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Viral Infections of the Respiratory Tract

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Viral infections of the respiratory tract are responsible for large amounts of time lost from the workplace and significant morbidity and mortality in the very young and the very old. The worldwide pandemic of influenza in 1918 was alone responsible for nearly 30 million deaths in excess of those expected for influenza. Viral respiratory infections are the most frequent illnesses in human beings. The most frequent causes of respiratory infections are adenoviruses, influenza viruses, parainfluenza viruses, respiratory syncytial viruses, and rhinoviruses. Frequency and severity of infection are increased in the very young and the elderly, worsened by crowding and inhaling pollutants, and influenced by anatomic, metabolic, genetic, and immunologic disorders. Respiratory infections are the leading cause of death in children under age 5 living in underdeveloped countries.[1]

Viruses Involved with Upper Respiratory Tract Infections

Table 10.1 compares the results of studies over the past 15 years detailing the prevalence rates of the common respiratory viruses. These prevalence rates include data from various parts of the world, and all age groups. Prevalence rates as high as 35% reflect the reason why these viruses are such common causes of disease.[2–13]

Viral Identification and Specimen Collection

Three techniques are commonly utilized to obtain specimens for viral identification. Nasopharyngeal swabs are sterile swabs inserted 3 to 4 cm into one nostril, left in place about 5 seconds, then removed and placed in a culturette containing modified Stuart's medium for transport to the lab. (One such system is the Becton Dickinson Microbiology Systems Mini-Tip Culturette, San Diego, CA.) Nasopharyngeal wash specimens are collected according to the method described by Hall and Douglas.[14] A 1-ounce rubber ear syringe (Davol, Inc., Cranston, RI) is loaded with 3 to 5 mL of sterile phosphate-buffered saline. With

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TABLE 10.1. Prevalence Rates of the Common Respiratory Viruses

	Flu A	Flu B	Para	Adeno	RSV	Rhino	Corona	Flu A & B
Croatia study[2]			2.3		7.6	33.6		0.6
Indian hospital study[3]			5	3	5			6
Nursing home study[4]			2		12	9.4		
COPD study[5]			8	0.7	3.1	6	5	4.2
Hospitalized colds[6]						12.5	4.7	
Cost-effective study[7]	5.9	1.2		0.35	18			
Early detection study[8]	1.8		2.7	4.5	12.8	35.8		
Pediatric inpatients, Taiwan[9]	5.5	2.6	2.0	4.0	1.7	12.7		
Chronically ill patients[10]	7.2	0.1	7.5	1.1	10.3	4.2	2.5	
Hospitalized Korean children[11]	4.8	1.3	6.5	3.9	11.8			
Hospitalized German children[12]	7.0	1.3	2.8	7.7	12.6			
Children in Jordan[13]		4.0	2.0	14.0				

COPD = chronic obstructive pulmonary disease; RSV = respiratory syncytial virus.

the patient's head tipped back about 70 degrees, the bulb tip is inserted until it occludes the nostril. With one complete squeeze and release, the nasal wash is collected in the bulb. The bulb contents are then emptied into a sterile screw-top tube for transport to the lab. Nasopharyngeal aspirate specimens are collected using a pediatric suction catherer (Safe-T-Vac, Kendall Healthcare Products, Mansfield, MA). Normal saline, 2 to 3 mL, is instilled into a nostril and the specimen is aspirated moments later into a sterile specimen trap.

Laboratory Testing

The standard to which laboratory tests for viral identification are compared is viral culture on monkey kidney, human lung laryngeal epidermoid carcinoma (Hep-2), and human embryonal diploid lung cell tissue culture. These cultures are studied daily for evidence of cytopathic effect. Cultures may become positive in several days to several weeks. Sensitivity of viral culture ranges from 7% to 94%. Specificity is very high. The Bartels viral respiratory screening and identification kit is an indirect fluorescence antibody procedure that contains monoclonal antibodies for seven respiratory viruses. This type of test has sensitivity of 84% to 88% and results are available in less than 24 hours after specimen collection.[15] Several laboratories are developing rapid reverse-transcription polymerase chain reaction (RT-PCR) tests (Prodesse, Inc., Milwaukee, WI) that improve sensitivity and shorten reporting time for respiratory virus identification. Sensitivities for rhinoviruses improved from 8% for tissue culture methods to 56% for the RT-PCR method.[8,16] Tests based on the reaction between viral neuraminidase from influenza viruses and a chromogenic substrate (Z Statflu Test, Zymetx, Oklahoma City, OK, USA) are available to detect influenza types A and B. Sensitivity approaches 78% and specificity nears 91% for this method with turnaround times of a few hours using throat swab specimens.[17]

