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Infectious disease agents include viruses, bacteria, fungi, protozoa, parasites, and proteins called prions. Some patients are asymptomatic from their infection, whereas in other patients, clinical or subclinical illness affects the patient during the perioperative period. Transmission of the agents can occur through airborne inhalation, through contact with contaminated body fluids, via food, through physical contact, or through vector organisms. Additionally, patient-patient and patient-healthcare worker (HCW) transmission of infectious diseases remain a high concern. The perioperative period represents a unique challenge in the prevention of transmission. While diligent hand washing remains a staple in the standard of care, other measures must be implemented with certain infectious agents. Several of the major infectious diseases will be reviewed in this section, and universal precautions will be examined. Careful perioperative planning and situational awareness should be practiced by the healthcare worker taking care of patients with transmissible diseases.

Human Herpes Virus

The human herpes family viruses (HHV) consist of eight separate viruses, all with potential of causing human disease. The prevalence of *HSV-1* (HHV-1) and *HSV-2* (HHV-2) in the general population is 65 % and 29 %, respectively. HSV-1 is mostly transmitted through nonsexual contact and is most frequently associated with oral mucosal lesions, while HSV-2 is mostly transmitted through sexual contact and

commonly infects urogenital mucosa. Shortly after primary infection, the virus can be found in a dormant state in sensory neurons. Reactivation may occur at a later time. Immunocompromised patients are at increased risk for reactivation with subsequent disseminated disease. HSV reactivation in posttransplant patients can cause pneumonia, hepatitis, encephalitis, and disseminated disease. Oral acyclovir has been shown to be an effective prophylactic and treatment agent for HSV-1 and HSV-2.

Varicella zoster virus (VZV, HHV-3) is responsible for chickenpox and shingles in the healthy, immunocompetent population. However, it may cause significant, life-threatening disease in the immunocompromised population, such as posttransplant patients. Primary infection (chickenpox) or reactivation (shingles) in healthy patients with intact immune systems will manifest with a vesicular rash in a dermatomal pattern. Shortly after primary infection, VZV remains dormant in neurons of dorsal root ganglia. However, reactivation in posttransplant patients may manifest with cutaneous infection, encephalitis, myelitis, and pneumonia. Many studies have documented the efficacy of acyclovir and ganciclovir for the prophylaxis of VZV. Vaccination is available for patients and their close contacts and has shown to be effective in preventing disease.

Epstein-Barr virus (EBV, HHV-4) is the causative virus associated with infectious mononucleosis and the more serious (but rare) Burkitt's lymphoma, nasopharyngeal carcinoma, and posttransplant lymphoproliferative disorder (PTLD). About 90 % of the general population has been found to be seropositive for EBV. While patients generally demonstrate flu-like symptoms, more significant symptoms may occur. These include encephalitis, optic neuritis, and hepatosplenomegaly with increased risk of splenic rupture. Like VZV, EBV is generally transmitted through respiratory secretions and saliva. Shortly after primary infection, EBV can be found in a dormant state in B cells of the immune

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system. No vaccination currently exists for EBV, although some studies have shown the effectiveness of antiviral medications for treatment.

Cytomegalovirus (CMV, HHV-5) is a common infection with a prolonged latency period. Estimates of seropositivity rates range from 40 % in young adults to above 90 % in the elderly population. While most infections occur asymptotically in the healthy population, immunocompromised patients are at risk for disseminated disease. In particular, post-lung transplant patients are at risk for CMV pneumonitis, a common cause of bronchiolitis obliterans syndrome. Valganciclovir has been shown to be an effective prophylactic measure in these high-risk patients.

HHV-6, a common infection that occurs in over 90 % of the population, causes roseola infantum which is manifested by high fevers and a viral exanthem rash. After primary infection, it remains dormant in CD4 lymphocytes. Reactivation in immunocompromised patients may lead to neurologic symptoms, gastroenteritis, pneumonitis, hepatitis, and myelosuppression. While no vaccine currently exists, antiviral agents are an effective treatment.

HHV-8 gained attention as an opportunistic disease of AIDS patients, referred to as Kaposi sarcoma. In addition, HHV-8 is a causative agent in primary effusion lymphoma and multicentric Castleman disease in immunocompromised patients. While only 1.5 % of Americans are seropositive, up to 50 % of the sub-Saharan population is infected. Treatment of these diseases appears to be a reduction in the degree of immunosuppression, chemotherapy, radiation therapy and also resection of localized tumors, and treatment of other coinfections.

