What is new in Respiratory Viral detection in Children?

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Respiratory viral infections are common in children during the winter months in temperate climates. The seven most common respiratory viruses that are routinely detected by viral culture in the CMH microbiology laboratory are Influenza A, B, respiratory syncytial virus (RSV), Adenovirus, and Parainfluenza 1, 2 and 3.

Shell vial culture in CMH:
Rapid and sensitive identification of respiratory viruses is important for patient treatment and infection control. Although antigen tests for Flu and RSV provide rapid results, they have suboptimal sensitivities. Hence for the respiratory season 2007/08 the CMH microbiology laboratory has implemented a reflex policy to setup a 48 hour shell vial (SV) culture on respiratory specimens previously testing negative for Flu and/or RSV antigen. The policy is restricted to specimens obtained from outpatients who were subsequently hospitalized. As of January 19, 2008, a total of 96/373 (26%) specimens were positive for a respiratory virus by SV culture; the individual viruses are RSV (53), adenovirus (23), Influenza A (2), influenza B (2), Parainfluenza 1 (11), Parainfluenza 2 (4), Parainfluenza 3 (1). The high isolation rates of viruses and reporting within 2 days should improve patient management decisions.

Newly Described Respiratory viruses in Children:
Since 2001, using viral culture or molecular techniques, several newer respiratory viruses has been discovered in children worldwide. The newly identified viruses are human metapneumovirus (HMPV), human Boca virus (HBoV), some human corona viruses (HCoV) including HKU1, NL63, and a few polyoma viruses such as WU and K1. All of these viruses have been associated with one or more of a variety of respiratory manifestations including cough, wheezing, asthma, bronchiolitis, and pneumonia.

**Human metapneumovirus:** HMPV is a single stranded RNA virus in the Family Paramyxoviridae and is genetically closely related to RSV. It was originally detected in 2001 in a cohort of Dutch children suffering from bronchiolitis. The virus was isolated in tissue culture cells and found to produce cytopathic effect similar to RSV. Interestingly seroepidemiological studies have shown that this virus may have circulated for more than 50 years in the human population. Several studies have shown a worldwide distribution of this virus and an incidence around 4-25% in patients suffering from acute respiratory infections. It occurs more commonly during the winter and spring months. Indeed, it has been implied that HMPV may be the second most common virus associated with bronchiolitis following RSV. It can cause fatal disease in the elderly and the immunocompromised patient due to pneumonia. Like RSV two genotypes of HMPV have been identified, A and B. Each genotype has two lineages with a total of four different lineages A1, A2, B1 and B2. The incidence of lineages varies from season to season. Natural infection does not seem to be protective. Although HMPV can be isolated by culture, nucleic acid amplification technique (NAAT) is a more sensitive method.

**Human Boca virus:** HBoV is a newly discovered DNA virus belonging to the Family Parvoviridae. HBoV belongs to the same genus as the bovine parvovirus 1 and minute virus of canines; hence the name Boca virus (Bo-bovine, Ca-canine). The other human virus closely related to HBoV are the parvovirus B19 and adeno-associated viruses. It was first isolated in 2005 by random amplification of nucleic acids isolated from pooled respiratory specimens previously negative for common respiratory viruses. Laboratories have been unsuccessful in their attempts to isolate the virus. Viremia is not uncommon and usually seen during the early stages of the disease and in patients who excrete high viral loads in the
respiratory specimen (>10,000 copies/ml). Serological response with an increase in IgG titer and/or IgM detection was found commonly in patients with high viral load, viremic patients and patients for whom HBoV was the only respiratory pathogen. Evidence from worldwide studies suggests that HBoV is capable of causing severe lower respiratory infections in children. Interestingly HBoV has also been frequently associated in co-infection with other respiratory viruses, more commonly the adenovirus. A study from Israel demonstrated that greater than 70% of adenovirus-positive respiratory specimens were co-infected with HBoV. Persistence of low level of HBoV in the respiratory specimens has also been documented. HBoV has also been detected in stool specimens indicating a possible role in gastroenteritis. Reagents are unavailable for clinical testing for this virus, while some research based NAAT and serological methods have been described.

*Human Corona viruses:* Corona viruses have a crown-like appearance by electron microscopy and are single stranded RNA viruses. OC43 and 229E are two human Corona viruses identified in humans in the 1960s; however, not much is known about these viruses because they were traditionally discounted as viruses that cause common cold, until the first deadly corona virus namely SARS was discovered in 2003. The SARS epidemic spanned 29 countries with a total of 774 deaths from a total of 8098 confirmed infections and a mortality rate of 10%. Interest in corona viruses resurged and investigators have detected new strains of corona viruses namely NL63 and HKU1. The NL63 virus was first discovered in 2004 in a 7 month old girl with coryza, conjunctivitis, fever and bronchiolitis. Subsequently studies have shown the incidence to be around 1-10% worldwide and the virus seems to be associated with both upper and lower respiratory symptoms and commonly causing croup in children. Fever, cough, and wheezing were common in patients infected with NL63 and the virus was excreted for a period of 3 weeks following infection. HKU1 virus was identified in a 71 year old man with fever, cough and infiltrate on chest radiograph. The virus was detected by a NAAT that was designed for SARS. Incidence of HKU1 is less than 3% from few studies completed in Hong Kong and USA. The virus has not been isolated in cell culture and reagents are currently not available for clinical testing.

*Polyoma virus:* In 2007 two new polyoma viruses have been discovered in respiratory specimens in children. Researchers at the Karolinska institute in Sweden discovered a novel polyoma virus in 2007 by molecular methods and named it K1. The incidence of K1 in Swedish population was about 1%, while a recent study from Australia puts the incidence around 3%. Subsequently researchers at Washington University in St. Louis, Missouri identified another polyomavirus from respiratory specimen and named it WU virus. The incidence of WU virus is between 2-4 % from limited studies completed in USA and Australia.

Epidemiological studies conducted around the world allow us to understand the incidence and role of these viruses in respiratory infections in children. The development of reagents and tests for clinical use will improve respiratory viral detection in children.