20.1 Introduction

Viruses are significant causes of nosocomial infections, but their importance has been underappreciated in the past. However, outbreak of severe acute respiratory syndrome (SARS), avian and pandemic influenza with high morbidity and mortality rates increased the awareness of intensivists regarding the devastating effects of nosocomial spread of viral infections in intensive care units (ICU).

Advances in medicine have led to a large number of immunocompromised patients susceptible to severe viral infections. Many such patients are cared for in the ICU and in turn become an infectious hazard for other vulnerable patients. Health care workers can acquire common viral infections from the community and spread them to susceptible patients in the ICU. Patients in neonatal (NICU) and paediatric (PICU) ICUs are most vulnerable because of the lack of prior immunity against many viruses circulating in the community. Recent improvements in diagnostic methods have enabled the rapid diagnosis and monitoring of many viral infections. Rapid and accurate typing of viral strains using a molecular technique can help identify the source of outbreaks. Also, specific postexposure prophylaxis and treatment are now available for many important nosocomial viral infections. In this chapter, we discuss some of the important viruses that could be associated with nosocomial infections in the ICU, according to their usual route of transmission (Table 20.1). Infection control measures recommended for preventing these viral infections are listed in Table 20.2.
Table 20.1 Mode of viral infection transmission in the intensive care unit

|                          | Respiratory route | Faecal–oral route | Blood and body fluid | Direct contact/ fomites |
|--------------------------|------------------|------------------|-----------------------|------------------------|
| Influenza viruses        | +++              | –                | –                     | ++                     |
| Respiratory syncytial virus | +++              | –                | –                     | ++                     |
| Parainfluenza viruses    | +++              | –                | –                     | ++                     |
| Adenovirus               | +++              | ++               | –                     | +++                    |
| SARS coronavirus         | +++              | ±                | –                     | ++                     |
| Varicella zoster virus (chickenpox) | +++ | – | – | ++ |
| Rotavirus                | +                | +++              | –                     | ++                     |
| Norovirus                | ++               | +++              | –                     | ++                     |
| Enterovirus/parechovirus | +                | +++              | –                     | ++                     |
| Hepatitis A virus        | –                | +++              | ±                     | ++                     |
| Hepatitis B virus        | –                | –                | +++                   | –                      |
| Hepatitis C virus        | –                | –                | ++                    | –                      |
| Human immunodeficiency virus | –            | –                | ++                    | –                      |
| Haemorrhagic fever viruses | ±                | –                | ++++                  | +++                    |
| Cytomegalovirus          | –                | –                | +                     | ++                     |
| Herpes simplex virus     | –                | –                | –                     | ++                     |
| Varicella-zoster virus (zoster) | –         | –                | –                     | ++                     |
| Rabies                   | –                | –                | ±                     | ++                     |

SARS severe respiratory distress syndrome; – Unlikely; ± possible; + common (the number of + is an arbitrary indicator of transmissibility)

20.2 Viruses Transmitted by Droplets and Airborne Route

20.2.1 Influenza Viruses

Influenza viruses (family Orthomyxoviridae) are classified into types A, B and C. Annual seasonal outbreaks of influenza are caused by minor antigenic changes (antigenic drift) seen in influenza A and B viruses. Major changes in antigenic subtypes (antigenic shift) are only found in influenza A virus and typically involve the emergence of novel hemagglutinin (H) and/or neuraminidase (N) proteins on the viral envelope. Pandemic influenza occurs when a new influenza A strain emerges, to which the majority of the world’s population has little or no immunity.
| Virus                                | Isolation or cohorting | Hand washing | Apron/ gown+ | Gloves | Masks/ goggles | Incubation | Duration of infectivity |
|--------------------------------------|------------------------|--------------|--------------|--------|----------------|------------|------------------------|
| Influenza viruses                     | ✓ (negative pressure) IB ✓ ✓ ✓ ✓ | ✓ IB         | ✓ IA         | ✓ IB   | 1–4 days       |            | Prodromal phase and 7 days after onset |
| Respiratory syncytial viruses (RSV)  | ✓ II                    | ✓ IA IB IA IA | ✓ IB IA     | ✓ IB   | 2–8 days       |            | 48 h before symptoms and 7 days from onset; longer in immunocompromised (up to 30 days) |
| Parainfluenza viruses                 | ✓                       | ✓ ✓ ✓ ✓      | ✓            | ✓      | 2–4 days       |            | As long as symptoms last |
| Adenovirus                            | ✓                       | ✓ ✓ ✓ ✓      | ✓            | ✓      | 5–10 days      |            | As long as symptoms last |
| SARS coronavirus                      | ✓ (negative pressure) IA ✓ ✓ ✓ ✓ | ✓ (FFP3 or N95) IB | ✓            | ✓      | 4–6 days (max. reported 14 days) |            | Peak at day 10 of illness, no reported transmission 10 days beyond resolution of fever |
| Varicella-zoster virus (chickenpox)   | ✓ (negative pressure) IB ✓ ✓ ✓ ✓ | ✓ IB         | ✓ IA         | ✓ IB   | 10–21 days     |            | 2 days before first vesicle until all lesions are crusted |
| Rotavirus                             | ✓                       | ✓ ✓ ✓ ✓      | ✓            | ✓      | 2–3 days       |            | 2 days before symptoms and up to 4–7 days after onset of illness |
| Norovirus                             | ✓ IB                    | ✓ IA IB IB IB | ✓ IB ±        |        | 15–48 h        |            | Up to 48 h after becoming symptom free |
| Enterovirus/ parechovirus             | ✓ (young infants often require care in SCBU or NICU) ✓ ✓ ✓ ✓ | ✓            | ✓            | ✓      | 2–25 days      |            | 7–14 days from onset of illness; asymptomatic shedding common |
| Hepatitis A virus                     | ✓                       | ✓ ✓ ✓ ✓      | ✓            | ✓      | 2–6 weeks      |            | Infectious 1 week before onset of illness, infectivity declines rapidly after onset of illness |
| Hepatitis B virus                     | ✓                       | ✓ ✓          | ✓            | ✓      | 2–3 months     |            | As long as patient is viremic |

