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Hospital-acquired Viral Pathogens in the Neonatal Intensive Care Unit

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Hospital-acquired infections caused by viruses are a cause of considerable morbidity and occasional mortality in critically ill neonates. The intensive care environment allows for efficient spread of viral pathogens, and secondary cases among both patients and healthcare workers are frequently observed. We review the common viral causes of hospital-acquired infections in neonates, including rotavirus, respiratory syncytial virus, and others, discuss epidemiology and clinical syndromes, and summarize recommendations for control in outbreak situations. Chemoprophylaxis, isolation procedures, and care of affected staff are also addressed.
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*H*ospital-acquired infections are a major source of excess morbidity and mortality in the already fragile patient population that inhabits neonatal intensive care units (NICUs).[1] Hospital-acquired pathogens add to the difficulty of caring for critically ill neonates and can prolong hospitalization, worsen patient outcomes, increase costs, and, in the case of an outbreak, place considerable strain on physicians, nurses, infection control practitioners, and the clinical microbiology laboratory.[2] Data from the National Nosocomial Infections Surveillance System (NNIS) show that bloodstream infections are, by far, the most common hospital-acquired infections in NICUs, followed by pneumonias. Both of these infection sites had pathology entirely due to bacterial or fungal pathogens in the most recent NNIS report. Viruses were confined to causing 30% of episodes of hospital-acquired gastrointestinal infections and 5.1% of eye, ear, nose, and throat infections.[3] Congenital infections such as cytomegalovirus (CMV) and herpes simplex virus (HSV), which rarely pose infection control problems,

are the more conventional scenarios in which viruses are discussed in neonatal units. Why, then, include a section on hospital-acquired viral pathogens in this volume? Viruses can cause considerable pathology, often present atypically in NICU patients, may be difficult to detect (many require specific antibody studies or viral isolation techniques, and thus need to specifically considered to be diagnosed), and can spread rapidly within NICUs. Control of outbreaks caused by viral pathogens often involves prolonged and strict adherence to isolation precautions and may not be achieved until after many patients and/or staff are affected. Unlike some bacterial pathogens, hospital-acquired viral infections may affect immune-competent children without traditional risk factors for hospital-acquired infections (eg, indwelling catheters or ventilators) and may be of increased relevance in well-baby nurseries or lower-acuity NICUs as well. An understanding of the range of viral pathogens that may be involved in hospital-acquired infections, their modes of spread, and potential methods of control are important to limit the scope of an outbreak.

Enteric Viruses

Most hospital-acquired viral infections in the NICU are the result of pathogens that are spread via the fecal-oral route. These can cause a range of clinical sequelae, but are nearly universally contained through the use of contact isolation. The Centers for Disease Control & Prevention recommendation for each of the viruses listed in this section is to maintain contact isolation (Ta-

ble 1) for the duration of illness. It is important to realize that even after the resolution of symptoms, neonates may continue to shed many of the viral pathogens discussed below and thus may serve as a reservoir for further spread. Documentation of viral clearance prior to removal of isolation precautions may be of benefit in this population.

Rotavirus

Rotavirus (RV) was isolated in >95% of the cases of hospital-acquired viral gastroenteritis reported to NNIS.[3] While other viral pathogens (eg, enteric adenoviruses, calicivirus, astrovirus) appear to be capable of causing clusters of disease in neonates,[4] it is clear that the greatest

Table 1. Summary of Infection Control Data for Nosocomial Viral Pathogens in the NICU

