



Biocontainment Principles for Pediatric Patients

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Introduction

Preparing for highly hazardous communicable diseases (HHCD) in healthcare centers must include pediatric hospitals. While much of this preparation is similar between adult and pediatric populations, there are clear differences which must be appreciated when considering the clinical care of the highly infectious pediatric patient, as well as for providing safe and compassionate care for the patient and their families. Specialized biocontainment units, largely funded by academic institutions, have been created to care for children with suspected (person under investigation or “PUI”) or confirmed patients with highly hazardous communicable diseases. Care of patients with some pathogens, notably Ebola and other viral hemorrhagic fevers, require the use of special isolation and personal protective equipment by highly trained volunteers representing the interdisciplinary healthcare team including nurses, physicians, respiratory therapists, environmental services, laboratory technologists, and waste management. This was exemplified by the remarkable care of adult patients with Ebola Virus Disease (EVD) in the biocontainment units at the University of Nebraska, Emory, the National Institutes of Health, and Bellevue Hospital. Units that are now capable of caring for children with highly hazardous pathogens, including but not limited to Ebola virus, fully acknowledge their debt to the units that care for adults, but there are notable differences. Developmental issues, parental presence, specialized supplies, and equipment are important considerations when caring for children with suspected or proven EIDs. Currently, there are nine pediatric-specific institutions designated by the CDC as Ebola treatment

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Centers, but *all* institutions caring for children should be capable of mastering the tenets of infection prevention and control, biocontainment and isolation of children with a suspected or confirmed HHCD.

Pediatric Specific CDC Designated Ebola Treatment Centers in the United States

- Children’s Hospital Colorado; Aurora, Colorado
- Ann & Robert H. Lurie Children’s Hospital of Chicago; Chicago, Illinois
- Boston Children’s Hospital; Boston, Massachusetts
- Children’s Hospitals and Clinics of Minnesota – Saint Paul campus; St. Paul, Minnesota
- Children’s Hospital of Philadelphia; Philadelphia, Pennsylvania
- Texas Children’s Hospital; Houston, Texas
- Children’s Hospital of Wisconsin, Milwaukee; Milwaukee, Wisconsin
- Children’s National Medical Center; Washington, D.C.
- Seattle Children’s Hospital; Seattle, Washington

Highly Hazardous Pathogens in the Pediatric Population

There are differences between adult and pediatric epidemiology when it comes to highly hazardous pathogens. Here we will briefly examine three of the most recent threatening of the emerging pathogens: SARS-CoV, MERS-CoV, and Ebola virus.

Coronaviruses: Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle Eastern Respiratory Syndrome Coronavirus (MERS-Cov)

SARS-CoV

The SARS-CoV epidemic of 2003 is a prime example of how quickly an emerging infectious disease can spread. When reviewing pediatric data available from this epidemic, which occurred from November 2002 through July 2003, the factors most strongly associated with pediatric infections included close contact with adult SARS-CoV patients [1]. In a study looking at pediatric SARS-CoV patients in Toronto, Canada between February and June 2003, SARS-CoV was found to be a relatively mild illness in previously healthy children, resulting in only mild respiratory symptoms, supported in other published reports from pediatric patients from Hong Kong [1–3]. While there were serious diagnostic limitations to these studies, including the lack of serologic data and true confirmation of positive cases, data from all available pediatric studies suggest the majority of pediatric cases had contact with infected adults, resulting in less severe clinical courses in younger patients

(<12 years of age) as compared to teenagers and adult patients, many of whom required mechanical ventilation. SARS-CoV case fatality rate in pediatric patients was estimated to be <1% in patients less than 25 years of age, compared to a case fatality rate of >50% in patients >65 years of age [4].