(continued)
### Table 20.2 (continued)

| Virus                                  | Isolation or cohorting | Hand washing | Apron/gown† | Gloves | Masks/goggles | Incubation | Duration of infectivity |
|----------------------------------------|------------------------|--------------|-------------|--------|---------------|------------|------------------------|
| **Hepatitis C virus**                  | †                      | ✓            | ✓           | ✓      |               | 2–3 months | As long as patient is viremic |
| **Human immunodeficiency virus (HIV)** | †                      | ✓            | ✓           | ✓      |               | 3–6 weeks  | Indefinitely, though viremia can be controlled by therapy |
| **Viral hemorrhagic fever viruses (VHF)** | ✓ (high security isolation) | ✓  | ✓  | ✓     | ✓       | 3–21 days  | High infectivity during illness |
| **Cytomegalovirus (CMV)**              | ✓                      | ✓ (congenital CMV) | ✓ (congenital CMV) |        |               | 3–6 weeks from primary infection. | Congenital infection—from birth. Asymptomatic shedding common |
| **Herpes simplex virus (HSV)**         | ✓                      | ✓            | ✓           |        |               | Often due to reactivation | Until lesions have healed |
| **Varicella-zoster virus (shingles)**   | ✓                      | ✓            | ✓           |        |               | Due to reactivation | Until vesicles crusted over |
| **Rabies virus**                       | ✓                      | ✓            | ✓           | ✓      | ✓             | 2–8 weeks or longer | Duration of illness |

Categorisation of recommendations: IA strongly recommended for all hospitals and strongly supported by well-designed experimental or epidemiological studies; IB strongly recommended for all hospitals and viewed as effective by experts in the field (these recommendations are based on strong rationale and suggestive evidence, even though scientific studies may not have been performed). II suggested for implementation in many hospitals (these recommendations may be supported by suggestive clinical or epidemiological studies, a strong theoretical rationale or definitive studies applicable to some but not all hospitals.

**FFP3 or N95** high-filtration respirators, **SCBU** special care baby unit, **NICU** neonatal intensive care unit, ✓ recommended and suggested for implementation in most settings, **SARS** severe acute respiratory distress syndrome, **HIV** human immune deficiency virus, **VHF** viral haemorrhagic fevers, **CMV** cytomegalovirus.
There were three influenza pandemics in the last century, of which the pandemic in 1918 due to the H1N1 virus was the most severe. The first pandemic of this century occurred in 2009 [1] and was due to another H1N1 variant that emerged through a quadruple reassortment of viral RNAs derived from human, avian, Eurasian and North American swine influenza sources [2]. The presence of animal influenza subtypes, particularly avian influenza viruses such as H5N1, is of continuous concern, as these could be the source of future pandemics. Though with relatively high case-fatality rate, H5N1 avian influenza virus has so far only caused a limited number of human infections in restricted geographical locations with little evidence of human to human spread. However, the 2009 pandemic H1N1 virus proved to be a major burden for ICU staff [3].

Clinically, influenza infection is characterised by abrupt onset of fever, sore throat, myalgia, cough, headache and malaise. Young children may develop croup, pneumonia or middle ear infection. With seasonal influenza, complications are often seen in the elderly, the immunocompromised and those with pre-existing chronic heart or lung disease or diabetes. During the 2009 H1N1 pandemic, children and young adults were more susceptible [4]. Overall fatality rate was <0.5%, but as many as 9–31% of hospitalised patients needed ICU admission [5]. Severe disease and high mortality rates were seen in pregnant women, patients with underlying medical pulmonary, cardiac, metabolic, neuromuscular illness and severe obesity, and those in whom the diagnosis and admission was delayed [6–8]. Respiratory failures could be caused by viral pneumonia and acute respiratory distress syndrome (ARDS). In addition, secondary bacterial infection with *Streptococcus pneumoniae* or *Staphylococcus aureus* (often methicillin resistant) were found in 20–24% of ICU patients and 26–38% of patients who died [3, 5, 9]. Fatal cases were often complicated by multiorgan failure.