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV), a single-stranded RNA paramyxovirus, is the leading cause of pneumonia and bronchiolitis in infants and children. Virtually 100% of young children are infected with RSV by age 3. Two antigenically distinct groups of RSV (A and B) are recognized. Community outbreaks of RSV usually appear during the winter and spring in temperate climates. The diagnosis of RSV in the acute setting is usually made by viral culture of nasopharyngeal secretions. A rapid diagnostic test (Abbott test pack RSV; Directigen RSV by Becton Dickinson) employing antigen detection in nasal secretions is 95% sensitive and 99% specific. Results are available in an hour.

The spectrum of illness associated with RSV is broad, ranging from mild nasal congestion to high fever and respiratory distress. What seems to begin as a simple cold may suddenly become a life-threatening illness. Modes of spread are primarily via large-droplet inoculation (requiring close contact) and self-inoculation via contaminated fomites or skin. RSV is recoverable from counter-

tops for up to 6 hours from the time of contamination, from rubber gloves for up to 90 minutes, and from skin for up to 20 minutes. Viral shedding of RSV in infants is a prolonged process averaging 7 days. Strategies for controlling spread of RSV should be aimed at interrupting hand carriage of the virus and self-inoculation of the eyes and nose. Masks commonly employed for respiratory viruses have not been shown to be an effective measure for curtailing RSV outbreaks on pediatric wards. Hand washing is probably the single most important infection control measure for RSV.

Influenza Viruses

Influenza, considered a benign disease today, has ravaged human populations recently enough that there are still those living who can recall the 1918 worldwide pandemic, called the "Spanish flu." This particular influenza began as an ordinary attack of influenza and rapidly developed into severe pneumonia. Within hours, the patients had mahogany-colored spots over the cheekbones and cyanosis began to spread over the face. Death shortly overcame them as they struggled for air and suffocated. It is important to realize that although worldwide 30 million deaths were attributed to influenza, 97% of people who were infected had a 3-day course of fever and malaise and recovered. Of the 3% who died, most died of pneumonia. A small subset died very rapidly of massive pulmonary edema and hemorrhage. Influenza pandemics occur about every 7 to 11 years. They are always associated with extensive morbidity and a marked increase in mortality.

Type A influenza is an RNA virus with a negative-sense segmented genome. It undergoes continuous antigenic drift because it has no proofreading mechanism, and is prone to mutate during replication. Influenza virus is chimeric, existing in wild bird and swine reservoirs, with minor antigenic drifts making the same virus infectious among birds, humans, or swine.[18]

In addition to the predominant influenza virus that invades an area each season, many types, subtypes, or variants are identified during each epidemic period. During the early stage of an epidemic, a disproportionate number of cases involve school-age children, 10 to 19 years old. Later in the epidemic, more cases are diagnosed in younger children and adults. The age shift suggests that the early spread of influenza viruses in a community is concentrated among schoolchildren.

Parainfluenza Viruses

Parainfluenza is a single-stranded RNA virus of which four serotypes and two subtypes are recognized (parainfluenza types 1, 2, 3, 4A, and 4B). Bronchiolitis, croup, and pneumonia occur with all parainfluenza types. In children under 1 year of age, bronchiolitis is associated mostly with type 2. In older children, croup is most commonly associated with types 1 and 2. Immunosuppression, chronic cardiac, or pulmonary diseases are associated with increased risk of parainfluenza infection.[19] Most persons have been infected with parainfluenza virus by age 5.

Immunity to parainfluenza is incomplete, and, as with RSV, reinfection occurs throughout life and probably plays a major role in the spread of virus to the young infant.

Parainfluenza types 1 and 2 tend to peak during the autumn of the year, whereas parainfluenza type 3 shows an increased prevalence during late spring. Adult infection results in mild upper respiratory tract symptoms, although pneumonia occasionally occurs. Outbreaks of parainfluenza types 1 and 3 have been reported from long-term-care facilities.[20] Illness is characterized by fever, sore throat, rhinorrhea, and cough. The rate of pneumonia is relatively high.

