Common Viral Respiratory Infections

(See also *Harrison's Principles of Internal Medicine*, 17th Edition, Chapter 31)

Definition

- Acute viral respiratory illnesses are among the most common of human diseases.
  - Account for one-half or more of all acute illnesses
  - Most common manifestation: the "common cold"
  - May also manifest as pharyngitis, croup, tracheitis, bronchiolitis, bronchitis, and pneumonia
- Common infectious agents include:
  - Rhinovirus
  - Coronavirus
    - See SARS (Severe Acute Respiratory Syndrome).
  - Respiratory syncytial virus (RSV)
  - Human metapneumovirus (HMPV)
  - Parainfluenza virus
  - Adenovirus
  - Influenza virus
    - See Influenza.
  - Herpes simplex virus
    - see Herpes Simplex Virus Infections.
  - Enterovirus
    - See Coxsackievirus and Echovirus Infections.

Epidemiology

Acute viral respiratory illnesses

- Incidence in the U.S.
  - Overall
    - 3–5.6 cases per person per year
  - Age
    - Rates highest among children <1 year of age (6.1–8.3 cases per year)
    - Rates remain high until the age of 6 years and then decrease.
    - In adults: 3–4 cases per person per year

Specific viral infections

Rhinovirus

- Prevalence
  - A major cause of the common cold
  - Isolated from 15–40% of adults with common cold–like illnesses

- Distribution: worldwide
- Age
  - Rates of infection are higher among infants and young children and decrease with increasing age.
  - Often introduced into families by preschool or grade-school children <6 years of age
  - 25–70% of initial illnesses in family settings lead to secondary cases.
  - Highest attack rates among the youngest siblings at home
  - Attack rates increase with family size.
- Seasonality
  - Infections occur throughout the year.
  - Seasonal peaks in early fall and spring in temperate climates

Coronavirus

- Prevalence
  - Accounts for 10–35% of common colds, depending on the season
- Distribution: worldwide
- Age
  - Serum antibodies are acquired early in life and increase in prevalence with advancing age.
- Seasonality
  - Particularly prevalent in late fall, winter, and early spring (in contrast to rhinovirus)

RSV

- Prevalence/distribution
  - Annual epidemics worldwide
    - Last up to 5 months
  - Nearly 100% attack rates among susceptible infants and children in such settings as day-care centers
- Age
  - RSV is the major respiratory pathogen of young children and the foremost cause of lower respiratory disease in infants.
    - Illness rates highest among infants 1–6 months of age
      - Peaks between 2 and 3 months of age
    - Virtually all children infected by 2 years of age
  - Young infants and children
    - RSV accounts for:
      - 20–25% of hospital admissions for pneumonia
      - Up to 75% of cases of bronchiolitis
    - Half of infants at risk become infected during an epidemic.
  - Older children and adults
    - Reinfection with RSV is common.
    - Disease is milder than in infancy.
      - A common cold–like syndrome is frequent in adults.
    - Severe lower respiratory tract disease with pneumonitis may occur in elderly (often institutionalized) adults and immunocompromised patients.
- Seasonality
  - Late fall, winter, or spring
  - Rarely encountered during the summer

- Important nosocomial pathogen
    - Patients and up to 25–50% of staff members on pediatric wards are affected during outbreaks.

HMPV

- Prevalence
    - Serum antibodies present in nearly all children by the age of 5 years.
    - Accounts for 4% of respiratory tract illnesses requiring hospitalization of children and for a higher percentage of lower respiratory tract infections in nonhospitalized children
    - Accounts for 2–4% of acute respiratory illnesses in ambulatory adults and elderly patients
    - Detected in a few cases of SARS, but role (if any) not established
    - Assessment of the overall significance of HMPV infections awaits large-scale epidemiologic studies.
- Distribution: worldwide
- Age
    - Infections occur early in life.
    - Have been reported in a wide variety of age groups
- Seasonality
    - Most frequent during the winter