Virus	Incubation Period	Common Diagnostic Methods	Precautions (standard plus)	Viral Shedding (protracted in neonates)	Prophylaxis in Outbreak Setting
Rotavirus	1-3 d	EIA	Contact	Up to 5 d after cessation of symptoms	None
Hepatitis A	2-6 wk average 25-30 d	Serology (total and IgM)	Contact	2 wk prior to 1 wk after symptoms (infants likely asymptomatic)	IVIG HAV vaccine for HCW
Enteroviruses	3-6 d conjunctivitis 2-3 d	Viral isolation MA	Contact	3-4 d prior to 2 wk after symptoms (respiratory shedding < 1 wk)	None
RSV	2-8 d	IFA EIA Viral isolation MA	Contact	3 d prior to until cessation of respiratory symptoms Infants 3 d-4 wk	Palivizumab (investigational)
Influenza	1-3 d	IFA EIA Viral isolation MA	Droplet	1 d before symptoms appear through duration of symptomatic period	Amantadine or oseltamivir for HCW
Adenovirus	respiratory: 2-14 d GI: 3-10 d	IFA EIA Viral isolation MA	Contact and droplet	Several weeks possible	None
Parainfluenza	2-6 d	IFA Viral isolation MA	Contact	3-6 d prior to onset of symptoms until 10 d after resolution	None
Varicella	10-21 d Prolonged up to 28 d by VZIG	IFA Viral isolation MA	Airborne and contact	4 d before to 5 d after rash appears	VZIG Varicella vaccine for susceptible HCW
HSV	2 d to 2 wk	IFA Viral isolation MA	Contact	Skin: lesion onset until crusting Disseminated or mucosal may be prolonged.	N/A
CMV	Unknown	Serology Antigen detection Molecular detection	Standard	Prolonged, intermittent	N/A

NOTE. *Standard precautions:* handwashing, gloves for body fluid contact, masks/face and eye shields/gowns to avoid contact with fluids during procedures, patient care equipment disinfection. *Contact precautions:* Private room or cohorting of patients; gloves, hand washing, gowns. *Droplet precautions:* Private room or cohorting of patients; masks. *Airborne precautions:* Private room or cohorting; negative-pressure if possible; masks for susceptible personnel.

Abbreviations: RSV, respiratory syncytial virus; HSV, herpes simplex virus; CMV, cytomegalovirus; IFA, immunofluorescent assay; EIA, enzyme immunoassay; MA, molecular amplification (eg, polymerase chain reaction); N/A, not applicable; GI, gastrointestinal; IVIG, intravenous immune globulin; VZIG, varicella-zoster immune globulin; HCW, health care workers.

burden comes from this single agent. RV is a worldwide public health threat and causes >500,000 deaths annually.[5] However, symptomatic neonatal RV infection is relatively uncommon.[6,7] Maternal antibodies passed transplacentally are thought to afford some protection from symptomatic infection.[8,9] Effective protection from passive antibody acquired via breast-feeding has been less consistently shown.[10,11] Infection early in life, even with only mild or no symptoms, has been shown to be protective against later disease,[12] but neonatal RV may be acutely associated with electrolyte disturbances and poor weight gain. Reports of co-occurrence of RV with either necrotizing enterocolitis[13] or apnea and bradycardia[14] exist in the literature, but the significance of these associations remains unknown.

The epidemiology of RV can be confusing. Although there is a well-described seasonal variation in RV in the general population,[15] rates of disease in nurseries may not correspond to community trends.[6] Ill healthcare workers are often the initial source of RV infection, but this reservoir is not always clearly implicated. Some have raised the possibility that the relatively constant temperature and humidity within the NICU blunt these seasonal trends. Some nurseries show fluctuating rates of RV with increases in the colder months and fewer infants shedding the virus in the warmer months, and other studies show constant rates of shedding.[4] There may also be variation among units in the rate of symptomatic infections compared to asymptomatic carriage.[4]

RV may be introduced into the NICU by several routes. Reports of high levels of viral excretion during the first two days of life provide some evidence for vertical transmission of RV.[6,16] Any of the wide variety of non-newborns (physicians, nurses, hospital staff, family members) who come in contact with infants in the NICU may contribute to RV spread. Infant-to-infant transfer of RV via the hands of personnel or direct contact with people (especially ill healthcare workers) excreting the virus are possible mechanisms.[17] Although airborne infection,[18] fomites,[19] and contaminated formula are potential mechanisms of spread, there are no reports of NICU transmission through these means.