Influenza has a short incubation time of 1–4 days. The virus is transmitted via droplets, and patients are infectious during the prodromal phase and up to 7 days after symptom onset. Rapid antigen detection from respiratory secretions is available, but this was found to be insensitive for the 2009 H1N1 pandemic virus [10]. More sensitive and specific real-time polymerase chain reaction (PCR) methods had to be used [11]. Due to the infection-control hazards of taking nasopharyngeal aspirates or bronchoalveolar lavage, the use of throat and nasal swabs were advocated. A complete respiratory diagnostic workup needed to be performed to exclude other viral, bacterial and noninfectious causes. A single negative influenza PCR result on an upper respiratory sample did not definitively exclude the diagnosis [12]. In addition, other concurrent or secondary infections had to be considered. Protocols needed to be in place to ensure satisfactory triage of patients according to severity [13]. Early administration of specific neuraminidase inhibitors, such as oral doses of oseltamivir or inhalation zanamivir, seemed to be beneficial [14]. In more refractory cases, the off-license use of intravenously administered zanamivir or peramivir was tried. Extracorporeal membrane oxygenation (ECMO) was found to be useful in very severe cases [12].

The risk of nosocomial transmission to other hospitalised patients and staff is well documented. Infected patients should ideally be cared for in a single room
or cohorted together. Health care workers should be protected through the proper use of personal protective equipments, including respirators or masks, eye protection, gowns/aprons and gloves [15, 16]. High-filtration respirator to FFP3 (Europe) or N95/N99 (USA) standard should be used for staff carrying out aerosol-generating procedures after fit testing and training. Surgical masks should be adequate for nonaerosol contacts [16]. Environmental contamination is an important source of transmission. Good hand hygiene can prevent transmission through this route.

Vaccination is the most specific preventative measure. Annual seasonal influenza vaccination to vulnerable individuals and health care workers has been advocated. A specific vaccine against the H1N1 pandemic strain was developed within months of the onset of the outbreak. However, vaccine uptake rates amongst health care workers are usually poor, and more needs to be done to educate both patients and staff.

20.2.2 Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) (family Paramyxoviridae) is a major cause of lower respiratory tract infections in young children and infants. There are two subtypes, A and B, with varying dominance in different years [17]. The incidence of RSV is seasonal in temperate climates, and hospital admissions usually peak during winter months. Prematurity, bronchopulmonary dysplasia and congenital heart disease are associated with a significant risk for admission to high-dependency units or PICU. In Switzerland, it was estimated that approximately 1–2% of each annual birth cohort required such admission. RSV can also cause significant disease in adults, particularly in immunocompromised individuals such as patients undergoing therapy for haematological malignancies, the elderly and those with chronic pulmonary disease [18].

The most rapid diagnosis of RSV is by direct antigen detection methods such as chromatographic immunoassays. A typical rapid test method is completed within 30 min and can be used as a point of care testing method in emergency rooms and ICUs. However, these rapid tests lack sensitivity [19]. More recently, many laboratories have begun using multiplex real-time nucleic acid amplification techniques (NAAT) to diagnose respiratory tract infections, including RSV [20]. Although NAAT is highly sensitive, it is not a rapid testing method. Hence, it is desirable to have a mixed strategy of diagnostic approaches, such as an initial rapid direct antigen test followed by retesting of negative samples by NAAT.

Nosocomial transmission of RSV in the ICU and haemoncology units has frequently been reported. It is important to identify infected patients and to apply prompt and effective infection control measures (Table 20.2). It is recognised that a combination of cohorting patients using dedicated health care staff, contact isolation of patients, strict adherence to hand hygiene; and screening visitors, family members and health care staff for upper respiratory tract infection symptoms significantly reduce the cross-infection rate of RSV. In haemoncology units,
the practice of enhanced seasonal infection control programs for RSV has been shown to be effective [21]. The usefulness of wearing masks and goggles is less clear.

There is no safe and effective vaccine to prevent RSV infection. However, immunoprophylaxis in the form of RSV immunoglobulin (RSV-IG) or humanised monoclonal antibodies (palivizumab) is available as prophylaxis for some high-risk patients to prevent serious RSV disease or to limit further nosocomial spread. Both palivizumab and RSV-IG have been shown to decrease the incidence of RSV hospitalisation and ICU admission, although there was no significant reduction in the risk of mechanical ventilation or mortality rate. When given prophylaxis, infants born <35 weeks gestational age and those with chronic lung and congenital heart disease all had a significant reduction in the risk of RSV hospitalisation [22].