Parainfluenza virus

- Prevalence
    - Accounts for <10% of respiratory illnesses in adults
    - Important cause of respiratory illness in young children
        - Ranks second only to RSV as a cause of lower respiratory tract illness
        - Accounts for 4–22% of respiratory illnesses in children
        - Type 1: most common cause of croup (laryngotracheobronchitis) in children
        - Type 2: causes similar but generally less severe disease
        - Type 3: an important cause of bronchiolitis and pneumonia in infants
        - Type 4: associated illnesses generally mild
        - Unlike types 1 and 2, type 3 frequently causes illness during the first month of life, when passively acquired maternal antibody is still present.
        - Type 4 (subtypes 4A and 4B): reported less widely, probably because more difficult to culture
- Distribution: worldwide
- Age
    - Infection acquired in early childhood
    - Most children have antibodies to serotypes 1, 2, and 3 by the age of 5 years.
- Seasonality
    - Types 1 and 2 cause epidemics during the fall, often in an alternate-year pattern.
    - Type 3 is detected during all seasons, with annual epidemics in the spring.

Adenovirus

- Prevalence
    - Accounts for ~10% of acute respiratory infections in children
    - Accounts for <2% of respiratory illnesses in civilian adults
    - Nearly 100% of adults have serum antibody to multiple serotypes.

    - Types 1, 2, 3, and 5 are the most common isolates from children.
    - Types 4 and 7 (also 3, 14, and 21) are associated with outbreaks of acute respiratory disease among military recruits in winter and spring.
- Age
    - Most frequently affects infants and children
- Seasonality
    - Infections occur throughout the year.
    - Most common from fall to spring

Risk Factors

- Rhinovirus infections
    - Direct contact with infected secretions, usually respiratory droplets
    - Residence in a home with children <6 years of age who are in day care or school
    - Psychologically defined "stress" may contribute to development of symptoms.
    - Factors *not* associated with illness in volunteers include:
        - Cold exposure
        - Fatigue
        - Sleep deprivation
- Severe RSV infection in children
    - Prematurity
    - Congenital cardiac disease
    - Bronchopulmonary dysplasia
    - Nephrotic syndrome
    - Immunosuppression
    - Genetic factors (e.g., *CCR5* polymorphisms)
    - Co-infection with HMPV
- Adenovirus infections
    - Military recruits

Etiology

Rhinovirus

- Major cause of the common cold
- Virology
    - Picornaviridae family
    - Small (15- to 30-nm) nonenveloped viruses
    - Single-strand RNA genome
    - 102 distinct serotypes
- Transmission
    - Spread through direct contact with infected secretions, usually respiratory droplets
        - Hand-to-hand contact with subsequent self-inoculation of conjunctival or nasal mucosa
        - Large- or small-particle aerosol
        - Environmental surfaces probably contribute to transmission.
- Infection
    - Attachment to specific cellular receptor
        - Most serotypes attach to intercellular adhesion molecule 1.
        - A few serotypes use the low-density lipoprotein receptor.

    - Mediators linked to development of signs and symptoms
        - Bradykinin
        - Lysylbradykinin
        - Prostaglandins
        - Histamine
        - Interleukins 1, 6, and 8
- Incubation period: generally 1–2 days
- Virus shedding
    - Usually coincides with the onset of illness
    - May begin shortly before symptoms develop
- Immunity
    - Mechanisms of immunity are not well worked out.
    - In some studies, the presence of homotypic antibody has been associated with significantly reduced rates of subsequent infection and illness.
    - Data conflict regarding the relative importance of serum and local antibodies in protection from infection.

Coronavirus

- Virology
    - Pleomorphic, single-strand RNA viruses
    - Diameter: 100–150 nm
    - Named for crownlike appearance caused by club-shaped projections that stud the viral envelope
    - 3 antigenic groups represented by prototypes:
        - HCoV-229E
        - HCoV-OC43
        - Coronavirus associated with SARS (SARS-CoV)
- Strains HCoV-229E and HCoV-OC43 cause the common cold.
    - Mean incubation period: 3 days
- Viruses infect ciliated nasopharyngeal epithelial cells.
- Viral replication damages ciliated cells and leads to induction of chemokines and interleukins, resulting in symptoms.

