or maternal white blood cells in the affected neonatal lungs [2]. The bacterial aetiology of neonatal pneumonia is also influenced by nosocomial infection in neonatal intensive care units. High rates of *Streptococcus pneumoniae* have been reported in late onset neonatal pneumonia in some areas of the world [5].

Atypical bacterial pathogens, for example *Chlamydia trachomatis,* are well recognised as agents of late onset pneumonia causing infection at 1-3 months of age. The ability to now perform *C. trachomatis* polymerase chain reaction (PCR) testing on nasopharyngeal or endotracheal aspirates from infants with neonatal pneumonia has increased the rate of detection of this pathogen. It is assumed that *C. trachomatis* contributes significantly to neonatal pneumonia in countries where untreated sexually transmitted diseases in women are common. In addition, *Bordetella pertussis* may present as an early onset or late onset pneumonia, and is most commonly associated with close contact with an infected parent, siblings, relative or healthcare worker. Other atypical bacteria that have been associated with pneumonia or pneumonitis in the neonate are *Ureaplasma urealyticum* and *Ureaplasma parvum, Treponema pallidum, Mycobacterium tuberculosis* and *Listeria monocytogenes* [5].

A persistent neonatal pneumonia associated with a rapidly progressive presentation of congenital HIV infection has been previously described in two Southern Africa studies [6, 7]. Co-infections with *M. tuberculosis,* syphilis and cytomegalovirus were common and realistically contributed to the clinical presentation. Congenital HIV infection also increases the fatality risk from neonatal respiratory distress syndrome and sepsis associated with *S. pneumoniae* and *Staphylococcus aureus.*

Viral respiratory pathogens

Viral neonatal pneumonias can either be associated with intrauterine, early onset or late onset pneumonias, and may be acquired from the birth canal (e.g. herpes simplex virus –

HSV), infected siblings, parents and/or healthcare workers with or without nosocomial involvement (e.g. respiratory syncytial virus). HSV is usually transmitted during delivery through an infected maternal genital tract and respiratory symptoms are normally associated with multi-organ disease. Transplacental transmission of virus and hospital-acquired spread from one neonate to another by hospital personnel or family may account for 15% of cases. Mothers of neonates with HSV infection tend to have no history or symptoms of genital infection at the time of delivery.

The role of respiratory viruses (respiratory syncytial virus, influenza viruses, parainfluenza viruses, adenovirus and human metapneumovirus) in neonatal pneumonia is well described by retrospective reports [8] and is associated with seasonal late onset pneumonia where viral diagnostic techniques are accessible. Nosocomial outbreaks of respiratory viruses in neonatal nurseries and co-infections with respiratory syncytial virus and human metapneumovirus have also been described [9].

Diagnosis of neonatal respiratory infections

To diagnose neonatal respiratory infection, chest x-rays should be performed in any patient with respiratory abnormalities, and blood should be collected for culture in all cases of neonatal pneumonia. While the yield from blood cultures is low, blood, if possible, should be collected prior to antibiotic therapy to guide second-line treatment in the event of first-line antibiotic failure. Blood cultures collected simultaneously with endotracheal tube aspirates in mechanically ventilated neonates may also assist in determining the significance of endotracheal tube colonisation.

Conventional bacteriologic culture is used most widely and is currently most helpful in diagnosing neonatal pneumonia. The culture of fungi, viruses, *Ureaplasma urealyticum,* and other unusual organisms often requires different microbiologic processing but may be warranted in suggestive clinical settings. A number of factors may interfere with the ability to cultivate a likely pathogen from the sites noted, including (but not limited to): pretreatment with antibiotics that limit *in vitro* but not *in vivo* growth; contaminants that overgrow the pathogen; pathogens that do not replicate in currently available culture systems; sampling of an inappropriate site; and patients in whom the process is inflammatory but not infectious, such as with meconium aspiration.