Most studies suggest direct person-to-person transmission. Parainfluenza is stable in small-particle aerosols at the low humidity found in hospitals. Outbreaks tend to proceed more slowly than influenza or other aerosol-spread infections.[21] Infection control policies should emphasize hand washing and isolation of patients.

Rhinoviruses

Rhinovirus is a non-enveloped, 30-nm, RNA virus with over 100 serotypes. It only replicates in primates. It is characterized by a single positive stranded genome not only acting as a template for RNA synthesis, but also encoding for a single polypeptide necessary for viral replication. It belongs to the picornavirus family, a diverse group of viral pathogens that together are the most common causes of infection in human beings. Within the picornavirus family are found the rhinoviruses, the enteroviruses, and the hepatoviruses (including hepatitis A). Rhinovirus infection is transmitted by direct contact with the eye or nasal mucous membrane. The most efficient modes of spread are hand-to-hand contact or contact with a contaminated surface followed by inoculation of the nose or conjunctiva. Rhinoviruses remain infectious for as long as 3 hours on nonporous surfaces. Transmission can be decreased by hand washing and disinfecting environmental surfaces. After deposition on nasal mucosa, the virus binds to intercellular adhesion molecule type 1 (ICAM-1) receptors on epithelial cells, initiating a cascade of inflammatory responses. Viral replication occurs in the nose, and viral shedding continues for up to 3 weeks. The cascade of interleukin-6, -8, and -16, histamine, bradykinin, and cytokines recruit neutrophils and produce the rhinorrhea, vascongestion, sinus congestion, sore throat, cough, wheezing, and middle ear inflammation.[22,23]

There is now evidence that direct invasion of the lower respiratory tract does occur, causing bronchitis and possibly triggering asthma attacks and exacerbation of chronic obstructive pulmonary disease (COPD). New antirhinoviral treatments are being tested. Intranasal interferon prevents infection, but provides no therapeutic benefit. Oral pleconaril shows therapeutic promise. Intranasal tremacamra and AG7088 are under investigation.[24,25] For the time being, treatment is mostly symptomatic, with antibiotics and steroids showing no benefit.

Coronaviruses

Coronaviruses, members of the Coronaviridae family, are single-stranded RNA viruses first identified in 1962. They do not appear to replicate in any animal models and are almost impossible to isolate in standard tissue cultures. Acute and convalescent sera for enzyme immunoassay will identify the two common subtypes, 229E and OC43. The enzyme-linked immunosorbent assay (ELISA) has been used to identify coronaviruses in nasal secretions.[26] A 1997 study of frail older persons by Falsey and McCann[27] found 37 (8%) of 451 serologies positive for coronavirus 229E over 44 months. It was noted that illnesses were indistinguishable from RSV and influenza virus infections. Lower respiratory complications, such as pneumonia, occurred in one fourth of the infected residents.

Epidemics occur during late fall through early spring. Clinical symptoms usually include nasal congestion, headache, cough, sore throat, malaise, and low-grade fever similar to rhinoviral infections. Coronavirus infections have been associated with lower respiratory tract illnesses, including pneumonia and bronchiolitis in young children. Coronavirus is the second most frequent virus associated with asthma exacerbations; rhinovirus is the most frequent. Interferon-α, tremacamra, and pleconaril have shown promise in prevention and treatment of these infections.

Adenoviruses

Adenoviruses are double-stranded DNA viruses. There are 51 serotypes divided into six subgenera (A–F) that exhibit distinctly different organ tropisms. Adenoviruses cause a broad spectrum of diseases, including conjunctivitis, keratoconjunctivitis, pharyngoconjunctival fever, pharyngitis, tonsillitis, coryza, pneumonia, heart disease, hepatitis, nephritis, and gastroenteritis. All ages are affected, but the majority of illness occurs in children younger than 6 years old. Military recruits in the United States from 1971 to 1995 received adenovirus vaccine to types 4 and 7. Since vaccine production ceased in 1995, an average of 4555 cases of adenoviral respiratory disease occur annually on military bases, costing about $2.6 million per year.[28] Adenovirus is ubiquitous, found everywhere during all seasons of the year, with annual peaks of activity in midsummer and midwinter. Transmission can occur by aerosolized droplets, fomites, hand carriage, fecal-oral, and by contact with contaminated lake water while swimming. The virus can be isolated for prolonged periods from respiratory secretions, conjunctival secretions, and stools of infected patients. Adenoviruses are identified by cytopathic effect in tissue cultures from nasopharyngeal specimens. They are also detected by indirect fluorescence antibody procedures (e.g., Bartels, Issaquah, WA, Viral Respiratory Screening and Identification Kit) using monoclonal antibodies. Newer RT-PCR testing (Taqman PCR, Glaxo Wellcome, Research Triangle Park, NC) can provide very accurate results in 6 to 12 hours, and primers are available for all adenovirus serotypes.[18]