RSV

- Virology
    - Paramyxoviridae family (genus *Pneumovirus*)
    - Enveloped virus, ~150–300 nm in diameter
    - Single-strand RNA genome
    - Helical nucleocapsid
    - So named because viral replication leads to fusion of neighboring cells into large multinucleated syncytia
- Transmission
    - Close contact with contaminated fingers or fomites and self-inoculation of conjunctiva or anterior nares
    - Also spread by coarse aerosols produced by coughing or sneezing
    - Inefficiently spread by fine-particle aerosols

- Infection
  - The lipid envelope bears 2 glycoproteins.
    - G protein, by which the virus attaches to cells
    - F (fusion) protein, which facilitates cell entry by fusing host and viral membranes
- Incubation period: ~4–6 days
- Virus shedding
  - Lasts ≥2 weeks in children
  - Lasts for shorter periods in adults
  - Prolonged for weeks in immunosuppressed patients
- Immunity
  - Incompletely understood
  - In volunteers, nasal immunoglobulin (Ig) A neutralizing antibody correlates more closely with protection than does serum antibody.
  - However, maternally acquired antibody seems to provide some protection from lower respiratory tract disease in infants.
  - Cell-mediated immunity appears to be an important mechanism of host defense against RSV.

HMPV

- Newly described viral respiratory pathogen
- Virology
  - Paramyxoviridae family (genus *Metapneumovirus*)
  - HMPV particles:
    - May be spherical, filamentous, or pleomorphic
    - Measure 60–280 nm in diameter
  - 2 genetic subgroups or genotypes

Parainfluenza virus

- Virology
  - Paramyxoviridae family (genera *Respirovirus* and *Rubulavirus*)
  - Diameter: 150–200 nm
  - Enveloped, single-strand RNA genome
  - Helical nucleocapsid
  - 4 distinct serotypes
  - Share certain antigens with other Paramyxoviridae, including mumps and Newcastle disease viruses
- Transmission
  - Spread through infected respiratory secretions
  - Primarily by person-to-person contact and/or by large droplets
- Incubation period
  - Varies from 3–6 days in experimental infections
  - May be somewhat shorter for naturally occurring disease in children
- Immunity
  - Incompletely understood
  - Evidence suggests that immunity to infections with serotypes 1 and 2 is mediated by local IgA antibodies in the respiratory tract.
  - Passively acquired serum neutralizing antibodies also confer some protection against infection.
  - T cell–mediated immunity may also be important.

Adenovirus

- Virology
  - Complex linear double-strand DNA virus
  - Diameter: 70–80 nm
  - Icosahedral shell composed of 20 equilateral triangular faces and 12 vertices
  - 6 subgenera (A through F)
  - 51 serotypes
- Transmission
  - Inhalation of aerosolized virus
  - Inoculation of virus into conjunctival sacs
  - Probably spread by the fecal-oral route as well
- Immunity
  - Type-specific antibody generally develops after infection.
  - Antibody is associated with protection—albeit incomplete—against infection with the same serotype.

Symptoms & Signs

Rhinovirus infections

- Most frequent clinical manifestation: the common cold
  - Symptoms
    - Rhinorrhea
    - Sneezing
    - Nasal congestion
    - Sore throat common
      - May be initial symptom
    - Systemic symptoms (malaise and headache) mild or absent
    - Fever unusual
  - Nasal mucosa
    - Edematous
    - Often hyperemic
    - Covered by a mucoid discharge during acute illness
  - Illness lasts 4–9 days.
  - Generally resolves spontaneously without sequelae, but may cause exacerbations of asthma and chronic pulmonary disease in adults
- Deeper respiratory tract disease (bronchitis, bronchiolitis, bronchopneumonia) reported in children, but not common
- Severe and even fatal pneumonia in immunosuppressed patients, particularly bone-marrow transplant (BMT) recipients

Coronavirus infections

- Common colds with clinical features similar to those of rhinovirus infections
  - Mean incubation period: 3 days (longer than rhinovirus infections)
  - Mean duration of illness: 6–7 days (shorter than rhinovirus infections)
  - Nasal discharge somewhat greater in colds induced by coronaviruses than in rhinovirus infection in some studies

- Other syndromes in which coronaviruses have been recovered
  - Pneumonia in infants
  - Lower respiratory tract disease in military recruits
  - Worsening chronic bronchitis