Treating RSV infection is mainly supportive, including oxygen, ventilation and bronchodilatative drugs. Aerosolised ribavirin has often been used in severe cases, with or without gamma globulin i.v. [23]. However, evidence for the clinical efficacy of ribavirin in RSV infection remains inconclusive [24]. The use of aerosolised ribavirin needs to be carefully controlled, as there are potential teratogenic effects on pregnant staff and visitors. Others have tried a combination of palivizumab i.v. with or without ribavirin [25].

Another paramyxovirus, known as human metapneumovirus (hMPV), shares a similar spectrum of clinical illness as RSV. It is likely that general infection control measures against RSV would also be effective against hMPV.

### 20.2.3 Parainfluenza Viruses

There are four types of human parainfluenza virus (PIV) types: PIV 1–4 (family Paramyxoviridae). Infections with PIV1 and 2 are seasonal, with a peak in autumn affecting mainly children between 6 months and 6 years of age. Clinically, patients often present with croup or a febrile upper respiratory tract infection. In contrast, PIV3 is endemic throughout the year and infects mostly young infants in the first 6 month of life and up to 2 years of age. Clinically, there is no specific presentation in PIV3, but bronchiolitis and pneumonia are not uncommon. In immunocompromised adults, such as stem cell transplant recipients, PIV3 is associated with a high mortality rate. Such patients often present with severe pneumonia and many require admission to the ICU.

The diagnosis of PIV infection can be confirmed by immunofluorescence antigen detection or NAAT [26]. Nosocomial transmission is often due to PIV3 and has been documented in neonatal care and adult haematology units [27]. Infection control precautions are the same as for RSV. Despite several uncontrolled case series of apparent successful use of intravenously, orally or aerosolised administration of ribavirin to treat PIV infections, there is no clear evidence that ribavirin with or without immunoglobulin alters mortality rates from PIV3 pneumonia or decreases the duration of viral shedding from the nasopharynx [28]. Nevertheless, there may be a role for pre-emptive early therapy with ribavirin to prevent progression of upper airway infection to pneumonia.
20.2.4 Adenovirus

Adenovirus (family Adenoviridae) multiplies in the pharynx, conjunctiva or small intestine. Clinically, the infection is localised and typically presents with pharyngitis, conjunctivitis or gastroenteritis depending on serotype. However, in young infants and immunocompromised patients such as organ transplant recipients or AIDS patients, adenovirus can cause severe pneumonia, disseminated infection or haemorrhagic cystitis. The diagnosis can be confirmed by specific antigen detection tests on respiratory or stool samples. Viremia and viruria can be confirmed and quantified using real-time PCR.

In respiratory infections, the virus spreads via droplets or through contaminated hands or fomites. Nosocomial adenovirus infections have been reported and can be a particular problem in neonatal units. It is important to adhere to strict infection control procedures to prevent nosocomial spread (Table 20.2). In vitro, adenovirus is susceptible to antivirals such as cidofovir and ribavirin [29]. Use of cidofovir in selected patients may be successful [30].

20.2.5 Severe Acute Respiratory Syndrome: Coronavirus

A respiratory virus that caused a severe acute respiratory syndrome (SARS) emerged from southern China in 2002. The virus was subsequently identified as a novel virus from the Coronaviridae family and was named SARS coronavirus (SARS CoV) [31]. SARS was associated with a high mortality rate, and of the most concern to the international community was the potential in causing nosocomial infections. From a single index case in a Hong Kong hotel, a series of chains of outbreaks occurred in Vietnam, Singapore and Canada [32]. Subsequently, infections were reported in major cities in Asia, Europe and USA, transmitted through international travel. In total, 8,422 individuals were infected, with 916 deaths around the world. The emergence of SARS was the first wake-up call to the medical community regarding the need for comprehensive infection control policies in hospitals and ICU. This also led to the general provision of personal protective equipment (PPE) with training and fitting programmes for health care workers in many countries.

SARS is infectious from the onset of illness and infectiousness correlates with the degree of viral shedding. Incidences of superspreaders or superspreading events may have accounted for most of the large-scale transmissions. Older age and underlying comorbidity are major risk factors for fatality [33]. Viral loads in various anatomical sites also correlate with the severity of symptoms and mortality. Shedding of SARS CoV peaks at day 10 after the onset of symptoms. The disease pathology is characterized by uncontrolled viral replication, with a major proinflammatory response. The optimal therapy for SARS is still not clear, as there were no randomized controlled trials conducted. Treatment with interferon (IFN)-\(\alpha\), steroid, protease inhibitors (such as lopinavir) together with ribavirin, or convalescent plasma containing neutralising antibody, could all be useful.
Prophylaxis with IFN or hyperimmunoglobulin may also be considered as post-exposure prophylaxis [34].