Disease Presentations

Common Cold

The common cold, a disease of antiquity, is characterized by objective signs and subjective symptoms that are usually self-limited. Symptoms that occur with common colds include sneezing, watering of the eyes, nasal stuffiness, nasal obstruction, postnasal discharge, sore throat, hoarseness, cough, and sputum production. The common cold is a clinical diagnosis and lacks specificity because other ailments such as allergies and early symptoms of more serious illnesses mimic common cold symptoms. In the United States colds account for 23 million lost days of work and 26 million lost school days per year.

DIAGNOSIS

Rhinoviruses and coronaviruses are the most common causes of the common cold, with RSV and adenoviruses producing a similar set of signs and symptoms especially in adults. Mild cases of influenza and parainfluenza infection can be mistaken for the common cold. Because there are now a number of specific (as well as nonspecific and symptomatic) treatments for these viruses, it has become prudent medicine to undertake identification of the infecting virus, especially in more severe cases. Direct and indirect immunofluorescent staining techniques with virus-specific monoclonal antibodies (e.g., Chemicon International, Inc., Temecula, CA) or RT-PCR tests (e.g., Taqman PCR, Glaxo Wellcome) are well tested throughout the world and provide virus identification in a matter of hours almost anywhere.

MANAGEMENT

There are as many ways to manage the common cold as there are physicians. Gwaltney and Park[29] tested the therapeutic efficacy of clemastine fumarate, a second-generation antihistamine, and found reduction in total volume of rhinorrhea and number of sneezes in their patients challenged with rhinovirus. First-generation antihistamines reduce rhinorrhea and sneezing, and nonsteroidal antiinflammatory drugs reduce coughing, headache, malaise, and myalgias.

Intranasal steroid sprays reduce symptoms, but have little effect on duration of illness. Steroids may lengthen the period of viral shedding. Renewed interest in herbal and homeopathic remedies has produced clinical trials designed as randomized double-blind, placebo-controlled, multicenter studies mostly focused on symptom relief.[30] Jackson and Lesho[31] conducted a meta-analysis of 10 clinical trials on the use of zinc gluconate lozenges for treatment of the common cold. They concluded that evidence for effectiveness of zinc lozenges in reducing the duration of common colds is still lacking. Similar negative results have been reported from studies using heated, humidified air (steam) for cold treatment. Recent improved understanding of the pathophysiology of rhinoviral colds has focused attention on the neutrophilic inflammatory reaction, chemotaxis regulation,

cytokinesis, and upregulation of immunocompetent cells. Pleconaril 200 mg twice a day for 7 days decreases signs and symptoms as well as reducing viral shedding.[32] Tremacamra, a synthetic ICAM-1 glycoprotein acts as an antiadhesion molecule when sprayed into the nostrils. Tremacamra produces a significant decrease in symptoms.[33] Rest, adequate hydration, and time to recover should be stressed during management of the common cold. In the future, antirhinovirus drugs and interferon may reach development levels where alleviation of symptoms or prevention of infection exceeds side effects.

COMPLICATIONS AND SEQUELAE

When the diagnosis of the common cold is accurate, complications and sequelae are minimal. Complications generally result from assuming the cold symptoms are caused by rhinovirus or coronavirus, when in fact influenza, RSV, adenovirus, or a bacterial pathogen are responsible. Complications also occur in immunocompromised patients where rhinovirus can cause fatal pneumonia. Sequelae include asthma triggered by the rhinoviral-induced airway inflammation, and otitis media precipitated by viral-induced eustachian tube dysfunction with altered middle ear pressure.

Hand washing is the most important way to prevent transmission of these viruses. With rhinoviruses and RSV, direct contact with a contaminated surface followed by inoculation of the nose or conjunctiva can result in infection. Use of masks and gloves and isolation of infected persons is the most effective way to limit the spread of cold viruses.