RSV infections

- Wide spectrum of respiratory illnesses
- Infants
  - 25–40% of infections result in lower respiratory tract involvement.
    - Pneumonia
    - Bronchiolitis
    - Tracheobronchitis
  - Typical symptoms
    - Rhinorrhea
    - Low-grade fever
    - Mild systemic symptoms
    - Cough and wheezing common
    - Recovery gradual (over 1–2 weeks)
  - Severe illness
    - Tachypnea
    - Dyspnea
    - Frank hypoxia, cyanosis, and apnea can ensue.
    - Diffuse wheezing, rhonchi, and rales
- Adults
  - Most common symptoms: those of the common cold
    - Rhinorrhea
    - Sore throat
    - Cough
  - Occasional moderate systemic symptoms
    - Malaise
    - Headache
    - Fever
  - Pneumonia
    - May be severe in elderly persons, particularly nursing-home residents
    - Significant cause of morbidity and death in patients undergoing bone-marrow and solid-organ transplantation
  - Other syndromes associated with RSV infection in adults
    - Sinusitis
    - Otitis media
    - Worsening of chronic obstructive and reactive airway disease

HMPV infections

- Spectrum of clinical illnesses similar to that in RSV infections
- Upper and lower respiratory tract illnesses
  - Bronchiolitis
  - Croup
  - Pneumonia

Parainfluenza virus infections

- Young children
  - Initial infection with serotype 1, 2, or 3 usually associated with acute febrile illness (50–80% of cases)
  - Presentation
    - Coryza
    - Sore throat
    - Hoarseness
    - Cough (may or may not be croupy)
  - Severe croup
    - Persistent fever
    - Worsening coryza and sore throat
    - Brassy or barking cough may progress to frank stridor.
  - Most children recover over 1–2 days.
  - Progressive airway obstruction and hypoxia occasionally ensue.
  - Bronchiolitis or pneumonia
    - Progressive cough
    - Wheezing, tachypnea, and intercostal retractions
    - Modest increase in sputum production
    - Nasopharyngeal discharge
    - Oropharyngeal injection
    - Rhonchi, wheezes, or coarse breath sounds
- Older children and adults
  - Milder illness
  - Common cold or hoarseness, with or without cough
  - Lower respiratory tract involvement uncommon
  - Tracheobronchitis in adults has been reported.
  - Severe, prolonged, and even fatal parainfluenza infection
    - Reported in children and adults with severe immunosuppression (e.g., BMT and solid-organ transplant recipients)

Adenovirus infections

- Children
  - Acute upper respiratory tract infection
    - Most common clinical syndrome in children
    - Rhinitis prominent
  - Lower respiratory tract disease
    - Bronchiolitis
    - Pneumonia
  - Pharyngoconjunctival fever
    - Caused particularly often by types 3 and 7
    - Characteristic acute febrile illness of children
    - Occurs in outbreaks, most often in summer camps
    - Bilateral conjunctivitis
    - Bulbar and palpebral conjunctivae have a granular appearance.
    - Low-grade fever is often present for the first 3–5 days.
    - Rhinitis, sore throat, and cervical adenopathy develop.
    - Illness generally lasts 1–2 weeks and resolves spontaneously.
  - Febrile pharyngitis without conjunctivitis

    - Adenovirus has been isolated from cases of whooping cough with or without *Bordetella pertussis*.
        - Significance unknown
- Adults
    - Acute respiratory disease caused by types 4 and 7 in military recruits is the most commonly reported adenovirus syndrome in adults.
        - Prominent sore throat
        - Gradual onset of fever, which often reaches 39°C (102.2°F) on the second or third day of illness
        - Cough almost always present
        - Coryza and regional lymphadenopathy common
        - Pharyngeal edema, injection, and tonsillar enlargement with little or no exudate
        - Auscultation may indicate areas of patchy infiltration with pneumonia.
- Nonrespiratory tract diseases
    - Acute diarrheal illness caused by types 40 and 41 in young children
    - Hemorrhagic cystitis caused by types 11 and 21
    - Epidemic keratoconjunctivitis
        - Caused most frequently by types 8, 19, and 37
        - Associated with contaminated common sources, such as ophthalmic solutions and roller towels
    - Adenovirus nucleic acids have been detected in myocardial cells from patients with "idiopathic" myocardiopathies and have been suggested as causative agents in some cases.
    - Disseminated disease and pneumonia in immunosuppressed patients, including BMT or solid-organ transplant recipients
        - BMT recipients
            - Pneumonia
            - Hepatitis
            - Nephritis
            - Colitis
            - Encephalitis
            - Hemorrhagic cystitis
        - Solid-organ transplant recipients
            - Adenovirus infection may involve the transplanted organ.
            - Can disseminate to other organs as well
    - In patients with AIDS
        - Adenovirus serotypes have been isolated, usually in the setting of low CD4+ cell counts.
        - Frequently, isolation is not clearly linked to disease manifestations.