Once RV has been introduced to a NICU, it may be difficult to prevent spread. Fecal excretion of virus may begin prior to the onset of clinical illness (if present). Affected infants may excrete a large viral load with 10^8 to 10^{11} viral particles per gram of stool. In one study of RV in neonates, an infant with convulsions was transferred to a premature ward that had been RV free.[20,21] This child was later found to be infected with RV. Subsequently, 63% of the infants in that ward and 46% of infants in the nursery were found to be RV positive. Some infections occurred as early as 24 hours after the index case was diagnosed. The average time to diagnosis was 5 days after admission to the hospital or detection of the index case. Of note, all cases of RV in this outbreak were identical by molecular typing, indicating nosocomial spread. One week after the index case was admitted, infection control procedures were instituted. Although this decreased the number of new cases, it took weeks for the outbreak to subside.[21]

Because asymptomatic and prolonged shedding of RV is common, vigilance regarding hand washing and standard precautions are necessary to prevent outbreaks. These infection control practices must be in place routinely and adhered to continually, and not just when a case has been identified. Regular disinfection of surfaces and of potential fomites (eg, stethoscopes) may help in preventing spread as RV may remain viable on inanimate surfaces for prolonged periods.[22] Alcohol-based disinfectants and hand cleansers are important resources in the interruption of RV transmission. RV should be included in the differential diagnosis of a neonate with diarrhea and should be tested for promptly so that contact precautions, which should be instituted at the onset of diarrhea, and further case investigation can begin.

Hepatitis A

Infections with hepatitis A virus (HAV) are rare in NICUs, and affected infants usually have subclinical illness. However, the NICU appears to provide an excellent environment for the propagation of spread of HAV to other infants and health-care workers. There are multiple reports of HAV outbreaks in NICUs.[23-26] In these, the index cases were infected through various means including vertical transmission, blood transfusion, and undetermined causes. Al-

though each of these modes of transmission is rare, the common factor in each of these outbreaks was the rapidity of spread and the longevity of HAV in a NICU environment. In each case, HAV spread through the nursery to both infants and caregivers, and, in some cases, transfer of neonates to other facilities increased the extent of the outbreak. All neonatal infections in these descriptions were subclinical, and the outbreaks were detected as a result of clinical symptoms in caregivers.

Once HAV has been introduced, several aspects of the NICU setting appear to encourage spread of virus: 1) The likelihood that affected neonates may be asymptomatic; 2) Fecal-oral spread by personnel who care for multiple patients with tasks that may include the changing of diapers and the placement or manipulation of enteral feeding equipment; 3) Lack of adherence to hand washing and glove wearing; and 4) Increased duration of viral shedding among infants. In a study of risk factors for transmission during an outbreak, Rosenblum et al[26] noted that in addition to "nurse-sharing" between cases and uninfected infants, breaks in infection control procedure including drinking beverages in the NICU and not wearing gloves while manipulating intravenous tubing were associated with higher rates of spread. Outbreak control is best attained by strict adherence to contact precautions designed to prevent fecal-oral spread. Exclusion of symptomatic healthcare workers from patient care duties may be warranted.

One outbreak of HAV has been described in which the index case was thought to have acquired the infection vertically.[25] Although vertical transmission is rare[27] and disease in infants is usually subclinical, some experts recommend giving a single dose of immunoglobulin to an infant whose mother developed symptoms during the period from 2 weeks prior to delivery through 1 week postpartum.[28] In an outbreak setting, personnel with significant exposure should receive immunoglobulin.[28] Although there is no published recommendation regarding treatment of potentially exposed neonates with immunoglobulin during an outbreak, this intervention has been described by at least 1 group.[23] There is no role for postexposure hepatitis A vaccine in children under 2 years of age, and the vaccine has not been studied for postexposure prophylaxis of adults in an outbreak

setting. Since all of the described NICU outbreaks of HAV involved healthcare workers, education of that population as well as occupational health providers about the importance of screening exposed infants if a worker develops hepatitis A disease may be helpful in the early recognition of an outbreak. Vaccination of all NICU workers against HAV is not routinely recommended but merits study.