Influenza

Influenza has one of the more characteristic sets of clinical findings. The onset is usually sudden, with shivering, sweating, headache, aching in the orbits, and general malaise and misery. Cough is often found early in the course, aggravating headaches and causing generalized aching. The onset is generally explosive, with fever in adults ranging up to 102°F. In children the fever may be higher than 102°F, and sore throat may be an early sign. The most consistent signs are the presence of polymyalgias, weakness, and malaise.

DIAGNOSIS

Not surprisingly, the diagnosis of influenza is more accurate during epidemics and less accurate during nonepidemic periods. Influenza in the United States usually occurs during December, January, and February. Successful presumptive diagnosis requires appropriate clinical symptomatology at the right time of the year and a knowledge of the pattern of influenza illness around the world. Virologic studies, including cultures from throat swabs and nasopharyngeal washings, cells from nasopharyngeal washings stained with monoclonal antibody fluorescence stains, and complement fixation studies on paired serum samples can confirm the diagnosis. The Zstatflu test (Zymetx, Oklahoma City, OK, USA) is a rapid de-

tection kit for both type A and type B influenza. It is based on the reaction between influenza neuraminidase and a chromogenic substrate. Throat swab or nasopharyngeal swab specimens will generate results in a few hours. There are several rapid flu A and flu B tests available currently that report results in less than an hour.

MANAGEMENT

Because several new effective medications are now readily available for treatment of influenza, virologic testing to confirm the diagnosis and type the virus is important. Amantadine (Symmetrel) 100 mg twice a day, is effective treatment for influenza type A, but not type B. Patients with compromised renal function should reduce the dose to 100 mg once a day. The dose in children up to age 10 is 3 mg/pound/day as a single dose. More recently, rimantadine (Flumadine) in the same doses offers the same good results with fewer side effects. Within the past 2 years, two neuraminidase inhibitors, zanamivir (Relenza) and oseltamivir (Tamiflu), have been approved for use and are widely available to treat both types of influenza. Zanamivir is inhaled as 10 mg twice a day. Oseltamivir is taken orally as 75 mg twice a day for adults and 2 mg/kg twice a day for children, used daily for 5 days. Because of the severity of the myalgias and headache associated with influenza, aspirin and nonsteroidal antiinflammatory drugs (NSAIDs) may not suffice and a narcotic-containing product is frequently indicated.

COMPLICATIONS AND SEQUELAE

Most statistical methods for assessing excess morbidity and mortality are based on an index of influenza complicated by pneumonia, which may produce an underestimation of the serious morbidity and mortality. During an influenza outbreak, there is usually an increased death rate among the elderly mostly due to pneumonia and cardiovascular disease. Influenza itself can cause severe and rapidly evolving viral pneumonia with multiorgan failure. Children under 5 years of age have the highest rates of hospitalization for acute upper and lower respiratory tract disease when infected with influenza. Pandemic strains of extreme virulence such as the 1918 influenza can cause far-reaching complications. The 1918 Spanish flu caused 5 million cases of encephalitis lethargica (of von Economo) with symptoms of acute encephalitis with or without death and postencephalitic Parkinson's disease. The 1957 pandemic produced a small number of people with massive pulmonary edema and hemorrhage with rapid death as was seen commonly in 1918. Even in the years where the circulating influenza strains are mild, there is a rise in the number of cases of otitis media, bronchitis, asthma, and exacerbation of COPD.

CONTROL AND PREVENTION

Influenza vaccine is produced on the recommendation of the Food and Drug Administration (FDA) Vaccines and Related Biologicals Advisory Commit-

tee. Antigenic choices are based on (1) the viruses that have been seen during the previous year, (2) the viruses that are being seen in other parts of the world during the current year, and (3) the estimated antibody response in persons previously infected or vaccinated to these viruses. The current strategy is to immunize high-risk groups (the elderly and children with underlying conditions including heart, pulmonary, malignant, and some metabolic diseases). Unfortunately, the level of acceptance by patients and the overall delivery of vaccines to high-risk children has been consistently poor. This approach leaves most of the population unvaccinated, which produces a large "at-risk" population to be infected. Another approach to the control of influenza is to immunize all schoolchildren, children in day care, college students, military personnel, and employees of large companies. These groups have the highest susceptibility and, because of the nature of their activities, are the principal vectors of influenza virus in the community. They are also an accessible population with a structured environment that permits effective distribution of influenza vaccine. Efforts should also be directed toward immunizing as many high-risk patients as possible or to start them on chemotherapy at the first evidence of an epidemic.