Paramyxovirus

Respiratory syncytial virus (RSV) and parainfluenza are part of the paramyxovirus family that is a frequent cause of both upper and lower respiratory tract infections in children. Peak seasonal appearance occurs in the winter, similar to influenza. Immunocompromised patients, such as posttransplant and lymphopenic patients, are more likely to have progression of the infection into the lower respiratory tract with significantly higher mortality rates. The paramyxoviruses have been associated with posttransplant complications, including post-viral obliterative bronchiolitis, a cause of chronic rejection. While vaccination is not available, RSV prophylaxis can be effectively managed with immunoglobulin and monoclonal antibodies. Treatment centers on the use of ribavirin, RSV antibodies, and supportive measures. In comparison, there are no proven preventative or treatment measures for parainfluenza.

Influenza Virus

Perhaps the one virus that has gained global notoriety in history for global epidemics has been the influenza virus. Despite widespread vaccination, the potential for antigenic shift and drift exists, a situation that could contribute to worldwide pandemics. Influenza A and B are RNA viruses that cause upper and lower respiratory tract disease. Like RSV, the progression to lower respiratory tract disease is more prevalent in immunocompromised patients and disease peaks in the winter. Neuraminidase inhibitors, such as oseltamivir and zanamivir, are effective treatments, especially when begun early in the viral course. These treatments are augmented by amantadine and rimantadine. Vaccination is available, but it may not cover all strains of the virus.

Blood-Borne Viruses

Blood-borne viruses are a major concern in the hospital for both the patient and healthcare providers. Virus transmission from an infected host during percutaneous or mucosal penetration is reported to be 0.3 % for human immunodeficiency virus (HIV), 3 % for hepatitis C, and 30 % for hepatitis B. In order to calculate risk of transmission from percutaneous or mucous membrane injury, several factors must be considered, including method of transmission (needle penetration versus blood splash to mucous membrane), needle type (hollow-bore needle such as an IV needle versus solid-bore needle such as suture needle), needle gauge, penetration of needle into patient and healthcare worker, presence of blood on needle, access of the needle to the patient's bloodstream, or whether the needle has passed through gloves or other barriers prior to entering the skin. Personal protective equipment and situational awareness remain the mainstays of prevention. Effective protection methods to minimize risk of transmission of blood-borne diseases include gloves, double gloving if needed, face shields or other eye protection, sleeve reinforcements, knee-high trauma boots, plastic aprons under surgical gowns, and avoidance of blind suturing techniques.

HIV is an RNA retrovirus that produces reverse transcriptase, which allows the creation of complimentary DNA that is substituted into the host cell. The virus attacks the host and causes cell lysis, with subsequent loss of helper CD4 T cells. Although mandatory preoperative HIV screening has been advocated by many, ethical concerns in addition to financial concerns are barriers to this screening. Furthermore, consent must be obtained before performing testing. Instead, a more accepted practice among many practitioners seems to be

testing either high-risk patients or those undergoing higher risk procedures. Regardless of the patient's infection status, universal precautions are standard practice. Upon receiving a percutaneous or mucosal injury from a patient with unknown HIV status, prophylactic treatment is begun and consent for HIV testing is obtained from the patient. If the host was determined to have asymptomatic disease, a two-drug regimen is recommended. However, if the patient was symptomatic at the time of exposure, a three-drug regimen is commenced for at least 4 weeks.

Hepatitis B is mainly transmitted through intravenous drug abuse, blood transfusions, and sexual contact. Viral replication of the virus occurs in hepatocytes. After exposure, 25 % of patients demonstrate clinical symptoms of hepatitis. About 95 % of patients exposed will have spontaneous clinical resolution, while 5 % will be antigen positive for life with potential for progression to chronic hepatitis, cirrhosis, portal hypertension, and hepatocellular carcinoma. The state of exposure for hepatitis can be determined through antibody testing. The presence of the core antibody indicates previous exposure, and the presence of core antigen indicates persistent disease. The presence of the "e" antigen indicates active viral replication, a marker of higher infectivity. If the surface antibody is the only antibody present, this signifies previous vaccination against hepatitis B. Despite the high transmission of hepatitis B through percutaneous injury, vaccination effectively eliminates transmission. However, those with unreactive antibody testing or no prior vaccination history are at risk and should receive postexposure prophylaxis. These individuals should receive the HBV immunoglobulin and either a booster dose of the vaccine or the full vaccination series.