Enteroviruses

Whereas hepatitis A is rare and often asymptomatic in infants, the nonpolio enteroviruses (including enteroviruses, coxsackie viruses, and echoviruses) are common and may be associated with substantial morbidity and mortality in this population. The most common presentation of enteroviral infection is a nonspecific febrile illness; however, enteroviruses may be responsible for sepsis-like syndromes, myocarditis, meningitis, hepatitis or death.[29] Enteroviruses may spread via fecal-oral and respiratory routes as well as via fomites. Introduction of enteroviruses into a NICU frequently occurs as a result of transmission from an infected mother (often with a nonspecific febrile illness during the summer months) to her newborn infant.[2] Neonatal infections are relatively common[30] and many outbreaks in NICUs have been described,[31-35] some with high rates of serious disease. Viral shedding may occur without signs of active infection, and although respiratory tract shedding generally lasts for a week or less, fecal viral shedding can continue for several weeks. In temperate climates, outbreaks may occur in the general population yearly most often in the summer and autumn.[35] ICU cases may parallel community outbreaks.[36,37] In healthy infants, some data suggest that breast-feeding may protect against developing infection.[30] However, this has not been described in neonatal intensive care populations.

Eisenhut et al[38] recently reported a fatal case of coxsackie A9 infection caused by myocarditis in a full-term infant that occurred during an outbreak.[38] Infection control measures and the use of pooled human immunoglobulin appear to have been effective in halting spread. An outbreak of echovirus 33 (EV33) infection occurred in a newborn unit and involved 9 patients during an 11-day period.[35] Of these, 5 patients devel-

oped meningitis, 3 developed coagulopathy, and 1 died. The level of maternal antibody to EV33 appeared to be a predictor of severity of illness. Similar outbreaks with multiple infants developing systemic symptoms within days of the index case have been described with other echoviruses.[33,34] However, in other cases, the outbreak occurred weeks after admission of the index patient, while the patient was still excreting virus.[31,32]

Although some enteroviruses can be passed transplacentally, the more common means of maternal-infant transmission appears to be after birth via fecal-oral or respiratory spread. Spread among patients likely occurs more efficiently via the fecal-oral route than via the respiratory route, and prolonged shedding in the stool of patients and healthcare workers may facilitate the continuation of an outbreak as described above for RV.[39]

While there is no widely accepted treatment for enteroviral disease, several authors have described the use of immunoglobulin (IVIG) in outbreak settings and in life-threatening infections. Abzug et al[40] showed more rapid resolution of viremia and viruria in patients who received IVIG with high titers of neutralizing antibodies against the specific type of enterovirus with which they were infected. Pasic et al. described the use of prophylactic IVIG during a NICU outbreak of echovirus.[41] This decreased the risk of symptomatic viral infection from 19% in the untreated group to 5% in the group receiving IVIG. However, larger studies would be required before immunoglobulin could be routinely recommended for this use. Pleconaril is an antiviral agent with activity against enteroviruses.[42] While some data regarding treatment of severe enteroviral infections in neonates are available,[43] its role in the control of in-hospital spread of enteroviruses is unknown.

Respiratory Viruses

Respiratory viruses comprise the other major group of hospital-acquired viral pathogens affecting hospitalized infants, and while the causative agents are many of the same ones that affect other pediatric populations,[44] largely during the winter months, the clinical presentations may be quite different. Nonspecific clinical findings (eg, apnea, feeding intolerance) and a low

index of suspicion leading to failure to order specific viral tests likely contribute to a delay in the institution of proper isolation and to the propagation of outbreaks. Although the target organ of these viruses is the respiratory tract, control of the spread of respiratory syncytial virus (RSV), the most common respiratory virus affecting neonates, is achieved via contact isolation. Some other viral respiratory pathogens spread via droplets and require precautions to prevent that means of spread (Table 1).