MERS-CoV

MERS-CoV is a more recently described coronavirus, and while similar to SARS-CoV, presents with more severe clinical symptoms [5]. First isolated in the Kingdom of Saudi Arabia in 2012 from a Saudi businessman who died of pneumonia [6], this respiratory disease has remained primarily isolated to the Arabian Peninsula, with the exception of one significant outbreak in South Korea in 2015 [7]. Isolated from infected camels with confirmed camel-to-human transmission, the exact mode of transmission remains undetermined. Similar to SARS-CoV, hospital acquired infections play an important role in the spread of the virus [5, 8]. Interestingly, a large MERS-CoV outbreak occurred in South Korea in 2015 resulting from the exposure to a *single* infected patient in a crowded emergency room, resulting in MERS-CoV infections in 82 individuals (33 patients, 8 healthcare staff, and 41 visitors), highlighting the need for improved preparedness in early identification and isolation of patients with highly hazardous communicable diseases [8]. Much like with SARS-CoV, pediatric data are limited, as MERS-CoV is primarily a disease seen in the adult population. Of reported pediatric cases, MERS-CoV infections in previously healthy children typically result in non-specific clinical symptoms including fever, cough, shortness of breath and breathing difficulties, and pneumonia, which can progress to acute respiratory distress syndrome and subsequent multi-organ failure [9–12]. From June 2012 through April 2016, only 31 cases (2 known fatalities) of children with MERS-CoV were reported in the Kingdom of Saudi Arabia, compared to a total of 1561 adult cases of MERS-CoV, with 633 fatalities from June 2012 through February 2017. Of the children with more severe symptoms who progressed to death, both had pre-existing conditions (cystic fibrosis and nephrotic syndrome) [10]. Due to non-specific clinical symptoms of both SARS-CoV and MERS-CoV which are similar to other common respiratory pathogens including influenza and Respiratory Syncytial Virus (RSV), a travel and family history is critical in identifying and isolating these patients rapidly upon arrival to any emergency center or primary care setting for proper diagnosis and treatment [13, 14].

Viral Hemorrhagic Fevers: Ebola Virus

Examples of Viral Hemorrhagic fevers in the pediatric population requiring special isolation include Ebola virus, Marburg virus, and Lassa Fever. There is no better example of a viral hemorrhagic fever outbreak than the 2014–2016 Ebola virus disease (EVD) outbreak, which provided new information on pediatric patients with EVD. Much like SARS-CoV and MERS-CoV described above, pediatric patients represented a minority of all patients presenting with suspected or confirmed

EVD. In contrast, the case fatality rate in these children, especially those under 5 years, was quite high, with mortality rates for neonates reaching 100% [15].

Major risk factors for pediatric infections during the 2014–2016 EVD outbreak in West Africa, such as washing of bodies during ritual burials and direct care of sick relatives, were less likely to occur in children and likely partially accounted the lower overall incidence of infection in children, in addition to likely underreporting, and perhaps a faster progression to death in children [16].

In pediatric EVD cases, there is a wide range of symptoms that occur. After an incubation of 2–21 days, these patients usually develop fever, chills, anorexia, headache, and myalgia. In contrast to adults, children more often present with fever and are less likely to report specific complaints of pain, dyspnea, dysphagia, and hiccups. Although designated as a hemorrhagic fever, significant bleeding or bloody diarrhea is seen in a minority of patients. Gastrointestinal involvement predominates after the initial symptomatology, which may include significant diarrhea, emesis, and abdominal pain. It has been suggested that young children are less likely to be able to report such symptoms, which may distort these differences [17].

Special Issues in Pediatric Populations

When preparing for highly hazardous communicable diseases such as SARS-CoV, MERS-CoV, and viral hemorrhagic fevers in pediatric populations, there are special issues facing children and their families which must be carefully considered and include the following:

- General preparedness in pediatric institutions
- Clinical care considerations
- Building a pediatric response team for patients with HHCDs
- Social and ethical considerations specific to the pediatric population
- Pediatric biocontainment unit considerations

General Preparedness in Pediatric Institutions

The majority of pediatric providers will never work in a biocontainment unit, but all frontline providers caring for children should be prepared to identify and isolate suspected patients, as well as rapidly inform the proper individuals if they are faced with a pediatric patient suspected of having a HHCD. Identification of these children with potential exposure to high-risk pathogens can be extremely challenging, particularly in the height of influenza and respiratory virus seasons, where seemingly every child evaluated has symptoms including cough, fever, and diarrhea. Preparedness efforts are therefore time-consuming, costly, and challenging, but potential solutions exist [18]. Travel screening at all points of entry is critical. High-risk travel screening in busy pediatric institutions is a difficult but an essential part

of identifying patients with potential HHCDs and properly isolating those patients to limit the spread of disease. Hospitals and clinics should use appropriate travel screening algorithms, ideally built into the electronic medical record admission process and available at all possible points of entry in pediatric centers, including emergency centers, ambulatory clinics, as well as inpatient settings.

While it becomes increasingly difficult in the era of multiple “electronic flags” in the medical record to add another checkpoint for triage, it is necessary to build within these algorithms links to current travel alerts [19]. Additionally, travel screening is useless if positively identified patients are not properly identified and immediately isolated, followed by timely notification of appropriate personnel.

In each institution, pediatric-specific triage screening questions should be developed with the help of infectious disease experts. Example screening questions include:

- “In the past 3 weeks have you or your child traveled outside the U.S. **or** had close contact with someone who traveled outside the U.S.?”
- “Has your child had fever, rash, diarrhea or new skin lesions?”
- “Has your child had difficulty breathing or cough?”
- “Are there ill family members with these symptoms to whom your child was exposed prior to travel?”