Differential Diagnosis

- The differential diagnosis primarily includes infections with other viral respiratory agents.
- Viral croup
    - Acute epiglottitis caused by *Haemophilus influenzae* type b
    - Influenza A virus croup
- Adenovirus infection
    - *Mycoplasma pneumoniae* infection

Diagnostic Approach

- Signs, symptoms, and routine chemistry/hematology laboratory tests do not distinguish reliably among viral agents causing respiratory infections.
- Common cold
  - Diagnosis is made clinically.
  - The causative virus generally is not identified because of the benign, self-limited nature of the illness.
- Bronchiolitis or pneumonia
  - Diagnosis often suspected on the basis of epidemiologic setting, history, and physical examination findings
  - Identification of the specific viral pathogen is possible with respiratory secretion studies (viral culture, rapid antigen assays, or nucleic acid testing) or serologic testing.
    - Particularly important for patients with severe illness or immunocompromise
    - Also important for guiding infection-control measures in hospitalized patients
    - Diagnosis of a specific virus is not always necessary in other settings.

Laboratory Tests

Rhinovirus infections

- Virus can be isolated from nasal washes or secretions in tissue culture.
- Detection of rhinovirus RNA by polymerase chain reaction (PCR)
  - More sensitive than detection by tissue culture
  - Largely a research procedure
- Serum antibody testing impractical, given the many serotypes
- Common laboratory tests (white cell count and sedimentation rate) not helpful

Coronavirus infections

- Virus difficult to cultivate
- Research procedures used to detect coronaviruses in unusual settings
  - Enzyme-linked immunosorbent assay (ELISA)
  - Immunofluorescence assays
  - Reverse-transcriptase PCR (RT-PCR) for viral RNA
- SARS
  - See SARS (Severe Acute Respiratory Syndrome).

RSV infections

- Virus can be isolated from respiratory secretions (sputum, throat swabs, nasopharyngeal washes) in tissue culture.
- Rapid viral diagnosis from secretions (immunofluorescence, ELISA, other techniques)
  - Nasopharyngeal washes/aspirates better than nasopharyngeal swabs
  - Sensitivities and specificities of 80–95% with specimens from children
  - Less sensitive with specimens from adults
- Serologic diagnosis
  - Made by comparison of acute- and convalescent-phase serum specimens using:
    - ELISA

        - Neutralization tests
        - Complement fixation tests
    - May be useful in older children and adults
    - Less sensitive in children <4 months of age

HMPV infections

- Can be detected in nasal aspirates and respiratory secretions by:
    - PCR
    - Growth in rhesus monkey kidney (LLC-MK2) tissue cultures
- Serologic diagnosis
    - ELISA: uses HMPV-infected tissue culture lysates as sources of antigens

Parainfluenza virus infections

- Virus can be detected in:
    - Respiratory tract secretions
    - Throat swabs
    - Nasopharyngeal washings
- Viral growth in tissue culture
- Rapid viral diagnosis
    - Identification of parainfluenza antigens in exfoliated cells from the respiratory tract by immunofluorescence or ELISA
    - These techniques are less sensitive than tissue culture.
    - Highly specific and sensitive PCR assays have also been described.
- Serologic diagnosis
    - Hemagglutination inhibition tests
    - Complement fixation tests
    - Neutralization tests of acute- and convalescent-phase specimens
    - The serotype causing illness often cannot be distinguished from other serotypes by serologic techniques alone.