Hepatitis C is estimated that over four million people in the United States have been exposed to hepatitis C. Transmission occurs through intravenous drug abuse, sexual contact, and transfusions. Like hepatitis B, about 25 % of people exposed demonstrate clinical symptoms. However, unlike hepatitis B, 50–80 % of those patients with hepatitis C will go on to develop chronic disease. About 20 % of those with chronic disease will progress to cirrhosis and hepatocellular carcinoma. Antibody testing after exposure may yield a positive result for up to a year. Unfortunately, no effective vaccination or prophylaxis after exposure is available at this time.

Nosocomial Infections

Infectious bacterial organisms are a major concern when considering infection control measures to prevent patient-patient transmission. Nosocomial infections are a major source of morbidity and mortality, including vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant

Staphylococcus aureus (MRSA), quinolone-resistant *Pseudomonas*, and *Clostridium difficile*. Many interventions have been proposed to eradicate or control the spread of nosocomial infections. Infection control measures include proper hand washing techniques, implementation of contact precautions, active surveillance cultures from patients, staff education, and effective environmental cleaning. All of these interventions, especially when combined, have been shown to reduce the incidence of multidrug-resistant organisms and its spread.

The duration of patient isolation is an area of high debate. Some advocate that once a patient is labeled as a carrier, they should always be isolated as if they were a carrier and that any testing indicating that they have been cleared of their infection is a result of poor culturing, poor sensitivity, or removal of antibiotic selection pressure. However, the Hospital Infection Control Practices Advisory Committee (HICPAC) recommends removal of isolation precaution after three negative cultures, at least 1 week apart. This duration of colonization of these antibiotic-resistant organisms is highly variable and currently unknown.

MRSA In addition to its nosocomial origin, MRSA is now being found in the community and is an important source of skin and soft tissue infections presenting in the outpatient setting. In the inpatient setting, it is a leading cause of pneumonia, surgical site infections, and disseminated infections. Risk factors for contracting MRSA include advanced age, prior antibiotic use, previous surgery, and extended hospitalization. MRSA colonization occurs in asymptomatic patients on normal skin flora and in the nares. Furthermore, colonization in the nares has been shown to be a risk factor for development of surgical site infections. For this reason, many advocate MRSA screening with eradication therapy through antiseptic decontamination prior to surgery. Screening of asymptomatic patients also allows for more effective prevention of cross-contamination of other patients through implementation of isolation and barrier precautions. Despite these measures, the Center for Disease Control (CDC) recommends against routine active surveillance screening of all patients.

VRE Up to 9 % of nosocomial-acquired bloodstream bacterial infections are attributed to *Enterococcus*, with a significant percentage as VRE. Unlike MRSA, VRE has a low rate of asymptomatic carriers. When colonization occurs, it is most likely on the skin and in the gastrointestinal tract. A higher prevalence of VRE has been found in intensive care, dialysis, and oncology units. The most common mechanism of transfer among patients appears to be ineffective hand hygiene among healthcare workers. Contact precautions typically are not implemented until after a diagnosis or history of VRE is known.

Clostridium difficile is considered a part of the normal intestinal flora in 1–3 % of healthy patients. When *C. difficile* overgrows and dominates the intestinal flora secondary to

eradication of the other normal gut flora, clinical symptoms can occur, which can range from mild diarrhea to the more severe pseudomembranous colitis and toxic megacolon. The toxins released from the bacteria are implicated in causing mucosal damage and inflammation. Measures to control the spread of this infection include proper hand washing to remove the *C. difficile* spores, disinfection of the physical environment, implementation of contact precautions, and proper selection of antibiotics when necessary. Some experts have recommended that contact precautions be maintained until 48 h after resolution of diarrhea. Environmental cleaning after physical exposure by an infected patient can be accomplished with chlorine-containing agents or hydrogen peroxide.

Airborne Disease

Droplet transmission is limited by distance spread from host to less than 1 m due to particle size. The size of the particle is a source of controversy, but the World Health Organization (WHO) employs a particle size of $>5 \mu\text{m}$. In comparison, particles that undergo airborne transmission are usually $<5 \mu\text{m}$, may remain suspended in air for an extended amount of time, and may be spread to greater distances. In addition, smaller infectious particles are more likely to penetrate the lower respiratory tract, while larger particles generally settle in the upper respiratory tract. Proper precautions should be followed in the operating room. Laminar airflow systems with HEPA filters are effective in removing the majority of airborne particles. These systems can be ceiling or wall mounted, with frequent air changes that limit colony-forming units. Other measures to prevent infection transmission in the operating room include sterile surgical gowns and drapes, face masks, antiseptic hand scrub, and the timing of opening surgical instruments prior to performing a procedure.

