LAB NEWS

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Update in Adenovirus Diagnostic Options at YNHH

Adenovirus infections are common, with over 51 serotypes associated with a variety of diseases and involving all organ systems (Table 1). Infections are usually self-limited, but serious and even fatal pneumonias have occurred sporadically in otherwise healthy persons. Adenoviruses were initially isolated from latently infected human adenoid tissues ("adenoid-associated viruses"); thus adenoviruses are known to cause persistent or latent infections, which can also reactivate during immunosuppression.

Table 1. Adenovirus Clinical Manifestations

Clinical Syndrome	Principle serotypes	Hosts at greatest risk
URI; exudative pharyngitis	1-3, 5-7	Infants, young children
Pneumonia	4, 7	Military recruits
Pneumonia	1-3, 7	Infants, young children
Pharyngo-conjunctival fever	3, 7, 14	School aged children
Pertussis-like syndrome	5	Infants, young children
Epidemic keratoconjunctivitis	8, 11, 19,37	Adults
Mononucleosis syndrome/ hepatitis	1, 2, 5	Infants and children with liver transplants
Ulcerative genital lesions, cervicitis, urethritis	19, 37	Sexually active
Acute hemorrhagic cystitis	11,21,34,35	Young children; hematopoietic transplant recipients
Gastroenteritis	31, 40, 41	Infants, young children
Intussusception	1, 2, 5, 6	Infants and young children
Myocarditis	?	Children
Meningitis/ encephalitis	1, 2, 5	Children and compromised hosts
Disseminated disease in compromised hosts: "sepsis", pneumonia, hepatitis, meningitis, diarrhea, rash, cystitis, ulcerative lesions	1, 2, 4, 5, 6	Compromised hosts

Immunocompromised hosts: Adenoviruses have been increasingly recognized as important pathogens in immunocompromised individuals (1-3), especially in patients with suppression or loss of T-cell function. These include allogeneic stem cell transplant recipients, lymphoma patients on anti-CD52 antibody therapy, and solid organ transplant recipients. Children in these groups are at greatest risk. Experimental therapy with cidofovir has had positive but variable results, and not surprisingly, immune reconstitution has been found to be important in recovery. As with other latent viruses, however, asymptomatic shedding can also occur.

Viral load in plasma: Real-time quantitative PCR screening of plasma has been instrumental in identifying patients at risk for dissemination at an early stage of viremia, monitoring these patients for rising adenovirus in blood, and allowing for early intervention (1-3). Isolation or detection of adenovirus from multiple body sites is another indicator of viral burden that has been used to gauge the seriousness of infection.

PCR Method (YNHH): Real-time TaqMan PCR that targets the hexon gene and detects all 51 types (2).

Interpretation of quantitative adenovirus PCR in plasma: Detection of adenovirus in plasma by PCR is an early indicator of a potentially serious adenovirus infection. Quantification is used to determine trends in viral load, i.e. whether viral load is significantly and/or rapidly rising over time, as well as response to therapy. With a "type-common" PCR that detects all 51 serotypes, absolute quantification of a given serotype will vary depending on how good a match the primers and probe are for that given serotype and strain.

Since adenovirus may grow slowly or not at all in cell culture, the rapid time to result afforded by PCR is a distinct advantage. However, all PCR methods, despite targeting highly conserved areas of the viral genome, can occasionally give falsely negative or low results due to sequence variations or mutations in primer and probe binding sites (4).

Table 2. Diagnostic tests available for adenovirus at YNHH:

Test	Sample types	Usage
Respiratory DFA	NP swab or aspirate, BAL	Rapid screen for 7 different viruses; only 70% sensitive for adenovirus. Time to result 2 hrs from receipt in lab, 7 days a week during operating hours.
Conventional cell culture	Any sample type	Ability to detect multiple viruses including the "unexpected"; use for DFA-negative respiratory samples in hospitalized patients. Adenovirus requires 1-14 days to grow.
Rapid adenovirus centrifugation culture	Any sample type	Detects only adenovirus. Cultures stained by IF and read at 2 and 5 days.
Adenovirus PCR	Any sample type	Whenever adenovirus is considered in hospitalized or immunocompromised patients. Result within 24 hrs, Monday-Friday.
Adenovirus PCR with Quantitation	Plasma only (done reflexively on positive plasmas)	To monitor viral load in high risk compromised hosts. Qualitative result within 24 hrs, Mon-Fri; quantitative result within 2-3 days.

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References

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