Bronchitis

DIAGNOSIS

Bronchitis is an inflammation of the major and minor bronchial branches. It is characterized by a cough that is frequently productive of sputum, depending on the inflammatory cause. Bacterial causes of bronchitis generally produce purulent-looking sputum. Viral causes of bronchitis more commonly produce either clear sputum or a nonproductive cough. On physical examination, a patient with bronchitis has a noticeable cough, but the lungs are usually normal to auscultation. Rales, dullness to percussion, egophony, and other lower respiratory findings are usually absent. Cigarette smoking, other air pollutants, and chemical exposures that cause bronchial irritation may prolong an episode of bronchitis. Systemic lupus erythematosus is a cause of persistent bronchitis in a small number of affected patients.[34]

SPECTRUM OF INFECTION

Acute lower respiratory tract illness in previously well adults is usually labeled acute bronchitis and treated with antibiotics before establishing the etiology. An English study of 638 patients over 1 year identified pathogens in 55% of cases; viruses were identified as 28% of the pathogens. Outcome did not relate to pathogens. Most patients improved without antibiotics in spite of the pathogen identified.[35] Viral causes of acute bronchitis tend to be more common with influenza (types A and B), parainfluenza of all four serotypes, and RSV. RSV and parainfluenza viruses are found more commonly in the young population, and coronaviruses and adenoviruses occur in older patients. Influenza causes bron-

chitis at all ages. Increases in frequency of bronchitis as a reason for adult hospital admissions usually occur during influenza epidemics. RSV is a significant problem in elderly populations in nursing homes. Falsey and Walsh[36] found attack rates of up to 10% per year in nursing home patients, with up to 20% going on to pneumonia, and 5% dying.

Spasmodic Croup and Laryngotracheobronchitis

Though croup is a frightening family experience, especially for parents of very young children, it is a self-limited illness. There are two variations of croup presentation, episodic (spasmodic) croup and laryngotracheobronchitis (LTB). Episodic croup presents as the sudden onset without warning of inspiratory stridor, cough, and hoarseness. The young child has not been overtly ill, but is suddenly crouping. There is minimal or no fever and no other respiratory symptoms. LTB has early warning signs of respiratory infection for several days that gradually lead to cough and inspiratory stridor. Cool night air or a steamed bathroom will usually break episodic croup, and it does not tend to recur in the same time period. At most, one treatment of aerosolized racemic epinephrine (0.25–0.5 mL of a 2.25% solution in 3 mL of normal saline) will break the attack. On the other hand, LTB may break with one epinephrine treatment, improve, and then worsen again.

On occasion, LTB will become severe enough to warrant admission for repeated aerosol treatments or a croup tent with mist and oxygen. Steroids are effective in improving the outcome of croup when given within 6 hours of symptom onset. Prednisolone (Pediapred or Prelone) 5 to 60 mg po divided bid can be continued for several days. Steroids given prior to a racemic epinephrine treatment may reduce the likelihood of rebound return of crouping as the epinephrine wears off. Physicians should look for the coexistence of underlying illnesses and reassure the family that croup is a manageable illness. Munoz and Glasso[37] reported that 70% of croup cases were caused by parainfluenza viruses. Children under 15 years of age are more likely to croup with parainfluenza types 1 and 2. Croup has peak incidence at age 2 years, and is more common in the fall and winter months. Croup is not commonly associated with rhinovirus infections, but is associated with coronavirus infections. Adenovirus is a common cause of croup in children and occurs sporadically throughout the year, being most common during the winter and spring.

Bronchiolitis

Bronchiolitis is an acute viral respiratory disease generally found in children younger than 2 years old. The typical clinical presentation is an upper respiratory infection with cough that progresses to a more severe cough and tachypnea. Respirations become rapid and shallow with a prolonged expiratory phase. Because the infants are not able to breathe well, they are also unable to suck or drink and can become dehydrated.

DIAGNOSIS

Physical findings include intercostal retractions and nasal flaring, which suggest pneumonia. A chest roentgenogram shows only hyperinflation with no infiltrates. Tight expiratory sounds (not entirely typical of wheezes found with asthma) are usually present, as are some rhonchi. Rales and dullness to percussion suggest the coexistence of pneumonia. Bronchiolitis is most commonly caused by RSV, occurring predominantly during the winter and spring. Parainfluenza viruses, particularly types 1 and 2, can cause bronchiolitis during early winter. The most severe cases of bronchiolitis are usually caused by influenza viruses, especially type A. The virus involved can be identified by culture of nasopharyngeal secretions or by RT-PCR or immunofluorescent assay.

