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Nosocomial Infections in Newborn Nurseries and Neonatal Intensive Care Units

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Newborn immunity, microbial colonization and infection

Newborns in nurseries and neonatal intensive care units (NICU) are at risk for nosocomial infections due to an environment, which is dramatically different from the sterile environment of the uterus. Invasive devices and frequent use of antimicrobial substances represent particular risks.[1] Many of the newborn's defence mechanisms are not fully developed: for example phagocytic activity, immunoglobulin synthesis or T-lymphocyte function.[2] The immune deficiency is age-related, i.e. the earlier during gestation the infant is born, the higher is the susceptibility to infection. During the intrauterine period no immunologic significant stimuli are present to prime protective immune reactions. The infant therefore depends on passively acquired maternal antibodies, which are transmitted via the placenta starting from 24 to 26 weeks of gestation. Prematurely born infants demonstrate significantly lower IgG antibody levels than full term infants.[3] However, these passively acquired antibodies represent the mother's prior exposure which certainly was different to the antigenic challenges of a NICU. Due to the sterile intrauterine environment the newborn lacks any normal microbial flora. In healthy newborns colonization of mucous membranes and skin develops rapidly by transmission of microbes from the infant's mother and other family members. Neonates starting life in a NICU acquire their flora from their contacts with doctors and nurses and the environmental of the ward, possibly resulting in early colonization with antibiotic resistant bacteria. Skin and mucous membranes of premature children are markedly permeable to exogenic antigens thus increasing the risk for microbial invasion of tissues and the vascular system.[4]

Vertical and horizontal transmission

Besides human and inanimate sources of infection, neonates acquire microorganisms from the maternal birth canal, which may cause infection (Table 1).

Administration of breast milk may result in transmission of pathogens either from the milk, from the mother's skin or from devices used for withdrawing and preparing the milk. Relevant pathogens include CMV, HBV, HCV, HIV and HTLV-I and -II, HSV and rubella virus.[5] Controversy exists about prohibition of breastfeeding in HIV-positive mothers.

As far as CMV transmission via breast milk in term infants is concerned, morbidity is low, although a few cases of serious disease with hearing impairment and mental retardation have been reported. Very premature infants are more susceptible to CMV infection, since they may have been born receiving mother's protective immunoglobulins. Prevention of CMV transmission by pasteurisation of breast milk is successful, but certain nutritional and

Table 1: Vertical Spread, by contact transmitted pathogens[2]

Bacteria	Viruses	Others
Group B streptococci	Herpes simplex	*Candida albicans*
Listeria monocytogenes	Cytomegalovirus	*Chlamydia trachomatis*
Enterobacteriaceae	HIV	*Ureaplasma urealyticum*
Neisseria gonorrhoeae	Hepatitis B	*Mycoplasma hominis*
Staphylococcus aureus		

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immunological factors in the milk are destroyed. Freeze-thawing of the milk at -20°C for 4 - 10 days decreases the rate of transmission and observed infections have been asymptomatic.[6] Preliminary studies with heat inactivation of very thin milk films in a rotating flask at 62 °C for few seconds demonstrated loss of infectivity while enzymatic activity was at least partly preserved.[7]

Horizontal transmission of 'typical' nosocomial pathogens like *Staphylococcus aureus* (including MRSA), enterococci (including VRE), enterobacteriaceae, non fermenting gram-negative bacteria (*Acinetobacter*, *Pseudomonas*, *Flavobacterium*, *Stenotrophomonas* spp.), *Candida* spp. as well as viruses (rotavirus, norovirus) may occur by direct or indirect contact or (less frequently) aerosols. Moreover, use of blood products represents a potential for transmission of bloodborne pathogens.

Surveillance and descriptive epidemiology

There are few data on infection rates in newborn nurseries, where babies are healthy and the hospital stay is short. Reported rates of infection differ between 0.3 and 1.7/100 discharges.[8] Overall newborn nosocomial infection rates are of limited value because of considerable variation in type of hospital or nursery and methods of surveillance. Denominators most frequently used are number of admissions or discharges or, for maternity hospitals, infections per 1000 deliveries. In the NICU, where the infection risk is related to the duration of stay, patient days is a more appropriate denominator.[9]

A few big studies carried out in the 1990's clearly showed the relation between birth weight and infection (Table 2).