Pediatric patients and their caregiver must be promptly isolated if the answers to these questions are “yes” and evaluated by proper experts to determine if the child is indeed at risk for a HHCD requiring special isolation. Immediate isolation requires masking the patient, as well as recognizing that the accompanying family members may also be infected. These identified patients should preferably be placed in a negative pressure room **with their family member/caregiver** to limit exposure to other patients and staff. One nurse and attending physician should assess the patient, and contact should be limited. Once a patient has been identified, isolated, and assessed, internal and external stakeholders must be promptly informed to facilitate testing and, if needed, transport specimens and/or the patient.

Establishing protocols and relationships with all stakeholders in advance is critical to the successful implementation of this process. Attempting to create plans and partnerships during an event is exceedingly difficult and potentially unsafe. In clinical care planning, regional transport partners, waste management groups, and communications experts are essential for successful response to pediatric patients with HHCDs. Informing the proper individuals can be a complex process if not practiced as an institution prior to an event. Creating and maintaining updated telephone trees, developing protocols to rapidly alert health department contacts, and then performing tabletop exercises and simulations to test this communication infrastructure is invaluable to safe and effective care of a patient with a suspected or confirmed highly hazardous communicable disease.

Clinical Care Considerations

All institutions involved in caring for children with suspected or confirmed HHCDs should be capable of offering intensive care for these patients, including mechanical ventilation, management of severe electrolyte disturbances, cardiac arrhythmias, and potentially dialysis in the event of renal failure and/or fluid overload. This requires advanced planning and well defined, well-practiced protocols to provide this level of care both safely and effectively in the setting of special isolation. Having an established, on-call specialized response team who are trained in PPE, protocols, and management of these patients is ideal. Management of critically ill children can be challenging under normal circumstances in the pediatric ICU, but performing procedures and high-level care in PPE is a set of skills which must be practiced.

Building a Pediatric Response Team for Pediatric Patients with Highly Hazardous Communicable Diseases

Careful consideration should be given to choosing healthcare workers for pediatric special isolation teams. While caring for any critically ill child carries specific challenges, the added burden of doing so under the unique stressors of special isolation can be overwhelming, and special attention should be spent on building guidelines and screening tools to ensure that the right team is chosen to care for these special patients and that the proper support is available for the team. In training specialized care teams to care for these children, each institution must decide whether to do this based on the recruitment of volunteers only or if this training is to be mandatory, particularly for staff working in high-risk areas including the emergency center and pediatric intensive care unit. While critical care skills are ideal in the recruitment of these “special response teams,” a varied skill set ranging from acute care nurses to ICU nurses, as well as physicians with varied backgrounds, should be considered. Individuals should be carefully screened for behavioral components key to performing well on such a highly specialized team, including the ability to work well with others, self-control, and the ability to remain calm under pressure. In dealing with critically ill children, a pediatric care providers’ first instinct is to sacrifice self for patient, and this *cannot* be the case in a caring for a child with a HHCD. The ability to follow strict orders to ensure team safety is key combined with the ability to troubleshoot and think creatively in situations likely never before faced when caring for children. Additionally, members chosen for these specialized teams should undergo full health screens, including potentially fitness and agility testing, as working in personal protective equipment for prolonged periods in environments of high-stress can be incredibly taxing. Human resources should be involved in creating employee policies including sequestration or home monitoring, furlough, pay and benefits, housing for providers, housing for infected employees, food, child-care, and emotional and spiritual support. These actions and policies provide reassurance, a sense of safety, and reduce employee stress. Health and wellness programs

and employee assistance programs offering counseling and employee health teams should be incorporated in the support staff available for all team members of a special response team. Caring for children admitted with HHCDs, potentially in pandemic situations, is likely to cause great amounts of stress, and being able to combat stress and teach caregivers how to manage it is of highest priority in maintaining a healthy team [20].

Social and Ethical Considerations Specific to the Pediatric Population

The social and ethical considerations are complex when dealing with pediatric patients in special isolation, and answers to how these issues should be handled may vary from institution to institution. It is crucial to include the need and stressors of families of these patients, as well as the need to have a plan in place to screen family members for symptoms to both reduce the risk of spread of disease as well as address the needs of adult family members. It must be presumed that if a child is infected with a HHCD, family members are at high risk for exposure and require screening, evaluation, and potentially specialized treatment at an adult treatment center.