MANAGEMENT

Management of bronchiolitis depends on the progression of signs and symptoms. Hospitalization may be necessary to correct hypoxemia or dehydration. If fever is significant, pneumonia must be ruled out. Cases that appear to be recurrent bronchiolitis may be asthma, even if the child is younger than 1 year old.

Outpatient treatment is generally supportive, with careful attention to hydration. If hospitalization becomes necessary to correct hypoxemia or dehydration, treatment is focused on oxygenation, mist, and mechanically clearing the upper airway. There is no effective antiviral agent to treat RSV and parainfluenza viruses. Ribavirin (Virazole) has shown variable effectiveness in the most severe cases of bronchiolitis, especially respirator-dependent infants. Steroids are of no proven value; however, the tight airway that reminds one of asthma may respond to both steroids and bronchodilators such as albuterol.

Infants who are at highest risk of developing severe bronchiolitis (preterm birth, bronchopulmonary dysplasia, immunocompromise and other underlying chronic diseases) can be protected during the winter season by prophylaxis with human RSV immunoglobulin or monoclonal antibodies (Palivizumab).

COMPLICATIONS AND SEQUELAE

The most serious complication of bronchiolitis is respiratory failure requiring ventilatory assistance. It is best managed with continuous positive airway pressure and oxygen. RSV accounts for an estimated 90,000 hospitalizations and 4500 deaths per year in children under 16 years of age in the United States. Mortality rates in institutionalized elderly can reach 20%.

Bronchiolitis caused by RSV is strongly associated with postinfection wheezing for as long as 10 years. Careful studies have shown rates of asthma from 23% to 30% several years after hospitalization as an infant for RSV bronchiolitis.

Pharyngoconjunctival Fever

Pharyngoconjunctival fever is an upper respiratory illness that affects teenagers and adults. It manifests as pharyngitis, cough, fever, headache, myalgias, malaise,

and particularly conjunctivitis. This syndrome is caused by adenovirus, particularly serotypes 3 and 7, which are frequently found in natural bodies of water and reservoirs. Symptoms may be similar to those of influenza. Conjunctivitis is generally not present with influenza but is always found with pharyngoconjunctival fever and usually at an early stage. There is a spring and summer seasonal prevalence. It can be diagnosed by viral cultures of nasopharyngeal and throat swabs and the recently developed immunofluorescent and RT-PCR tests. Management of pharyngoconjunctival fever is symptomatic. There is no indication for systemic antibiotic treatment or ophthalmic antibiotics. There are no long-term complications or sequelae. Recovery is generally within 1 week.

Laryngitis

There are six distinct causes of laryngitis, the most common being viral infections of the upper respiratory tract. Vocal cord tumors can cause laryngitis; allergies are a frequent cause, and strain of the vocal cords caused by long periods of loud talking produces laryngitis. A fairly frequent cause of laryngitis is hard coughing associated with an upper or lower respiratory tract infection. The least frequent cause is a bacterial infection of the throat. Most of the causes of laryngitis are obvious. Viral laryngitis is difficult to distinguish from the less frequent bacterial laryngitis, which might require antibiotic treatment. Children over age 2 and adults rarely have significant swelling of the throat that would put them at risk of airway obstruction. Children under age 2 are more likely to develop airway obstruction. Viral causes of laryngitis include the parainfluenza viruses, rhinoviruses, adenoviruses, and the influenza viruses. Voice rest has the greatest impact on recovery. Patients who are able to gargle with warm, weak salt-water solution sometimes find it soothing. Patients should be told that laryngitis is not a serious disease and that adequate time to recover is the only therapy in most cases.