Adenovirus infections

- Detection of virus in tissue culture (as evidenced by cytopathic changes)
- Specific identification by immunofluorescence and other immunologic techniques
- Rapid viral diagnosis
    - Immunofluorescence or ELISA
        - Nasopharyngeal aspirates
        - Conjunctival or respiratory secretions
        - Urine
        - Stool
    - Highly sensitive and specific PCR assays
    - Nucleic acid hybridization
- Adenovirus types 40 and 41
    - Require special tissue-culture cells for isolation
    - Most commonly detected by direct ELISA of stool
- Serum antibody rises can be demonstrated by:
    - Complement fixation or neutralization tests
    - ELISA
    - Radioimmunoassay
    - HI tests (for adenoviruses that hemagglutinate red cells)

Imaging

- Chest radiography
  - Severe RSV infections
    - Hyperexpansion
    - Peribronchial thickening
    - Variable infiltrates ranging from diffuse interstitial to segmental or lobar consolidation
  - Parainfluenza virus infections (mainly in children)
    - Air trapping
    - Occasionally interstitial infiltrates
  - Adenovirus infections
    - May show areas of patchy infiltration

Diagnostic Procedures

- Bronchoalveolar lavage or lung tissue sampling may be required to:
  - Obtain diagnostic material from immunocompromised and/or severely ill patients
  - Exclude other diagnoses

Treatment Approach

- Treatment of viral illness with antibacterial agents is a major source of inappropriate drug use.
- Symptom-based therapy and supportive care are the mainstays of treatment.
- The only specific antiviral agent indicated is ribavirin, which is used to treat selected patients with RSV infection.
- Antibiotics are used to treat bacterial infections that may complicate viral respiratory infections.

Specific Treatments

Rhinovirus infections

- Generally mild and self-limited
- Treatment usually not necessary
- Symptom-based therapy
  - First-generation antihistamines
  - NSAIDs
  - Oral decongestants for troublesome nasal obstruction
  - Rest
  - Fluids
- Antibacterial agents only for complications (e.g., otitis media or sinusitis)
- Alternative remedies (zinc, vitamin C, echinacea): no clear benefit noted in studies of variable quality

Coronavirus infections

- Common colds treated similarly to rhinovirus infections
- SARS
  - No specific therapy of established efficacy

    - Ribavirin has been used but has:
        - Little, if any, activity against SARS-CoV in vitro
        - No demonstrated beneficial effect on the course of illness
    - Glucocorticoids have also been widely used.
        - Their benefit, if any, is likewise unestablished.
    - Supportive care to maintain pulmonary and other organ-system functions is the mainstay of therapy.
    - See SARS (Severe Acute Respiratory Syndrome) for details.

RSV infections

- Upper respiratory tract infections with RSV are treated similarly to rhinovirus infections.
- Lower respiratory tract infections
    - Respiratory therapy
        - Hydration
        - Suctioning of secretions
        - Humidified oxygen
        - Antibronchospastic agents
        - Intubation and ventilatory assistance for severe hypoxia
- Aerosolized ribavirin
    - Nucleoside analogue active in vitro against RSV
    - Has had a beneficial effect on the resolution of lower respiratory tract illness in infants
    - Recommended for infants who are severely ill or at high risk for complications of RSV infection
    - Efficacy in older children and adults not established
- Immunoglobulins have not been found to be beneficial against RSV pneumonia.
- Combined therapy with aerosolized ribavirin and palivizumab (chimeric mouse-human monoclonal IgG against RSV) is being evaluated in immunosuppressed patients with RSV pneumonia.

Parainfluenza virus infections

- Upper respiratory tract illness is treated similarly to rhinovirus infections.
- Mild cases of croup
    - Bed rest
    - Moist air generated by vaporizers
- Severe croup
    - Hospitalization and close observation for respiratory distress
    - Humidified oxygen
    - Intermittent racemic epinephrine
    - Aerosolized or systemically administered glucocorticoids beneficial
- No specific antiviral therapy
- Ribavirin
    - Active against parainfluenza viruses in vitro
    - Anecdotal reports describe clinical use, particularly in immunosuppressed patients.

Adenovirus infections

- Symptom-based treatment
- No clinically useful antiviral compounds have been identified.

- Ribavirin and cidofovir
  - Active in vitro against adenoviruses
  - Anecdotes describe use in disseminated infections.

Monitoring

- Usually, no specific monitoring is indicated.
- Patients who are immunocompromised, have coexisting lung disease, or are severely ill may require hospital monitoring.