The needs of parents and family members of isolated pediatric patients require advance planning, and each institution must decide upon their own policies and procedures prior to facing this situation in real time. First, institutions must decide upon a family visitation policy. These policies can range from several options: first, a “zero tolerance” visitation policy, where families are not allowed inside biocontainment areas but are still provided with video conferencing capabilities in order to interact with their children. Second, family members may primarily spend

time in a separate, designated family room, with only brief visitation to pediatric patients diagnosed with HHCDs. Third, the family or caregiver must remain at the patient’s bedside for the entirety of the admission, after demonstrating proper technique in both donning and doffing PPE [21].

As an example, at Texas Children’s Hospital in Houston, Texas, a child with a HHCD admitted to the Special Isolation Unit is strictly isolated to prevent further spread of the disease. It is the policy at this institution that parents and family will not be allowed into the unit but are provided with a private family room for respite, where videoconferencing is available. These decisions should be made in consultation with a team including infectious disease experts, state and/or local public health authorities, risk management, and the clinical care staff who will be involved in caring for the child. Additionally, if the decision is made to allow family visitation, this should be closely observed. The ability of families to follow instructions, including appropriate donning and doffing of personal protective equipment, should be carefully considered and may require a case-by-case evaluation. The impact of family visitation must also be balanced with the risk this may bring to staff members caring for the patient. While it is difficult enough to care for a child with a HHCD in full personal protective equipment (PPE), adding family members to the room

increases the responsibility of staff to care for and monitor not only the patient, but the family member in addition. It is also important to note that competency in PPE takes practice and suggested quarterly training, and it may be unrealistic to expect family members to be able to don and doff safely without the risk of contamination. Lastly, the decision to allow families to visit children in strict isolation may differ from pathogen to pathogen. The visitation guidelines which apply to a child diagnosed with Ebola virus may differ from those diagnosed with respiratory viruses, such as MERS-CoV.

Regardless of institutional policies, it is critical to address the obvious stress these issues will have upon family members, and it is important to develop policies and procedures to provide exceptional support to these families who are separated from their children, some of whom may be critically ill. This includes specialized training within the care team on ways to care for the family, including assigning “family liaisons,” who will serve as a point of contact for the parents and with whom they can develop a trusting relationship regarding the care of their child. The individuals chosen for this position should be excellent communicators and clinical leaders on the patient care team. Parents should be given information on how to obtain updates 24 h a day, with a way to easily communicate with the team caring for their child. Establishing a comfortable, secure, and private space where a family can find solace is recommended. Additionally, family members should be screened daily for symptoms and isolated immediately if there are signs or symptoms of disease.

While local health departments should be partners in the screening of family members, it is important to establish institutional protocols regarding how family will be cared for while their children are patients in special isolation. This includes considering how family will be shielded from media and scrutiny from the general public while entering and exiting the hospital, ensuring families are screened on a daily basis for new symptoms requiring evaluation for potential disease, and monitoring family movements within the hospital to ensure families which may in fact be contagious are confined to specific, controlled areas. This is particularly important with respiratory viruses, such as MERS-CoV and SARS-CoV, where symptoms may initially be vague and patients may be contagious before they are identified.

Caring for the Dying Child in Special Isolation

In caring for critically ill pediatric patients under special isolation, clinical judgment will be required to balance the risks and benefits of heroic therapies as well as the utilization of cardiopulmonary resuscitation (CPR) in the event of cardiopulmonary arrest. This should be decided on a case-by-case basis, always balancing the safety of the care team with the risks of contamination. In pediatrics specifically, children often have little reserve when experiencing severe electrolyte derangements, hypoxemia, and respiratory failure. In many cases, it will be reasonable to offer CPR to patients with these reversible abnormalities [22–24].

Alternatively, if the decision to provide CPR to a child with Ebola virus disease in the setting of massive pulmonary hemorrhage, for example, puts the care team at risk of contamination and infection, the decision to provide CPR should be questioned. These decisions in children are not easy and should be guided by leadership with careful consideration given to the medical team and the psychological effects this discussion will inevitably bring.

In cases of medical futility or the dying pediatric patient in special isolation, offering quality palliative care is not only feasible, but should be discussed prior to the event. Even in the cases where parents and family would not be allowed to visit their dying child (i.e., EVD patients), there are creative ways to involve the family in their child's care. This includes first and foremost offering support, including social work, child life, and chaplain services. Creating "memory tokens" may be useful, though careful consideration must be paid to which items these could be, as only materials which can be successfully autoclaved can be removed from the biocontainment area in cases such as viral hemorrhagic fevers [21]. Photographs and video may assist in helping the family say goodbye, as well as providing items of comfort (e.g., a favorite toy). In the case of some pathogens, such as Ebola virus, it may not be feasible to return these items, and this should be discussed with the family in advance. As with all pediatric end-of-life care, honest and open communication is essential to this process along with allowing the family to grieve, even if isolated from their child. Lastly, the psychological and emotional stress placed on the staff caring for these children must be acknowledged, and staff should be cared for with supportive leadership.