Viral Respiratory Tract Infections in Very Young and Very Old Patients

Patients younger than age 2 present some special problems. Perhaps as many as two thirds of pediatric emergency room visits for respiratory infections are inappropriate. Parents frequently need only reassurance that their child is not seriously ill. Although most viral respiratory infections in children appear to be self-limited and without complications, they are among the leading causes of death in the youngest children. Table 10.2 details the patterns of viral illness found in young children, adults, and elderly patients. The institutionalized elderly represent a subgroup of older people who are prone to excess morbidity and mortality from respiratory tract infections. Each year many elderly persons living in long-term-care facilities become ill with respiratory illnesses that are mistakenly

TABLE 10.2. Patterns of Viral Illness in Children and Elderly Patients

Virus	Signs and Symptoms		
	Young children	Adults	Elderly
Respiratory syncytial virus	Wheezing, bronchiolitis, pneumonia, bronchitis	Nasal congestion and cough	Nasal congestion, cough, fever, pneumonia, wheezing, bronchitis
Influenza	Sore throat, high fever, myalgias, bronchitis, croup, bronchiolitis, rhinorrhea, otitis media	Fever, headache, myalgias, malaise, cough, weakness, bronchitis, laryngitis	Bronchitis, low-grade fever, sore throat, pneumonia
Parainfluenza	Croup, bronchitis, pneumonia, sore throat, bronchiolitis	Common cold, laryngitis	Rhinorrhea, sore throat, cough, pneumonia, fever
Rhinoviruses	Sore throat, rhinorrhea	Rhinorrhea, sneezing, cough, sore throat, laryngitis	Rhinorrhea, cough, sneezing
Coronaviruses	Croup, sore throat	Common cold, malaise, headache, sore throat, low-grade fever	Exacerbation of chronic pulmonary disease, pneumonia, bronchitis
Adenoviruses	Croup, sore throat	Coryza, sore throat, pneumonia, pharyngoconjunctival fever, keratoconjunctivitis, laryngitis	Bronchitis rarely

attributed to bacterial pneumonia or influenza. The respiratory tract viruses listed in Table 10.2 (particularly RSV, parainfluenza virus, and influenza virus) are a significant cause of disease in this high-risk population. RSV ranks second to influenza as the most common cause of serious viral respiratory infections in long-term-care facility patients. The pattern of reported outbreaks of RSV in a long-term-care facility is usually a steady trickle of cases over several months—distinctly different from outbreaks of influenza, which tend to be explosive. Parainfluenza virus is a common cause of croup and bronchitis in young children; however, because full immunity does not develop, reinfection is common in the older population. In the institutionalized elderly, parainfluenza presents as rhinorrhea, pharyngitis, cough, and pneumonia.

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CASE PRESENTATION

Subjective

PATIENT PROFILE

Kendra Nelson is a 16-year-old single female high school sophomore.

PRESENTING PROBLEM

Fever and weakness.

PRESENT ILLNESS

For the past day-and-a-half, Kendra has felt weak and achy. She has had a temperature of 103°F at home. There is a generalized headache, a mild cough, and a decreased appetite. A few of her schoolmates have had similar symptoms.

PAST MEDICAL HISTORY

No prior hospitalization or serious injury.

SOCIAL HISTORY

Kendra lives with her parents. She is a "good student" and has had a steady boyfriend for the past year.

HABITS

She uses no tobacco, alcohol, or coffee.

FAMILY HISTORY

Her parents are living and well. She has one sibling, aged 19, who is away from home in the Army.

- What additional historical information might be useful, and why?
- What might be the meaning of this illness to the patient?
- Would further information regarding her classmates or boyfriend be helpful? Why?

- What are likely adaptations of this teenager to her illness? Why might this be pertinent?

Objective

VITAL SIGNS

Blood pressure, 104/60; pulse, 86; respirations, 22; temperature, 38.6°C.

EXAMINATION

The patient is alert and ambulatory but looks "ill." The tympanic membranes are normal. The pharynx is mildly injected. The neck is supple without adenopathy, and the thyroid gland is normal. Her chest is clear. The heart has a normal sinus rhythm with no murmurs present.

- What further information about the physical examination might be useful, and why?
- What other areas of the body—if any—should be examined? Why?
- What—if any—laboratory tests should be obtained today? Why?
- What—if any—diagnostic imaging studies should be obtained today?

Assessment

- What is the likely diagnosis, and how would you explain this to the patient and her parents?
- Kendra's mother asks if Kendra is likely to be even worse during the next few days and what to do if this occurs. How would you reply?
- If the patient also had a rash, what diagnoses would you consider?
- What are the family/community implications of this illness?

Plan

- What would be your therapeutic recommendation to Kendra regarding medication, diet, pain relief, and return to school?
- Kendra asks about the possibility of others catching her illness. How would you reply?
- Kendra's mother asks about preventing such an illness in the future. How would you respond?
- What continuing care would you recommend?