In 1999, the German Reference Center for Surveillance of Nosocomial Infections started the NEOKISS project for surveillance of nosocomial infections in NICUs, including infants with a birth weight from < 1500 g until discharge/ death/ > 1800 g (http://www.nrz-hygiene.de/surveillance/neo.htm). Surveillance includes three types of infection - pneumonia, primary bacteraemia (BSI) and necrotizing entercolitis (NEC) – using specific case definitions. Incidence densities (infections/1000 patients) and device-associated infection rates (infections/1000 device days - vascular catheter or ventilator) are calculated and stratified according to different birth weight categories starting at < 500 g (Table 3).

Infections associated with the use of invasive devices are a major problem in critically ill neonates; Table 4 shows the NEO-KISS data for neonates with extremely low birth weight (< 500g). Duration of hospital stay, administration of broad spectrum antibiotics, overcrowding of wards and understaffing have been identified as risk factors associated with increased rates of nosocomial infections.

Infections at specific sites

Most infections are superficial (skin, mucous membranes, and eye). Outbreaks (viral or bacterial gastrointestinal pathogens) may occur following admission of maternally infected or colonized infants or as a reflection of community outbreaks. Primary bacteraemia (bloodstream infection) and respiratory tract infection followed by gastrointestinal infection are most frequent nosocomial infections.

Table 2: Nosocomial infection rates in the NICU[2]

	Freiburg 1991[11]		Montreal 1992-1997[12]	
Birth weight (g)	inf./100admissions	inf./1000 pat.days	inf./100admissions	inf./1000pat.days
<1000	70.4	22.8	25.7	9.9
1'001-1'500	31.9	18.5	39.4	9.6
1'501-2'500	21.4	23.8	19.4	9.0
>2'500	13.6	23.5	9.6	7.1

Table 3: Infection rates according to NEO-KISS, January 2000 - December 2004 (No. of infections/patient days x 1000)

Birth weight (patient days)	Severe infection*	Primary BSI	Pneumonia	Necrotizing enterocolitis
-499g (8'951)	13.3	11.3	2.0	1.0
500 – 999g (138'756)	9.9	8.6	1.3	1.0
1000 – 1499g (117'050)	4.5	4.1	0.4	0.6

* primary BSI + pneumonia

Table 4: Device associated infections* according to NEO-KISS, January 2000 - December 2004 (Birth weight < 500g; no. of infections/device days x 1000)

Catheter-associated BSI	12.3	Ventilation-associated pneumonia	2.5
- central venous	14.2	- tube-associated	3.7
- peripheral venous	9.6	- CPAP-associated	0.8

*patient-days : 8'951

Early onset sepsis is caused by pathogens from the maternal birth canal which are transmitted to the infant immediately prior to delivery. Premature birth, low birth weight, premature rupture of the amniotic membranes, chorioamnionitis and maternal colonization with group B streptococci (GBS) have been identified as specific risk factors for this severe and very often fatal disease. Antibiotic prophylaxis is successful but may result in an increase of gram-negative pathogens such as *Escherichia coli*.[13] Late (5-7 day) onset sepsis, may be due either to maternal pathogens, or may be transmitted nosocomially. The commonest causes include *Staphylococcus aureus* and coagulase negative staphylococci, enterococci or enterobacteriaceae or at a later stage *Candida* spp. Most cases are associated with the use of intravascular catheters. Other risk factors include low birth weight, application of lipid-containing infusions or blood drawing through central catheters.[14]

Respiratory tract infections in neonates can also be divided into early and late onset pneumonia. In the first days of their life neonates with bronchopulmonary dysplasia or meconium aspiration syndrome may develop pneumonia due to maternal pathogens (GBS, *Listeria monocytogenes*, gramnegative enteric aerobes). Late onset infection is often associated with mechanical ventilation and predominantly caused by gram-negative rods or *S. aureus*. Diagnosis is difficult in the intubated newborn, especially in those with primary lung diseases. Therefore many infants are empirically treated with antibiotics. Viruses – in particular respiratory syncytial virus (RSV) – are important causes of neonatal respiratory tract infection and may be responsible for institution-wide outbreaks.[15] Transmission not only occurs by aerosols but also by contact, as RSV like other respiratory viruses (influenza, parainfluenza) can survive on contaminated surfaces. Ward staff may become infected asymptomatically and represent an important factor in the spread of the disease.