SARS CoV is identified as a zoonosis with a natural reservoir in Chinese horseshoe bats [35]. Its emergence is associated with local culinary practice in southern China, leading to captured palm civets acting as the amplifying host and passing on infection to human. As long as the reservoirs and amplifying hosts coexist, there is a potential for SARS to re-emerge. Intensivists should always be on the lookout for patients with unexplained severe respiratory infections and consider SARS as a possible differential diagnosis.

### 20.2.6 Varicella Zoster Virus: Chickenpox

Primary varicella zoster virus (VZV) (family Herpesviridae) infection causes chickenpox. This is a common self-limiting childhood infection characterised by a mild fever and a generalised vesicular rash. Risk factors for severe disease include immunosuppression, smoking and pregnancy. Complications include bacterial sepsis, pneumonia, encephalitis, ataxia, toxic shock, necrotising fasciitis and haemorrhagic chickenpox with disseminated coagulopathy and fatality [36].

Chickenpox is highly infectious and can be transmitted via inhalation of respiratory secretions or by direct contact. Patients are likely to be infective 48 h before the appearance of the rash until the last lesion has crusted over. Outbreaks in the ICU have frequently been reported [37, 38]. Infected patients should be promptly isolated, preferably in negative-pressure rooms.

A rapid diagnosis of chickenpox can be made by electron microscopy or immunofluorescence of scrapings from the vesicle base. A person who has had chickenpox does not develop chickenpox again, but the virus may reactivate as zoster/shingles. Susceptibility to chickenpox can be determined by testing for the presence of VZV immunoglobulin (Ig)G. Infected patients need to be isolated immediately, and exposed patients and staff investigated. Exposed staff who are susceptible to VZV should be excluded from contact with high-risk patients for 8–21 days postexposure. Susceptible individuals at risk of severe disease should receive varicella-zoster immunoglobulin (VZIG) prophylaxis, which could be given up to 10 days after exposure.

Neonates born to mothers who developed chickenpox 7 days before to 7 days after delivery are highly susceptible due to a lack of protective maternal antibodies. In such cases, VZIG prophylaxis to the neonate is recommended. The baby should also be isolated. Intravenously administered acyclovir should be started promptly at the first sign of illness. Most childhood chickenpox does not require treatment. However, in severe cases (e.g. pneumonitis, disseminated disease with visceral involvement and patients requiring hospitalisation), intravenously administered acyclovir (10 mg/kg 8 hourly) is the treatment of choice. Treatment of neonates will require a higher dose (20 mg/kg 8 hourly). A live attenuated vaccine against VZV is available. Susceptible health care workers should be immunised.
20.3 Viruses Transmitted by the Faecal–Oral Route

20.3.1 Rotavirus

Rotavirus (family Reoviridae) is highly infectious and a significant cause of nosocomial gastroenteritis, particularly in children <5 years of age. Patients present with sudden onset of fever, vomiting, abdominal pain and watery diarrhoea. Due to the high viral shedding in the faeces, a diagnosis can be easily obtained using antigen-detection enzyme-linked immunosorbent assay (ELISA) or electron microscopy.

In temperate climates the infection is seasonal with peaks in winter, and hospital outbreaks often coincide with outbreaks in the community. In Europe, it was found that 49–63% of paediatric nosocomial gastroenteritis was positive for rotavirus, with an incidence of 1–2.3 per 1,000 hospital days, leading to prolonged hospitalisation between 1.5 and 4.5 days [39]. Very sick infants with gastroenteritis may require intensive care and could, in turn, be the source of nosocomial infection in ICU. Premature and very low birth weight infants (<1,500 g) are particularly at risk, as severe complications such as necrotising enterocolitis and intestinal perforation are commonly reported. A Dutch study found that amongst all nosocomially acquired viral infections in NICUs, 10% were due to rotavirus, which demonstrates the importance of this infection in the ICU setting [40].

Nosocomial rotavirus infections in adults have also been reported and occasionally cause serious complications in the elderly and immunosuppressed patients. Nosocomial transmission has been previously associated with ungloved nasogastric feeding, contaminated toys, shortage of nurses, overcrowding and high patient turnover. Adherence to effective infection control measures (hand hygiene, enteric precautions; Table 20.3), as well as adequate staffing and patient cohorting/isolation can therefore help prevent or manage an outbreak [41]. The recently developed rotavirus vaccine could substantially reduce the incidence of nosocomial infections [42].