Techniques that may help overcome some of these limitations include antigen detection, serologic tests, nucleic acid probes and PCR-based assays. Particularly in the diagnosis of viral respiratory pathogens, molecular methods have significantly enhanced our ability to diagnose these infections. Additionally, these sensitive assays have led to the recognition of new viruses associated with the human respiratory tract, including in neonates, yet the significance of these as agents of disease remains unclear [10].

Conclusion

In summary, the global impact of neonatal pneumonia is significant, with a complex epidemiology and aetiology compared to the pneumonias in older children. Management and prevention strategies for neonatal pneumonia cross multiple levels of the population and health care provision, and have broader based effects that are sometimes difficult to measure.

Table 1. Pathogens associated with congenital and neonatal pneumonia.

Bacteria	*Serratia* spp.	**Fungii**
Acinetobacter spp.	*Staphylococcus aureus*	*Candida albicans*
Enterobacter aerogenes	*Staphylococcus epidermiditis*	*Pneumocystis jiroveci*
Enterococcus spp.	*Streptococcus pneumoniae*	**Atypical microorganisms**
Escherichia coli	*Streptococcus viridans* group	*Bordetella pertussis*
Group A Streptococcus *(S. pyogenes)*	**Viruses**	*Chlamydia tracheomatis*
Group B Streptococcus *(S. agalactiae)*	Herpes simplex virus	*Listeria monocytogenes*
Group D & G streptococci	Human adenoviruses	*Mycobacterium tuberculosis*
Haemophilus influenzae (non-typable)	Human cytomegalovirus	*Treponema pallidum*
Klebsiella spp.	Human immunodeficiency virus	*Ureaplasma urealyticum*
Morganella spp.	Human metapneumovirus	*Ureaplasma parvum*
Neisseria meningitidis	Influenza A & B viruses	
Proteus spp.	Parainfluenzae viruses 1, 2 & 3	
Pseudomonas aeruginosa	Respiratory syncytial virus	
Salmonella spp.		

The growing prevalence of antibiotic resistance to common and affordable antibiotics will eventually impact on the morbidity and mortality rates for neonates, especially in the developing world, and emphasises the importance of the continuing development of universal maternal and preventative health programmes.

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Michael Nissen (BMedSc, MBBS, FRACP, FRCPA) is director of infectious diseases at the Royal Children's Hospital, Brisbane, unit director (medical) of the Queensland Paediatric Infectious Diseases (QPID) Laboratory, and clinical microbiologist overseeing the Serology, Virology and Molecular (SVM) Unit of Pathology Queensland Central based at Royal Brisbane Hospital, Brisbane. Michael's research interests include the characterisation and discovery of respiratory viruses such as WU and KI polyoma viruses, human metapneumovirus, bocavirus, coronaviruses NL-63 and HKU1, and new rhinovirus variants. He is also a chief investigator on three NHMRC project grants including one examining the viral aetiology of indigenous otitis media (OM).

Michael was a clinical research associate and post-graduate fellow in the Department of Molecular Microbiology and Pediatrics at the Washington University School of Medicine, St Louis and St Louis Children's Hospital, USA from 1996-1999, and the recipient of the Connaught Laboratories Inc. Fellowship in Infectious Diseases from the Infectious Diseases Society of America. He currently holds academic appointments with the School of Biomolecular and Physical Sciences, Griffith University, and the Biological and Chemical Sciences Faculty, University of Queensland, Brisbane.

Theo Sloots (PhD, GCM, MASM) has more than 25 years' experience in medical microbiology and is currently the unit director (research) at the Queensland Paediatric Infectious Diseases (QPID) Laboratory of the Royal Children's Hospital, Brisbane, as well as consultant virologist to Pathology Queensland Central. Research at the QPID Laboratory has focused on examining the significance of human metapneumovirus as a newly recognised respiratory pathogen, and the discovery of new viral agents associated with respiratory disease in children. Theo is a chief investigator on three separate research project grants funded by the NHMRC, and also holds academic appointments with the Biological and Chemical Sciences Faculty, University of Queensland, and the School of Biomolecular and Physical Sciences, Griffith University, Brisbane.