Necrotizing enterocolitis (NEC) is not strictly an infectious disease but a clinical syndrome of multifactorial origin including an immature gastrointestinal tract, bacterial overgrowth or infection (gram-negative enteric pathogens, *S. aureus, Clostridia*) as well as viral infection (rotavirus, coronavirus). Nasogastric tubes and enteral nutrition are factors which provide the basis for bacterial growth or toxin production.[16]

Infection control measures

Policies for infection prevention in nurseries have evolved over years from a combination of custom and ritual, common sense and epidemiologic study. Meanwhile the main focus moves from the nursery as an architectural and functional unit to the infant as a source as well as recipient of infection.[10]

Hand hygiene is the most important single infection control measure in nurseries and of utmost importance in the NICU. Data from two NICUs demonstrated that each neonate or immediate environment was touched 78 times during a 12 h shift; more than half of these touches were carried out by nurses.[17] In a more recent study of infections in neonates caused by gram-negative bacilli, the pathogen was transmitted by hand contact in 42% of cases.[18]

Hygienic hand disinfection is of paramount significance in preventing transfer of pathogens to the infants before starting a shift, between patient contacts, before "critical" manipulations like preparation of infusions or formula, and after touching potentially infectious materials and objects. The hand disinfection measure of choice is alcohol-based rubs, which are effective, fast in their action, skinfriendly and can be applied at the bedside. The next part of the hand hygiene policy is noncontamination, i.e., use gloves when contact with an infectious substance is expected or suspected. Gloves must be removed and disposed of immediately after any contamination – prior to touching other objects – followed by a hygienic hand rub. Unlike hand hygiene, the use of special gowns when entering the NICU has been shown to have no effect on colonization and infection rates.[19] Strictly, patient-related gowns should be used when isolation is required and when infants are taken outside their incubator by the staff or family members.

Particular attention has to be drawn to minimizing the use of invasive devices and to their proper care if used. Infection control recommendations for insertion and maintenance of intravascular catheters, endotracheal tubes and urinary catheters are similar to those for adult patients. Ready-to-feed commercial formula should be used within 4 h of uncapping. Preparations of formula from liquid or powder concentrates have to be made under strict aseptic conditions using sterile or at least boiled (5 min) water and should be refrigerated for a maximum of 24 hours. Nasogastric feeding sets should be changed every 24 h and nasogastric probes weekly.

The fundamental principle of barrier and isolation policies is that the flora of neonates should not be shared. In nurseries, standard precautions should be sufficient to prevent transmission between babies. Additional measures, in combination with cohorting, include the use of gloves, gowns, masks and goggles or face shields to prevent airborne transmission in cases of viral respiratory infection (RSV, adenovirus, and influenza) or pertussis. Patients with varicella or measles require single room isolation; negative pressure ventilation is recommend by some institutions.[20] The visitation policy should be flexible, liberal and safe.[2] Parents and immediate family members should be allowed to visit the patient as often as possible but need instructions in barrier precautions theoretically as well as practically. From a psychological perspective, direct skin contact between parents and baby is necessary. Therefore parents should not wear gloves when taking the baby out of the incubator, but wear a gown (which can be easily opened by the mother for breastfeeding) and carry out a hygienic hand disinfection before and after contact with the patient.

Enormous progress has been made in the therapy and care of premature and critically ill neonates resulting in significant improvement concerning survival and prognosis. The price is an increased risk for healthcare-associated infections caused by invasive measures, hyperalimentation and antibiotics. We have to understand these problems and draw the correct conclusions to provide the safest environment possible for those infants who start their life in an intensive care unit.

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