Pediatric Biocontainment Unit Considerations

All institutions caring for pediatric patients should be prepared to either care for a patient who may present after exposure to a highly hazardous pathogen, with basic training in PPE, infection prevention and control and protocols to isolate and care for patients, or have in place protocols to transfer identified patients to facilities where this care is possible. In this day and age with the ever-expanding ease of international travel, it is crucial to prepare for these patients in advance, including what physical space is necessary to properly isolate and care for these children. In considering the requirements for proper biocontainment of patients with HHCDs, the same principles apply in pediatrics as described previously in the literature [25–28]; however, pediatric-friendly adjustments may need to be made when designing biocontainment units with consideration for pediatric patients.

An example of this is the 8-bed Pediatric Special Isolation Unit built at Texas Children's Hospital. Completed in 2015, this pediatric biocontainment unit exists within a tertiary pediatric hospital and includes all the features of a true biocontainment unit, while remaining pediatric-friendly. Examples of this include a unidirectional workflow in the unit from "clean" to "dirty," specialized air handling systems with negative airflow and HEPA filtration, cleanable surfaces with no grout, pass-through boxes into patient rooms to limit the need for staff entry, a BSL3 laboratory

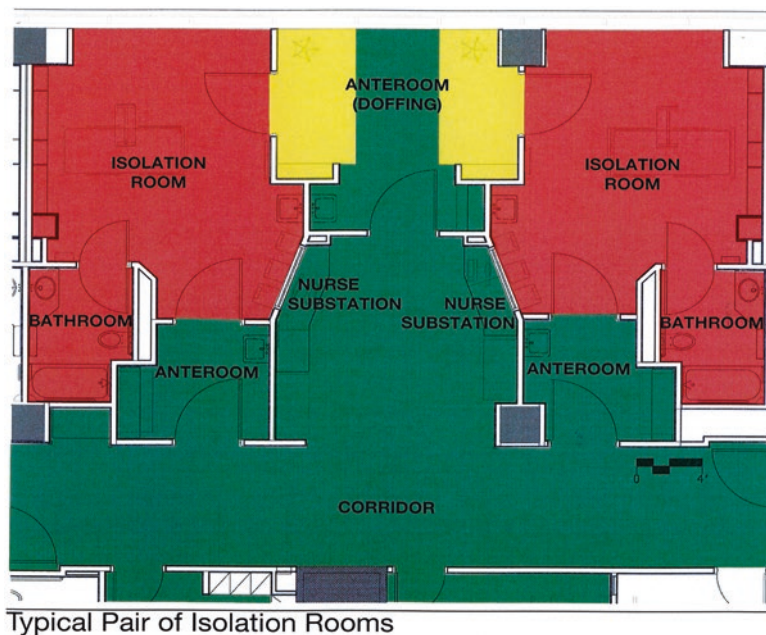


Fig. 10.1 Typical pair of special isolation rooms at Texas Children's Hospital, showing clean (green) to dirty (red) workflow

located within the unit, and three separate pass-through autoclaves capable of processing biohazardous category A waste (Fig. 10.1). Also important in the design of the unit was the ability for parents and families to be able to communicate with their children; therefore cameras were installed to allow family members to observe the room from a dedicated family room, located outside of the unit, when staff feels it is appropriate to do so. Additionally, rooms were built with high visibility so that medical staff could observe both the patient and the staff caring for the child easily from the outside. Rooms were designed in the same bright colors and pediatric themes as typical hospital rooms at Texas Children's Hospital.

Conclusion

Highly hazardous communicable diseases are not a new threat, and as history has shown, they will continue to remain a threat to mankind, both adults and children alike. Critical lessons have been learned in the past regarding how healthcare centers respond to public health emergencies and have highlighted the need for improved infection prevention and control, communication, isolation of HHCD patients, and the ability to care for them in specialized units. While it has been shown in past outbreaks of pathogens ranging from Ebola virus to MERS-CoV that

children may be less susceptible to these pathogens, critical illness and/or death can still occur. This requires that all healthcare facilities be prepared to identify, isolate, inform, and potentially provide prolonged care for these most vulnerable of patients and their families. The principles of preparedness in all pediatric institutions are achievable, with planning, practice, and dedication.

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