Complications

- Overall respiratory virus morbidity
  - Acute respiratory illness accounts for:
    - 30–50% of time lost from work by adults
    - 60–80% of time lost from school by children
- Bacterial infections related to obstruction of the eustachian tubes or sinus ostia
  - Otitis media
  - Acute sinusitis
- Severe and even fatal pneumonia in immunosuppressed patients, particularly BMT recipients

Prognosis

- In general, the prognosis for upper respiratory infections is excellent, as is the prognosis for lower respiratory infections among immunocompetent older children and adults.
- RSV infections
  - Mortality rate: 37% for infants with RSV pneumonia and congenital cardiac disease
  - RSV pneumonia in BMT and solid-organ transplant recipients
    - Significant cause of morbidity and death
    - Case-fatality rates: 20–80%
- Adenovirus
  - Disseminated infections in immunocompromised patients are associated with significant mortality.

Prevention

Rhinovirus infections

- Intranasal interferon sprays
  - Effective in the prophylaxis of rhinovirus infection
  - Associated with local irritation of the nasal mucosa
- Use of antibodies to intercellular adhesion molecule 1 or soluble purified receptors has yielded disappointing results.
- Experimental vaccines
  - Have been generated for certain serotypes
  - Usefulness questionable because of myriad serotypes and uncertainty about mechanisms of immunity
- Behaviors to reduce transmission
  - Thorough hand washing

  - Environmental decontamination
  - Protection against autoinoculation

Coronavirus infections

- Vaccines developed against several animal coronaviruses
- None against known human coronaviruses
- Infection control practices used to contain SARS epidemic
  - Case definitions established
  - Travel advisories proposed
  - Quarantines imposed in certain locales
- Emergence of SARS emphasized the importance of vaccine development.

RSV infections

- Cumulative effect of multiple reinfections tempers subsequent disease and provides some temporary measure of protection.
- Maternally acquired serum antibody
  - Provides some protection from lower respiratory tract disease in infants, but illness can be severe even in infants with moderate antibody levels.
- Monthly administration of RSVIg (currently not available) or palivizumab, which is approved as prophylaxis for children <2 years of age who:
  - Have bronchopulmonary dysplasia **or**
  - Are born prematurely
- Vaccines
  - Inactivated whole-virus vaccines ineffective
  - Other experimental approaches
    - Immunization with purified F and G surface glycoproteins of RSV
    - Generation of stable, live, attenuated virus vaccines
- Barrier methods
  - Protection of hands and conjunctivae can be useful in reducing virus spread.
  - Important in settings where transmission rates are high, such as pediatric wards

Parainfluenza virus infections

- Effective vaccines have not been developed.

Adenovirus infections

- Live vaccine
  - Developed against adenovirus types 4 and 7
  - Unattenuated virus administered in enteric-coated capsules
  - Used to control illness in military recruits
  - Not produced since 1999
- Vaccines from purified subunits of adenovirus are being investigated.

ICD-9-CM

- 465.9 Acute upper respiratory infections of unspecified site (includes viral, unspecified)

See Also

- Community-Acquired Pneumonia
- Coxsackievirus and Echovirus Infections
- Herpes Simplex Virus Infections
- Influenza
- Pharyngitis
- SARS (Severe Acute Respiratory Syndrome)

Internet Sites

- Professionals
  - Adenovirus
    U.S. Centers for Disease Control and Prevention
  - Human Parainfluenza Viruses
    U.S. Centers for Disease Control and Prevention
  - Respiratory Syncytial Virus
    U.S. Centers for Disease Control and Prevention
- Patients
  - Common Cold
    MedlinePlus
  - The Common Cold
    U.S. National Institute of Allergy and Infectious Diseases
  - Respiratory Syncytial Virus Infections
    MedlinePlus

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PEARLS

- Consider adenovirus infection in military recruits with respiratory syndromes.
- No strong evidence supports a benefit from "alternative" remedies for the common cold, such as zinc, vitamin C, and echinacea.
- Aggressive diagnostic efforts should be made when an immunocompromised host has a respiratory viral syndrome, so as to determine the utility of specific treatment (particularly for RSV) and to implement appropriate infection-control measures promptly.
- HMPV is being recognized increasingly as an important cause of respiratory infections in the community.