20.3.2 Norovirus

Norovirus (family Caliciviridae) is the most common cause of nosocomial outbreaks of gastroenteritis. Symptoms typically comprise profuse diarrhoea and projectile vomiting. The diagnosis can be confirmed by ELISA, RT-PCR or electron microscopy of stool samples. Noroviruses are highly infectious and are usually transmitted by direct contact via the faecal–oral route or via oropharyngeal exposure to aerosolised vomit. A number of outbreaks have recently been described in NICUs involving mainly premature neonates, some of whom developed necrotising enterocolitis. Neonates and immunocompromised patients can shed the virus for a prolonged time over months, which emphasises the need for rigorous adherence to effective infection control measures (Table 20.3). Additional measures such as increased hand hygiene and wiping of floors and
incubators with agents active against caliciviruses have been proven to be particularly useful in controlling outbreaks in NICU wards [43].

### 20.3.3 Enteroviruses and Parechoviruses

Both enteroviruses and parechoviruses (family Picornaviridae) have numerous subtypes. Enteroviruses include polioviruses, coxsackieviruses, echoviruses and other numbered enteroviruses. There are as many as 14 types of human parechoviruses [44]. Parechovirus type 3, in particular, can cause severe infection in young infants [45].

Both viruses are significant causes of nosocomial infections, particularly in the NICU. Enterovirus outbreaks involving up to 23 neonates have been reported [46], and an attack rate of 29% was reported. Enterovirus infections can present as neonatal sepsis, meningoencephalitis, myocarditis, hepatitis or gastroenteritis. Necrotising enterocolitis with pneumatosis intestinalis is a known complication in neonates. Some enteroviruses, such as Enterovirus 71, can cause severe and fatal illness in older children. Parechoviruses can cause meningoencephalitis [47] and a sepsis syndrome in young infants [48]. Enteroviruses and parechoviruses are genetically distinct from each other and require a different RT-PCR for diagnosis. Sequencing of the gene encoding the VP1 region of the virus has been used to identify outbreak strains.

With the global polio eradication programme, poliomyelitis is no longer a common nosocomial infection, although health care workers in the ICU who may

### Table 20.3 General measures to control outbreak of viral gastroenteritis [41]

| Measure | Category |
|---------|----------|
| Hand washing (liquid soap) or decontamination (aqueous antiseptic/alcohol based-hand rub) | A |
| Wear disposable gloves and aprons when contact with stool or vomitus is likely | B |
| Isolate symptomatic individuals (particularly with uncontrolled diarrhoea, incontinence, and children) | B |
| Avoid unnecessary movement of patients to unaffected areas | B |
| Staff working in affected areas must not work in unaffected areas within 72 h | B |
| Exclude symptomatic staff members from duty until symptom free for 72 h | B |
| If a large number of patients is involved and no further isolation facilities are available, close the unit to new admissions or transfers until 72 h after the last new case | B |
| Terminal cleaning of the environment, using freshly prepared hypochlorite (1,000 ppm) on hard surfaces | B |
| Caution visitors and emphasise hand hygiene | B |

Categorisation of recommendations: A strongly recommended for all hospitals and strongly supported by well-designed experimental or epidemiological studies; B strongly recommended for all hospitals and viewed as effective by experts in the field.
be in contact with live vaccine poliovirus shedding infants should ensure that they are immunised.

Rigorous hand washing (Table 20.3) is the most important measure during an outbreak. Cohort nursing, source isolation and screening are other measures frequently used (Table 20.3). Clearance of the virus by the host is antibody-mediated and many have advocated the use of normal human immunoglobulin (NHIG).

20.3.4 Hepatitis A Virus

Hepatitis A virus (family Picornaviridae) belongs to the same family as enteroviruses and is usually transmitted via the faecal–oral route. Nosocomial transmission of hepatitis A virus is well documented. An outbreak in an adult ICU (AICU) occurred as a result of inadequate precautions taken while handling bile of a patient not suspected of incubating hepatitis A [49]. Most other outbreaks occurred in PICUs or NICUs, with attack rates varying between 15 and 25%. Risk factors for outbreaks have been attributed to handling soiled bed pads, nappies or gowns of an index patient, failure to wash hands, and eating in the ICU. In the NICU, vertical transmission and blood transfusion have been implicated as the cause of infection in the index case. The effect of nosocomial hepatitis A infection varies from asymptomatic to classic presentation with acute hepatitis. Diagnosis is by serological detection of hepatitis-A-specific IgM. The use of molecular techniques such as RT-PCR can help identify early infection or in difficult cases, such as those with immunodeficiency. Sequencing of PCR products is useful in establishing epidemiological linkage during outbreaks. NHIG has been successfully used for postexposure prophylaxis to control outbreaks. There is now increasing evidence that hepatitis A vaccine can be used for prophylaxis if the contact occurs within 14 days from onset of illness in the index case [50].