Respiratory Syncytial Virus

Although RSV was known to be an important pediatric pathogen for several years prior,[45] it was not until 1979 that Hall et al[46] described the role of RSV in neonatal intensive care units. Neonatal RSV was found to be a protean disease, affecting premature infants far more frequently than had previously been appreciated, capable of causing considerable pathology, and involving a high percentage of NICU staff.[46] Since then, numerous reports of outbreaks in NICUs have confirmed these findings,[47-50] and RSV currently represents a major infectious cause of disease among critically ill neonates. Symptomatic RSV disease is less common in term neonates than in preterm infants, presumably due to transplacental acquisition of maternal antibodies. Numerous NICU outbreaks have shown that prematurity is a significant risk factor for acquisition of hospital-acquired RSV infection.[46,47]

There is strong evidence that compliance with contact precautions (gowning and gloves) prevents nosocomial spread of this virus.[51,52] However, despite increased vigilance, there continue to be hospital-acquired RSV outbreaks in NICUs with high attack rates and considerable morbidity. In addition, several reports exist of concurrent outbreaks of RSV and other respiratory pathogens (including rhinovirus, echovirus, and parainfluenza) in NICUs,[53-55] adding to difficulties in diagnosis, isolation, and containment of spread.

Spread of RSV within hospitals occurs largely on the unwashed or insufficiently washed hands of healthcare workers.[56] Cessation of outbreaks by enforcement of compliance with hand hygiene has been described,[57] and the use of gowns and gloves may confer additional benefit.[58] The high rate of transmission of RSV is also

thought to be related to its ability to survive on inanimate surfaces for minutes to hours. Even if hand washing takes place around the time of patient contact, the hands of caregivers may become contaminated by touching environmental surfaces. This can lead to spread to other patients and, often, to the caregiver. Affected caregivers are major components of many published outbreaks and contribute to inter-patient spread.[46] The development of antigen-based rapid diagnostic tests has contributed to the tracking and control of outbreaks.[59]

A targeted infection control program has been shown to decrease the amount of hospital-acquired RSV in a pediatric hospital and to be cost effective.[60] The measures undertaken in that particular program included education of staff, cohorting of infective patients and the nursing staff caring for them, maintenance of a high index of suspicion for new cases, contact precautions, and regular surveillance. This study included NICU patients, although the program was used in other pediatric populations as well. A strict infection control policy proved effective at decreasing spread during a NICU RSV outbreak.[47] In this study, cases of RSV were separated from other infants, and a separate team of nurses and physicians was assigned to that nursery. A policy of strict wearing of gowns, masks, and gloves during the handling of infected infants was observed. The nursery was cleaned and fumigated. Eight cases were found prior to the institution of these infection-control policies, but no new cases of RSV developed once they were in place. While these measures exceed those generally used to combat transmission of RSV in a NICU, they may be justified during an outbreak.

In addition to strict infection control measures, pharmacologic means have been explored to prevent the spread of RSV in the NICU. Infants meeting criteria laid out by the American Academy of Pediatrics routinely receive palivizumab to prevent severe RSV disease; however, the data regarding prevention of nosocomial spread of RSV by palivizumab are limited.[61] Cox et al[62] recently studied the use of palivizumab to prevent hospital-acquired RSV in infants at high risk for RSV (defined as infants <=35 weeks gestation or those with bronchopulmonary dysplasia) during an outbreak.[62] Palivizumab administration to susceptible infants correlated

with the end of an outbreak after increased infection control had failed. However, it is difficult to determine the role of palivizumab in ending the outbreak as there were a variety of measures in place. Controlled studies directed toward this question are needed.

Influenza

Outbreaks of influenza in NICUs are rarely reported, and cases in neonates are generally mild in part due to the presence of maternal antibody.[63-67] However, severe disease can occur, especially in premature infants. Diagnosis is important to ensure rapid institution of appropriate control measures as the short incubation period and droplet transmission by neonates may allow for rapid spread.[68] Rapid diagnosis may be made by direct immunofluorescence of nasopharyngeal aspirates. The presence of influenza in the general population should alert NICU personnel to suspect influenza in their patients.