Tuberculosis (TB) is currently the eighth leading cause of death worldwide, and an estimated 1/3 of the world's population is infected. The highest concentration is focused in the less developed areas of sub-Saharan Africa, India, Southeast and Central Asia, Eastern Europe, and Micronesia. Tuberculosis is spread through respiratory droplets by individuals with active pulmonary disease. While most healthy patients exposed will have an asymptomatic and localized course, this infection may remain dormant in pulmonary tissue for years, referred to as latent tuberculosis infection. Reactivation may occur years later in normal healthy patients. However, reactivation is more likely to occur in immunocompromised patients, such as patients with malignancies, HIV, end-stage renal disease, diabetes, and patients on immunosuppressive medications.

Active tuberculosis is characterized by chest X-ray findings of infiltrates found in the apical-posterior segments of

the upper lobes and may include cavitations. Symptoms most frequently associated with TB infection include the constitutional symptoms of fevers, night sweats, cough, and unintended weight loss. Diagnosis of latent TB infection is made by tuberculin skin testing (TST), with interpretation of test results based on prevalence and risk of the patient. Active disease is diagnosed through a combination of chest X-ray findings, culture results, and acid-fast bacilli detection from either sputum testing or bronchoalveolar lavage. Treatment is usually accomplished through direct observational therapy (DOT) with at least 6 months of treatment. While latent TB can be effectively treated with one agent, the danger of multidrug-resistant organisms necessitates the use of multiple medications. Patients found to have active tuberculosis infection should be kept in a negative-pressure isolation room with at least 6 air exchanges per hour until clinical resolution of symptoms is achieved with three consecutive negative results of sputum testing. Healthcare providers should wear N95 masks that have been individually fit-tested when caring for patients with active disease.

Severe Acute Respiratory Syndrome (SARS) In 2003, SARS, a form of *Coronavirus*, was responsible for a major pandemic that affected many healthcare providers. This virus was spread through respiratory droplets and was found to have a high level of infectivity. There has been some debate on whether this virus was also spread to greater distances from the host through airborne transmission. Flu-like symptoms were associated with mild acute infection and symptoms of serious infection included reactive hepatitis, a severe acute neurologic syndrome, and pulmonary involvement with pneumonia and acute respiratory distress syndrome (ARDS). Healthcare providers were found to be at significant risk for contraction of the virus, especially when caring for patients that required oxygen therapy, positive-pressure ventilation, and resuscitation. Recommendations for healthcare providers caring for these patients involve strict contact and droplet precautions. However, airborne precautions, such as the use of N95 fitted mask, must also be observed when performing procedures that may generate aerosols, such as bronchoscopy.

Prions

Creutzfeldt-Jakob disease (CJD), a family of neurodegenerative disorders, has become a surgical concern over the past couple decades. The infectious entity of this disease has been found to be mutated prions that are protease resistant. Mean incubation period until appearance of symptoms has averaged over 10 years with subacute progression of neurologic disease. However, average survival after the appearance of symptoms is only a few months. Diagnosis can only be made through biopsy of infected tissue.

Prion disease may be transmitted through familial, sporadic, or iatrogenic spread. In particular, the iatrogenic form is concerning for infection control precautions, as more than 400 patients have been exposed to prion-contaminated surgical equipment. Certain surgical operations such as ophthalmologic and neurosurgical procedures are considered high risk for prion transmission. Historically, EEG electrodes, human pituitary hormone, cornea transplant, and dura mater grafts have also been implicated. A few case reports have found transmission through blood transfusion from an infected donor. These mutated prions have been shown to be less susceptible to standard methods of sterilization. WHO has made specific recommendations regarding the sterilization of surgical instruments that have come into contact with tissues that carry a risk of high infectivity or patients with suspected or confirmed prion disease. Moreover, some experts recommend the use of disposable surgical instruments in these situations.

Clinical Review

- Vaccinations exist for all of the following viruses, except:
 - Influenza
 - Varicella
 - Hepatitis C
 - Hepatitis B
- Chronic liver disease is most likely to develop with infection with the following virus:
 - Hepatitis C
 - Hepatitis B
 - Human immunodeficiency virus
 - Herpes virus
- Following is the most common cause of death due to infection:
 - Tuberculosis
 - Human immunodeficiency virus
 - Hepatitis C
 - Lower respiratory tract infections

- Effective hand hygiene is important in preventing spread of infections:
 - True.
 - False.
 - Is irrelevant.
 - Double gloving has been shown superior to hand hygiene.

Answers: 1. C, 2. A, 3. D, 4. A

Further Reading

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