20.4 Viruses Transmitted by Blood and Body Fluid

The most commonly encountered nosocomial blood-borne viruses are hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The main risks are transmission from patients to health care workers. However, transmissions between patients and from health care workers to patients have been reported. The best way to prevent occupational exposure of blood-borne viruses is to practice universal precautions. Blood and body fluids (Table 20.4) from any patient, whether or not there are identifiable risk factors, should be considered as a potential risk. This encourages good and safe practice and helps prevent unnecessary accidents. Physical isolation of patients with blood-borne virus infection is generally not necessary unless there is profuse uncontrolled bleeding. Infection-control teams and occupational health departments should adopt a proactive approach to educate and prevent sharps injury (Table 20.5). There should also be specific instructions on how to deal with blood and body fluid exposure (Table 20.6).
20.4.1 Hepatitis B Virus

HBV is the most infectious of the three common blood-borne viruses. The risk of transmission depends on the viral load of the source patient. An HBV-infected individual with hepatitis B “e” antigen (HBeAg) tends to have a high viral load and is therefore more infectious than carriers without HBeAg. Estimate of infectivity ranges from 2% (HBeAg absent) to 40% (HBeAg present). All health care workers should be immunised against HBV. Exposed health care workers who are susceptible (not immunised or vaccine nonresponders) should receive hepatitis B immunoglobulin for postexposure prophylaxis. A booster dose of vaccine should be given to those exposed individual who had previously been successfully immunised.

20.4.2 Hepatitis C Virus

HCV is probably the commonest blood-borne virus encountered in Western countries. In the UK over a 3-year period, 462 incidences of occupational exposure to HCV were reported in comparison with 293 of HIV and 151 of HBV [51]. Follow-up studies of health care workers who sustained a percutaneous exposure to blood from a patient known to have HCV infection have reported an average incidence of seroconversion of 1.8% (range 0–7%). No vaccine or postexposure prophylaxis was available to prevent HCV transmission. Early diagnosis is essential, as early interferon treatment after seroconversion has a high success rate for eradication [52]. Exposed health care workers should be followed up at 6 and

Table 20.4 Body fluids that may pose a risk for hepatitis B and C virus (HBV, HCV) and human immunodeficiency virus (HIV) after significant exposure

- Amniotic fluid
- Breast milk
- Cerebrospinal fluid
- Exudate from burns or skin lesions
- Pericardial fluid
- Peritoneal fluid
- Pleural fluid
- Saliva after dental treatment
- Synovial fluid
- Unfixed tissues or organs
- Any other fluid if visibly blood stained

Saliva, urine, vomitus or stool that are not blood stained are not considered as high risk for blood borne viruses
12 weeks for HCV RNA testing and promptly referred for treatment if found infected.

### 20.4.3 Human Immunodeficiency Virus

The average risk of HIV transmission after percutaneous exposure to HIV-infected blood is about 0.3%. After mucocutaneous exposure, the risk is estimated to be <0.1%. A case-control study [53] identified four factors with increased risk of transmission:

- deep injury;
- visible blood on the device that caused the injury;
- injury with a needle that has been placed in a source patient’s artery or vein;
- terminal HIV-related illness in the source patient.

This study also showed that the use of zidovudine prophylaxis reduce the risk of transmission by 80%. Postexposure prophylaxis (PEP) should therefore be offered to all health care workers who have significant exposure to blood or body fluid from a patient known to be at high risk of or to have HIV infection. Various PEP options are available depending on national recommendations. This should be started as soon as possible after exposure and continued for 4 weeks.
20.4.4 Viral Haemorrhagic Fevers

Viral haemorrhagic fevers (VHFs) are severe and life-threatening diseases caused by a range of viruses. They are either zoonotic or arthropod-borne infections and are often endemic in certain parts of the world. They are often highly infectious through close contact with infected blood and body fluid and therefore pose a significant risk of hospital-acquired infection. As many patients with VHF present with shock and require vigorous supportive treatment, it is a potential problem in the ICU. The major viruses of nosocomial concern in this setting are Marburg, Ebola, Rift Valley fever, Lassa and Crimean Congo haemorrhagic fever (Table 20.7). The incubation period for these VHFs ranges from 3–21 days. Initial symptoms are often nonspecific but may eventually lead to haemorrhage and shock. Any febrile patient who has returned from an endemic area of one of the VHF agents or has a history of contact with cases suspected to have VHF within 3 weeks should be considered as at risk. However, malaria should always be excluded. A risk assessment needs to be performed, and any patient known or strongly suspected to be suffering from VHF should be admitted to a high-security infectious disease unit that is designed to manage these patients. While awaiting transfer to a secure unit, such patients should be placed in a negative-pressure room with strict source isolation. Specimens for patient management should be processed in a high-security laboratory designated for category 4 pathogens, and the aetiological agent established using PCR, serology and virus culture. All areas and materials in contact with infected patients should be autoclaved, incinerated or treated with hypochlorite (10,000 ppm of available chlorine). If the patient dies, the body should be placed in a sealable body bag sprayed or wiped with hypochlorite. Individuals who have been in contact with a case of VHF should be put under surveillance for 3 weeks. The successful i.v. use of ribavirin has been reported in some cases of VHFs (Lassa, Crimean Congo haemorrhagic fever and Hantaan). Apart from yellow fever, no vaccines are available.