Sagrera et al[63] described 2 outbreaks of influenza A over a 9-month period in 2 separate neonatal units in Barcelona, Spain.[63] In all, 30 of 95 infants in 2 NICUs were found to be infected with influenza A, of whom 22 (73%) developed symptoms. Risk factors for infection included low birth weight (mean birth weight 1622 g among cases, 2594 g among unaffected patients), low gestational age (mean gestational age 31 weeks among cases, 36 weeks among unaffected patients), twin pregnancy, and mechanical ventilation. An attack rate of 35% was documented in a retrospective study of an outbreak in a Canadian NICU.[65]

While annual vaccination is recommended for nursery personnel as well as parents/visitors to nurseries,[28] actual vaccination rates among hospital staff are often very low. When NICU personnel were surveyed during outbreaks, rates ranged from 2% to 45%.[63,66] Amantadine prophylaxis has been used for staff in outbreak settings but is not approved for use in infants.[65] Neuraminidase inhibitors may hold some promise as prophylaxis or treatment during outbreaks, but studies in NICU populations are not available. The most effective means of outbreak control is likely to be the routine vaccination of healthcare workers. Vaccination of healthcare workers, screening of asymptomatic infants,

droplet isolation of cases, limitation of sibling visitation during community outbreaks, and exclusion of affected adults from the NICU may all be of value in limiting the scope of outbreaks.

Adenovirus

Adenovirus infection is easily transmissible and there have been several reported NICU outbreaks.[69-72] Neonates are thought to gain some protection from maternally acquired antibodies; however, when infection does occur it can disseminate rapidly and is associated with a poor outcome. Factors that play a role in transmission include the difficulty of eliminating viral particles from environmental surfaces, long incubation period, and the ability to transmit virus through aerosols and direct and indirect contact. Infection in the neonate may have high morbidity and be confused with bacterial sepsis. Other manifestations can include URI symptoms, lower respiratory tract symptoms, conjunctivitis, gastroenteritis (caused by specific serotypes, generally 40 and 41), and fever. In neonates, disseminated disease including pneumonia, meningitis, or encephalitis may also occur.[2] Although long incubation periods may make outbreaks difficult to detect, early recognition of adenoviral infection may allow for limitation of viral spread. Coinfection of patients with adenovirus and other viral pathogens has contributed to delayed diagnosis (due to attribution of symptoms to another virus) with subsequent spread to staff members and other patients.[70] Another report of adenovirus spread within a NICU described a lower attack rate and less disseminated disease.[71] Significantly, healthcare workers were affected in that outbreak as well as in one of adenoviral conjunctivitis related to contaminated ophthalmology equipment.[69]

Control measures for adenovirus disease include contact and droplet precautions, strict enforcement of hand washing, proper disinfection of ophthalmologic and other medical equipment, cohorting of patients in outbreak situations, and exclusion of affected staff and parents from the unit. Protective eyewear for healthcare workers may be of use when caring for patients with adenoviral conjunctivitis to provide an additional barrier to patient-to-caregiver spread. Severe outbreaks may result in unit closure.[70]

Other Respiratory Viruses

Other respiratory viruses such as parainfluenza,[54,73-75] rhinovirus,[53] and coronavirus[76-78] may cause clusters of cases in NICU settings. These are generally associated with milder disease than RSV, and control follows the general principles outlined above.

Varicella-Zoster Virus

Neonatal varicella can occur via vertical transmission or hospital-acquired infection. Transmission of varicella zoster virus (VZV) occurs via direct contact with lesions or less commonly by aerosolized droplets. A long incubation period (10-21 days) and a period of maximum infectivity that lasts from 1 to 2 days before until 5 days after the onset of lesions make control of outbreaks difficult. Fortunately, such outbreaks seem to be rare and hospital-acquired disease is generally mild.[44]

The risk of horizontal transmission in nurseries is thought to be low because of physical barriers (such as isolettes) as well as high rates of passive immunity; only 5% to 10% of women born in the United States are thought to be susceptible to varicella,[79] and there is good transplacental passage of varicella antibody. Nonetheless, there are several reports of varicella outbreaks in NICUs.[80,81] Premature infants may be at increased risk because of decreased levels of antibody, although antibody may still be detectable in many of these infants.[82,83] The cornerstone of infection control management is to place infants who have had exposure on airborne isolation and provide passive immunization to high-risk infants with varicella zoster immunoglobulin (VZIG). Candidates for VZIG, according to the recommendations of the American Academy of Pediatrics,[28] are all hospitalized premature infants born at less than 28 weeks' gestation or 1000 g, those 28 weeks or greater if the mother has no reliable history or serologic evidence of varicella immunity, and those whose mother developed varicella between 5 days prior to and 48 hours after delivery. However, several reports show negative VZV antibody status and/or cases of varicella in infants of 28 to 32 weeks' gestation despite a positive maternal history of VZV.[80,81,84] Therefore, testing or empiric treatment in that subgroup may be justified. All

NICU healthcare workers should be vaccinated against varicella or show evidence of immunity. Of note, some commercially available serologic tests have low sensitivity and specificity for VZV antibodies in immunized adults.[85] In an outbreak setting, postexposure vaccine may be of benefit in exposed people over 1 year of age (eg, healthcare workers, family members).[28] With the increasing use of varicella vaccine in the community and a demonstrated decrease in disease,[86] it is likely that NICU exposures will be even less common in the near future.

Less Common Hospital-acquired Viral Pathogens

Herpes Simplex Virus

While HSV is a common and significant cause of disease in the neonatal period,[87] the vast majority of cases are acquired at the time of birth. Spread of HSV from caretakers with oral lesions or herpetic whitlow has been described, but outbreaks are rare.[88,89] Contact precautions and exclusion of caretakers with whitlow or with large oral lesions are generally sufficient to prevent spread. Workers with small oral lesions may continue to work provided that the lesions are adequately covered and proper infection control procedures are followed.

Cytomegalovirus

Greater than 1% of children excrete CMV in the neonatal period (and the number may be greater in populations with high rates of maternal immunity to CMV),[90] making it one of the most common congenital infections. Shedding in the urine or the saliva can be prolonged in neonates, but transmission in a NICU setting is rare. Child-to-child transmission of CMV is well described in the daycare environment.[91] However, routine hand washing seems to prevent spread in the NICU. Hospital-associated transmission has been documented by molecular techniques,[92] but a multiyear study by Adler et al[93] showed that the most common means of hospital-acquired CMV acquisition in neonates is via red blood cell transfusion.[93] Exclusion of pregnant caretakers from the care of CMV-excreting infants is not recommended, as healthcare workers frequently care for CMV-excreting children without an increased risk of acquiring

CMV infection.[94] Standard precautions are recommended for children known to be shedding CMV.

Transfusion-associated Viruses (Human Immunodeficiency Virus, Hepatitis B & C)

HIV, hepatitis B, and hepatitis C are of concern in the postnatal period mostly because of congenital infection. Transmission of these and other blood-borne pathogens is possible via transfusion of blood products, but current screening methods make this extremely unlikely. Secondary spread within a NICU has not been described, and standard precautions for patients with HIV, hepatitis B, and hepatitis C are indicated.

Conclusion

A wide variety of viral pathogens may be spread within neonatal units. Reported outbreaks and studies using video surveillance[95] and DNA markers[96] show an enormous capacity for spread of infectious organisms in this environment. Low gestational age and birth weight, incomplete transfer of maternal antibody, and atypical clinical presentations put these patients at increased risk of complications from viral infections. In addition, aspects of the NICU environment itself may predispose to rapid spread of these agents among patients, with healthcare workers as a common means of transmission. Clinical suspicion, rapid diagnosis, and prompt institution of proper infection control precautions, including occupational health service evaluation and possible exclusion of affected staff and family members from patient care areas, are critical components of an infection control program that can limit the impact that hospital-acquired viral infections have on NICU populations.

Acknowledgment

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