| Virus                        | Geographic distribution                                                                 | Reservoir | Vector   |
|------------------------------|-----------------------------------------------------------------------------------------|-----------|----------|
| Marburg and Ebola            | Sub-Sahara Africa                                                                      | Bats      | None     |
| Rift Valley fever            | Mainland Africa                                                                        | Sheep, cattle | Mosquito |
| Lassa                       | West Africa                                                                            | Rodents   | None     |
| Crimean Congo haemorrhagic fever | East, West and South Africa, North and Central Asia, Middle East, India and Pakistan, Balkans, West China | Cows, hares, birds, hedgehogs | Ticks |

Table 20.7 Viruses responsible for viral haemorrhagic fevers with nosocomial concern in the intensive care unit
20.5 Viruses Transmitted by Direct Contact

20.5.1 Varicella Zoster Virus; Shingles

Shingles or zoster is the result of the reactivation of latent VZV (family Herpesviridae) in the dorsal root or cranial nerve ganglia. The clinical presentation is a painful vesicular eruption covering the affected dermatome. The clinical diagnosis can be confirmed rapidly by immunofluorescence, electron microscopy or PCR of the cellular material obtained from a vesicular scraping. The infection is usually self-limiting but can be more severe in immunocompromised patients, in whom it may present over multiple dermatomes or as a disseminated infection. The latter cases should be managed as if they were chickenpox, and respiratory precautions for infection control have to be enforced.

Patients or health care staff members with classic shingles are contagious from the day the rash appears until the lesions are crusted over. There is some risk of nosocomial transmission if the lesions are on exposed areas of the body or in immunocompromised infected patients. Nonimmune (VZV-IgG negative) patients or health care staff members with no history of chickenpox are susceptible if they have close contact with shingles and should be managed as described for chickenpox contact.

20.5.2 Herpes Simplex Virus

The herpes simplex virus (HSV) (family Herpesviridae) consist of two types: HSV-1 and HSV-2. Clinically, they most commonly manifest with oral (mainly HSV-1) or genital (mainly HSV-2) ulcerations/vesicles, and reactivation is common, particularly in the ICU. Other presentations include keratitis, encephalitis, meningitis, herpetic whitlow or neonatal infection.

The diagnosis can be confirmed rapidly by immunofluorescence, electron microscopy or PCR of vesicle/ulcer scrapings. In the immunocompromised patient, HSV can cause life-threatening disseminated infection and, early treatment with acyclovir i.v. is recommended. It has also been suggested that occult herpes virus reactivation may increase the mortality risk of ICU patients [54].

As the infected lesions contain virus, there is an increased risk of nosocomial transmission until the lesions have crusted over. Standard isolation precautions should be in place to reduce transmission (Table 20.2). Patients with active lesions should be nursed away from high-risk patients (i.e. immunocompromised, severe eczema, burns, or neonates). As patients can be asymptomatic secretors, health care workers should wear gloves when dealing with mucosal secretions (i.e. saliva) to avoid infections such as herpetic whitlow. Infected staff should cover lesions if possible and should not attend those at risk.

Neonatal herpes is usually transmitted from mother to the child at the time of delivery and may not be noticed until the infant develops the disease. Universal precautions, in particularly, hand washing, should always be in place to reduce
transmission of infection. To contain or prevent an outbreak, infected cases should be cohorted and nursed by dedicated staff who will not attend noninfected infants.

**20.5.3 Rabies Virus**

Rabies virus (family Rhabdoviridae) is usually transmitted to humans following exposure to saliva of a rabid animal (e.g. dog, fox, bat) via a bite or scratch, but only 40% of exposed people develop disease. The virus spreads from the wound to the central nervous system causing fatal encephalitis, and the virus may be present in the patient’s saliva, skin, eye, and brain tissue. The diagnosis can be confirmed by demonstrating the virus directly in brain tissue or saliva by RT-PCR or by immunofluorescence detection of antigen in skin biopsies from the nape of the neck. Due to the severe and paralysing effect, patients may be admitted to the ICU. To date, no case of nosocomial transmission has been reported apart from two patients who received corneal transplants from infected donors. Suspected or proven cases should be placed in standard isolation and appropriate precautions taken when dealing with potential infectious secretions (e.g. wearing of mask if dealing with oral secretions). Any health care worker with a significant exposure (e.g. splash of secretion onto mucosa or broken skin) should receive rabies vaccine and specific immunoglobulin.

**20.6 Summary**

Viral infection can cause significant morbidity and mortality and has the potential to result in cross infection, involving patients as well as health care workers. Good infection-control practice is essential to prevent nosocomial infection. Intensivists should be on the alert for important viruses causing infections according to age group of patients and mode of transmission and should never be complacent. Good liaison with the laboratory is essential for determining correct diagnostic tests and timely report of results to help in patient management.

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